Volume 9, Number 4, (Cumulative No.31) Part 19 December 25, 2012 ISSN:1097-8135

Life Science Journal

Marsland Press

PO Box 180432, Richmond Hill, New York 11418, USA

Website:
http://www.sciencepub.net

Emails:
editor@sciencepub.net
sciencepub@gmail.com

Phone: (347) 321-7172

Life Science Journal 2012 Volume 9, Number 4, Part 19 ISSN:1097-8135

Volume 9, Number 4, Part 19 December 25, 2012 ISSN:1097-8135

Life Science Journal

ISSN 1097-8135

9 771097 813002

MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

Websites:
http://www.lifesciencesite.com
http://www.sciencepub.net

Emails:
lifesciencej@gmail.com
editor@sciencepub.net

Volume 9, Number 4, Part 19 December 25, 2012 ISSN:1097-8135

Life Science Journal

MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

Websites:
http://www.lifesciencesite.com
http://www.sciencepub.net

Emails:
lifesciencej@gmail.com
editor@sciencepub.net

ISSN: 1097-8135

Life Science Journal

Acta Zhengzhou University Oversea Version

(*Life Sci J*)

Life Science Journal, the Acta Zhengzhou University Oversea Version, is an international journal with the purpose to enhance our natural and scientific knowledge dissemination in the world under the free publication principle. The journal is calling for papers from all who are associated with Zhengzhou University-home and abroad. Any valuable papers or reports that are related to life science - in their broadest sense - are welcome. Other academic articles that are less relevant but are of high quality will also be considered and published. Papers submitted could be reviews, objective descriptions, research reports, opinions/debates, news, letters, and other types of writings. Let's work together to disseminate our research results and our opinions.

Introductions to Authors

1. General Information

(1) Goals: As an international journal published both in print and on internet, **Life Science Journal** is dedicated to the dissemination of fundamental knowledge in all areas of nature and science. The main purpose of **Life Science Journal** is to enhance our knowledge spreading in the world under the free publication principle. It publishes full-length papers (original contributions), reviews, rapid communications, and any debates and opinions in all the fields of nature and science.

(2) What to Do: The **Life Science Journal** provides a place for discussion of scientific news, research, theory, philosophy, profession and technology - that will drive scientific progress. Research reports and regular manuscripts that contain new and significant information of general interest are welcome.

(3) Who: All people are welcome to submit manuscripts in life science fields. Papers of other fields are also considered.

(4) Copyright and Responsibility of Authors to their Articles: When the manuscript(s) is submitted to the journal, the authors agree the following: All the authors have participated sufficiently in this work; The article is not published elsewhere; Authors are responsibility on the contents of the article; The journal and author(s) have same right for the copyright of the article and either of the journal or author(s) can use it by anyway without noting the other party.

(5) Publication Costs: US$500 per article to defray costs of the publication will be paid by the authors when it is received. Extra expense for color reproduction of figures will be paid by authors (estimate of cost will be provided by the publisher for the author's approval).

(6) Advertisements: The price will be calculated as US$400/page, i.e. US$200/a half page, US$100/a quarter page, etc. Any size of the advertisement is welcome.

2. Manuscript Preparation

Each manuscript is suggested to include the following components but authors can do their own ways:

(1) Title: including the complete article title; each author's full name; institution(s) with which each author is affiliated, with city, state/province, zip code, and country; and the name, complete mailing address, telephone number, facsimile number (if available), and at least one email address for author(s). **(2) Abstract**: including Background, Materials and Methods, Results, and Discussions. **(3) Key Words**. **(4) Introduction**. **(5) Materials and Methods**. **(6) Results**. **(7) Discussions**. (8) **Acknowledgments**. **(9) References**.

3. Manuscripts Submission

(1) Submission Methods: Submission through email (editor@sciencepub.net) is encouraged.

(2) Software: The Microsoft Word file will be preferred.

(3) Font: Normal, Times New Roman, 10 pt, single space.

(4) Indent: Type 2 space in the beginning of each new paragraph.

(5) Manuscript: Don't use "Footnote" or "Header and Footer".

(6) Email: At least one author's email must be put under title.

(7) Title: Use Title Case in the title and subtitles, e.g. "**Debt and Agency Costs".**

(8) Figures and Tables: Use full word of figure and table, e.g. **"Figure 1.** Annul Income of Different Groups**", Table 1. Annual Increase of Investment".**

(9) References: Cite references by "last name, year", e.g. "(Smith, 2003)". References should include all the authors' last names and initials, title, journal, year, volume, issue, and pages etc.

Reference Examples:

Journal Article: Hacker J, Hentschel U, Dobrindt U. Prokaryotic chromosomes and disease. Science 2003;301(34):790-3. **Book**: Berkowitz BA, Katzung BG. Basic and clinical evaluation of new drugs. In: Katzung BG, ed. Basic and clinical pharmacology. Appleton & Lance Publisher. Norwalk, Connecticut, USA. 1995:60-9.

(10) Submission Address: editor@sciencepub.net, Marsland Press, PO Box 180432, Richmond Hill, New York 11418, USA, 347-321-7172.

Marsland Press / Zhengzhou University
PO Box 180432, Richmond Hill, New York 11418, USA
http://www.lifesciencesite.com; http://www.sciencepub.net
lifesciencej@gmail.com; editor@sciencepub.net

CONTENTS

Statistical Evaluation of Sustainability of Selected Crop Production in Nigeria

Abayomi Samuel Oyekale

Department of Agricultural Economics and Extension, North-West University Mafikeng Campus, Mmabatho 2735 South Africa. asoyekale@gmail.com

Abstract: Sustainable agricultural production is a paramount goal of many developing countries in order to ensure that foods required for the growing population are available in the right quantity and quality. This paper evaluated the extent of sustainability of the Nigerian crop production sector using secondary data from the FAO statistical database. Inferences of sustainability was made with contingency table developed by Monteith (1990) after computing geometric growth rates of land use and crop outputs. Results show that production of majority of the crops was not recently sustainable. Between 1961 and 1980, cereals (4.07%), maize (8.17%), sorghum (5.16%), millet (3.76%), yam (1.08%), kolanut (0.92%), oil palm (0.93%), vegetables and melon (0.82%) and plantain (2.53%) were sustainably cultivated while only cocoa (0.14%) and kolanut (1.82) percent show sustainability between 1981 and 2000. The findings suggest that ensuring sustainability of crop production in Nigeria requires adequate investments in highly productive farm technologies to make up for degradation of soil resources.
[Abayomi Samuel Oyekale. **Statistical Evaluation of Sustainability of Selected Crop Production in Nigeria**. *Life Sci J* 2012;9(4):2769-2775] (ISSN:1097-8135). http://www.lifesciencesite.com.. 408

Keywords: sustainability, contingency table, crops, Nigeria

1. Introduction

Agriculture is the most dominant sector in the economies of many sub-Saharan African nations. This is partly because the food it provides is the basis for human existence. However, it is paradoxical to note that as population grows, the food need of nations increases, but the arable land needed to grow the food becomes scarcer. In Nigeria, persistent stagnation in agricultural production is now a matter of serious concern. Although outputs in some crops have recently increased, it had been realized that most of these increases resulted from increase in land areas cultivated (Falusi, 1997). Thus, increasing crop production puts more pressure on the forest, and it is not sure whether this can be sustained as population further increases.

A growing awareness now exists of the fact that attainment of food security has gone beyond availability of improved production technologies, but the natural resource base upon which crop production ultimately depends must be appropriately managed and conserved (Mwale, 1998). In this respect, national governments, international organizations and non-governmental organizations (NGOs) are now actively involved in the development of workable natural resource conservation strategies in order to reverse the negative synergy developing from increased demographic pressure, environmental degradation and food insecurity.

Moreover, it had been realized that the traditional agricultural production system was stable and biologically conducive to soil nutrient replenishment because of the long fallow period (Scherr, 1999). But with increasing demographic pressure in many of the SSA countries, crop production has expanded to marginal lands and fallow periods have drastically reduced. There is now increase in the rates of forest clearing for agricultural production, and degradation of farmlands and decline in yields of crops persists (Pinstrup-Andensen *et al.,* 2001).

Furthermore, the peculiar characteristics of the humid tropical soils which are sandy, highly weathered, low in organic matter, and highly susceptible to soil erosion, nutrient depletion and compaction have worsened the situation (Pinstrup-Andensen and Pandya-Lorch, 2001). The implication of all these on SSA agriculture now poses a great challenge of how to meet the food needs of the ever growing population without irreversibly damaging the fragile land resource base to food policy makers (Pretty, 2001).

In Nigeria, the issues of concern to sustainable agriculture include the problems of soil vis-à-vis human induced soil degradation, bush burning and soil compaction (FAO, 2000). The problem of resource degradation has been identified as the most crucial environmental challenge that faces the nation (World Bank, 1990a). This conclusion was reached based on its great economic significance, the wide area of land that is affected, and the large number of people whose economic activities are directly hampered. Specifically, the problem of land degradation affects about 50 million Nigerians, and an estimated annual cost of US $3 billion is to be borne by the Federal Government. However, this conservative estimate only reflects the cost of food replacement through importation without considering

the costs of health hazards that could likely result (World Bank, 1990a). Similarly, natural resource degradation and accelerated rates of population growth have significantly undermined the productive capacity of majority of the Nigerian soils (FAO, 1991; Higgins and Antoine, 1991).

Moreover, the problem of sustaining growth in agricultural production emanates from unplanned land use and inability to give adequate attention to physical, biological and ecological implications of agricultural intensification (Barbier, 2001). Consequently, crop yields on some of the high potential and high input areas of the tropics have now started to decrease, while the reserves of unused lands are decreasing and the resource base of agriculture continues to be degraded (FAO, 1997).

Given the level of agricultural technology development in Nigeria, there are 40-50 million people in excess of the land's supporting capacity at present who are just mining the soil to support themselves (FAO, 2000). In addition, widespread poverty and income inequality also confront the households' decisions for any investment in soil conservation practices (Barbier, 2001). Without being addressed, such economic condition is liable of culminating into serious ecological crises (WCED, 1987). Sustainable development would therefore be compromised under impoverished situation where short-term survival takes precedence over long-term productivity. In some northern states, for instance, just as it is happening in some nations in North Africa, ecology degrading activities by the private and public sectors are in urgent need of remediation. Many irrigation projects have ended up displacing poor farmers and pastoralists from their traditional sources of water and land. Thus, they are forced to move to more fragile lands that are prone to erosion (Barbier and Thompson, 1998; Barbier, 2000).

Conventional wisdom therefore teaches that a central and crucial point in the performance of Nigerian agriculture in the last three decades is the issue of production sustainability. This can be vividly seen from the persistent stagnation in agricultural production resulting from low resource productivity of small-scale farmers that dominate the food production sub-sector. For instance, total cereal production index decreased from 142 in 1996 to 135.6 in 1997, before slightly increasing to 135.9 in 1998. Even between 1990 and 1997, cereal yield per hectare decreased from 1093.11 kg to 1008.44 kg (ECA, 1998).

Sustainable food production as a recent policy objective in Nigeria is far from being realized. Poor agricultural production has led to decline in the level of welfare among the rural and urban households. As food prices increase, poverty and malnutrition problems widen in dimensions. Worse still, 87 percent and 67 percent of the core poor were in agriculture in 1985 and 1992 respectively (FOS, 1999). It has also been found that 77 percent of farmers are poor, while 48 percent are in extreme poverty (FOS, 1999). Because crop yields are low, some farmers cannot even pay for hired labour and land rent at the end of the season. Many who are willing to invest in soil conservation technologies cannot get the means to do so. And because of the fight for survival, continuous cropping and deforestation continue in many ecological zones of the nation.

The importance of agriculture in Nigerian economy cannot be over-emphasized. Specifically, agriculture contributes more than 30 percent of the total annual GDP, employs about 68 percent of the labour force, accounts for over 70 percent of the non-oil exports, and provides over 80 percent of the food needs of the country. However, the small-scale farmers that dominate the sector are facing serious problems in getting good land due to progressive growth in population, land degradation, and inadequate planning in the use of available land (FAO, 1991; Barbier, 2000, 2001). In spite of massive government investment in the sector and related programmes over the years, in the form of input subsidies, the River Basin Development Authorities, Agricultural Development Projects (ADPs), Green Revolution, Operation Feed the Nation, Directorate for Food, Roads and Rural Infrastructure (DFRRI), among others, the sector's performance is still far below expectation.

The Nigerian small-scale farmers largely depend on traditional methods of farming. These farmers are facing various land use constraints, which is one of the major sources of declines in agricultural productivity. Even if rural households choose to stay on degraded land, its declining productivity will be unable to support growing rural populations, not to consider the nation as a whole. Thus, some households are forced to abandon existing agricultural areas in search of new forest land. Where land is scarce, continuous cropping on fragmented pieces of degraded farm plots persists with little or no soil conservation investments, and resource productivity eventually decreases (FAO, 1991).

Low resource productivity of Nigerian agriculture is a reflection of its comparatively low input use (FAO, 2000). Reardon (1998) noted that low use of fertilizer across African countries is a major cause of concern, both from the food production and environmental perspectives. FAO (1998) submitted that shortage of good quality agricultural land for smallholder is a problem in many regions of the world. Payment of compensation

in cash or in kind for the use of land no doubt affects land use intensity (Adegboye, 1986). According to Nwosu (1991), the government of Nigeria has been acquiring large tracts of land for agricultural and non-agricultural purposes. Therefore, access to land through ownership or secure tenure is a *sine qua non* for improving agricultural productivity.

In order to therefore address natural resource degradation and food insecurity, the logical and paramount goal that faces Nigerian food policy makers is the development of progress pathways that enhance sustainable natural resource management and increased food production. This is the only way to harmonize population growth with people's increasing food demand so that the nation can steadily achieve its medium term development goal.

Enough evidence abounds on the persistent weakness of the Nigeria's natural resource base to support increasing food demand of the growing population (World Bank, 1990a; 1990b). Food policy makers have now realized the need to integrate environmental matters into the frameworks of agricultural policies, and studies on agriculture-population-environment nexus are now highly demanded at all levels of agricultural development planning. This study then ranks most applicable to current Nigeria's goal of sustainable economic development, because it will provide some important inter-linkages on the issues of environmental degradation and sustainable agricultural production.

Policymakers in developing countries are increasingly frustrated as they try to increase agricultural production, reduce poverty, and sustain their resource base. Their frustration is compounded by lack of information about how to bring about these desired outcomes, and they are unsure about which sustainability targets they should aim for, what the short-term and long-term costs will be, and how to go about reaching these targets (Vosti, 1992). Therefore, economic planners in developing countries are facing serious dilemma on the need to strike a balance between meeting the immediate short-term needs of increasing agricultural production through forest clearing or destruction and the grave long-term cost of reduced agricultural productivity through land degradation. However, this study partially evaluates sustainability of Nigerian crop production sector using the trends of land areas and output. This is vital for addressing future food requirements of the country in relation to persistent degradation of land resources. In the remaining parts of the paper, materials and methods, results and discussions and conclusion have been presented.

2. Materials and methods

The area of study

This study was carried out in Nigeria. Nigeria is one of the Sub-Saharan African (SSA) nations located in the western part of Africa. The nation shares boundary with the Republic of Benin to the west, the Niger Republic to the north, the Republic of Cameroon and the Chad Republic to the east, and the Atlantic Ocean forms a coastline of about 960 Km^2 to the south. The country lies between the Latitudes 40^0 and 140^0 north of the equator. The climate varies from equatorial in the south to tropical in the center to arid in the north. It is equally blessed with a total land area of about 92,377,000 hectares, out of which about 91,077,000 hectares are solid land area. Its terrain consists mainly of southern lowlands, which merge into central hills and plateaus, mountains in the southeast, and plains in the north. Natural resources include petroleum, tin, columbite, iron ore and coal. Soil degradation, deforestation and droughts are the nation's primary environmental concerns.

Sources and limitations of data

The data used in this study were the national aggregates for land areas and output contained in the *Production Yearbook* published by the Food and Agriculture Organization (FAO), FAOSTAT web site (www.fao.org). The study period can be divided into two. First, 1961-1980, which was characterized by low population, low rate of urbanization, agricultural policies that were not too demanding on the environment and little threat from depletion of the ozone layers resulting into climatic vagaries. The second period, 1981-2000 can be described as the period of high population density, high rate of urbanization, increasing threats from climate vagaries, and adoption of agricultural policies like the Green Revolution and the Structural Adjustment Program (SAP) that largely characterized by increased use of agrochemicals. A comparison of the results of the data analysis was therefore made for the two periods.

Methods of data analysis

Standard deviation

The standard deviation is the square root of variance, and it gives us an index of dispersion expressed in the same units as the observations from where it is calculated (Frank and Althoen, 1994). The standard deviation is represented by the symbol *s* and is given by:

$$s = \sqrt{\frac{\sum_{i=1}^{n}(X_i - \bar{X})^2}{n-1}} \qquad 1.$$

Where X_i is the individual observation/score, X is the mean and n is the number of observations.

Test of statistical significant difference

The *t-test* was used to compare some computed means in order to test whether a significant difference exists between them. The formula is given as:

$$t_{cal} = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{S_1^2/n_1 - 1 + S_2^2/n_2 - 1}} \qquad 2.$$

Where:

t_{cal} = student's t distribution value calculated
X_1 = mean for variable X_1,
$\bar{X}_2$ = mean of for variable X_2,
S_1= standard deviation for variable X_1,
S_2= standard deviation for variable X_2,
n_1= number of observations in variable X_1,
n_2 = number of observation in variable X_2,

Crop production sustainability was inferred from the contingency table developed by Monteith (1990) (table 1). In order to determine the sustainability of crop production, the geometric growth indexes for the land areas harvested and the yields were calculated. These form the basis for conclusion. If the land index is greater than yield index, production is not sustainable, and vice versa.

Table 1: Contingency table for inferring production sustainability based on trends of system inputs and outputs

Output	Input		
	Decreasing	Constant	Increasing
Decreasing	Indeterminate	Unsustainable	Unsustainable
Constant	Sustainable	Sustainable	Unsustainable
Increasing	Sustainable	Sustainable	Indeterminate

Source: Monteith (1990)

The geometric growth (indices of sustainability) were computed from the equation below:

$$I_t = \sqrt[k]{(1+p_1)(1+p_2)..(1+p_k)} \qquad 3$$

Where: I_t =index of output and input used in period t

p_i = percentage growth rate between years t and t-1.

k = n -1 (where n is the number of observations)

3. Results and Discussions

Testing for statistical difference in land areas harvested and yield

In order to analyse the trend in the use agricultural land and crop yields, average land areas cultivated and yields for each crop in the 1961-1980 and 1981-2000 periods were computed, and using the *t-statistics*, statistical differences between them were tested. Table 2 shows that in grain crops the mean differences between land area cultivated to cereal crops, maize, and rice were all statistically significant at 1 percent level. Moreover, the average yields per hectare show statistical difference for cereal, rice, millet and sorghum at 1 percent level. It is worth noting that while maize shows statistical mean difference for land area, yields are not statistically different at 5 percent. This implies that over those periods, maize yields are still at almost the same level. Therefore, it could be inferred that recent increases in maize production in Nigeria have not really come from improvements in the yields, but from expansion in land areas. Falusi (1997) had earlier made this assertion. Millet land areas mean difference is with negative sign, while the yield difference is positive, just as it is recorded in all other cereal crops. This shows that despite the fact that land area cultivated to millet has declined over the years, the yields have increased significantly perhaps due to use of improved seeds, increase in land and fertilizer use that is more prevalent in some Northern States where sorghum is largely grown.

Table 2: Mean difference and t-statistics for some crops land areas and yields during 1961-1980 and 1981-2000

Crop	Cultivated Area		Yield Per Hectare (Kg/Ha)	
	Mean Difference	T-Statistics	Mean Difference	T-Statistics
Cereal	130,003,415	109.592*	473.78	9.7212*
Maize	2,482,200	6.3387*	197.5223	1.3911
Rice	1,099,110	8.1468*	410.230	4.4181*
Millet	-64,700	-0.1753	479.46	7.6181*
Sorghum	383,410	0.9119	368.75	6.0121*
Tuber/Roots	2,055,239.25	1.3976	1,173.77	1.2161
Cassava	1,127,340.4	5.9480*	688.25	2.9043*
Yam	808,600	4.8258*	-458.295	-0.2232
Potatoes	9,333.85	5.6017*	-321.98	7.0686*
Cocoa	23,125	4.1950*	13.555	0.565
Kolanut	-147,500	-2.5047**	69.565	0.2976
Oil-Palm	218,400	2.1636**	123.59	8.1774*
Plantain	18,225	1.6717	1,647.27	7.991*
Vegetables	343,176	6.5469*	791.469	5.4927*

Source: Computed from data from FAO Publications

Note: * Statistically significant at 1% level, ** Statistically significant at 5% level

In the roots and tuber crops, cassava, yam and potatoes all have their mean differences in land area harvested to be statistically significant at 1 percent level. However, it is only cassava and potatoes that show statistical difference for the average yields. It should be noted that the average yield differences in potatoes and yam are with negative sign. This negative sign implies that their production has not been sustainable over those years.

In cash crops, mean difference for cocoa land area shows statistical difference at 1 percent level, but no statistical difference is computed for the yield difference. Mean difference for kola nut land area harvested is with negative sign, and it is statistically significant at 5 percent level. Yield difference for kola nut is however with positive sign, but statistically insignificant at 10 percent level. It is only in oil palm that the land areas mean difference and yield difference are not equal to zero at 5 percent level and 1 percent level respectively.

Finally, in fruits and vegetables, only vegetables and melon have the mean difference land area not equal to zero, being statistically significant at 1 percent level, but both the mean differences of the yields in plantain and vegetables and melons are statistically significant at 1 percent level.

Geometric growth index as a measure of sustainable crop production in Nigeria

This study used the geometric growth index to determine the sustainability index of crop production in Nigeria. This is done in order to overcome the weaknesses of the time trends proposed by Monteith (1990). This weakness is noticed by its not being able to determine the sustainability state when both input and output move in the same direction. Using the geometric proportionate growth index, any production system is concluded sustainable if the proportionate yield growth index is greater than the proportionate land area growth index. However, it should be stressed that the analyses done here have some limitations in the sense that only land is considered as input, and nothing is known about the state of the land in respect of depletion and/or rejuvenation of soil nutrients. Taking all other factors to be constant, this section therefore uses the trend of output and input approach to partly infer production sustainability.

Table 3: Geometric growth index as a measure of sustainable crop production in Nigeria (1961 – 1980)

Crop	Yield Index	Land Index	Sustainability Index	Inference
Cereal	1.0202	0.9795	0.0407	Sustainable
Maize	1.0262	0.9445	0.0817	Sustainable
Rice	1.0429	1.0712	-0.0283	Sustainable
Sorghum	1.0335	0.9819	0.0516	Unsustainable
Millet	1.0169	0.9793	0.0376	Sustainable
Root and tubers	1.0107	1.0118	-0.0011	Unsustainable
Cassava	0.0006	1.0229	-0.0223	Unsustainable
Yam	1.0161	1.0053	0.0108	Sustainable
Potatoes	0.9842	1.0513	-0.0671	Unsustainable
Cocoa	0.9868	1.000	-0.0132	Unsustainable
Kolanut	1.0038	0.9946	0.0092	Sustainable
Oil palm	1.0000	0.9907	0.0093	Sustainable
Vegetable & Melon	1.0110	1.0028	0.0082	Sustainable
Plantain	1.0198	0.9945	0.0253	Sustainable

Source: Computed from data from FAO and Publications

The sustainability indices (table 3) show that out of the crops that were sustainably cultivated, maize has the highest sustainability index of 8.17 percent, while vegetables and melon have the lowest index of 0.82 percent. On a general note, the analysis shows that many of the food and cash crops were sustainably cultivated between 1961-1980. This could be traced to fertility of land. The fallow periods then could be as high as 3 -4 years. The pressure on land during that period was lower because of low population, and farmers readily got the needed fertilizer to add to their crops for increased productivity.

Table 4 shows that during the 1981–2000 period, agricultural production was mostly unsustainable. Only cocoa and kolanut were sustainably cultivated. This shows that land area is growing at higher rate than yield. This could be attributed to possible extension of crop production activities to marginal land and reduction of fallow period.

Cocoa and kolanut that were sustainably cultivated could be attributed to dissolution of the Commodity Boards for the enhancement of cash crop production under the SAP, which made farmers to be able to take better care of their cocoa farms due to better market prices as liberalization policy was fully implemented. As cocoa trees were being cared for, kolanut would not be left out since most farmers intercrop it with cocoa. All these would have

contributed to sustainability of cocoa and kolanut production.

Table 4: Geometric growth index as a measure of sustainable crop production in Nigeria (1981 – 2000)

Crop	Yield Index	Land Index	Sustainability Index	Inference
Cereal	1.0057	1.0512	-0.0455	Unsustainable
Maize	1.0025	1.1194	-0.1169	Unsustainable
Rice	0.9853	1.0754	-0.0901	Unsustainable
Sorghum	1.0001	1.0380	-0.0379	Unsustainable
Millet	0.9797	1.0619	-0.0822	Unsustainable
Root and Tubers	0.9995	1.0727	-0.0732	Unsustainable
Cassava	1.0079	1.0518	-0.0439	Unsustainable
Yam	0.9949	1.0932	-0.0983	Unsustainable
Potatoes	0.9881	1.0884	-0.1003	Unsustainable
Cocoa	1.0172	1.0032	0.014	Sustainable
Kolanut	0.9957	0.9775	0.0182	Sustainable
Oil palm	1.0034	1.0215	-0.0181	Unsustainable
Vegetable & Melon	1.0119	1.0437	-0.0318	Unsustainable
Plantain	1.0082	1.0238	-0.0156	Unsustainable

Source: Computed from data from FAO Publications

Table 5 also shows that only cocoa, kolanut and plantain were sustainable cultivated during the period 1961–2000. Sustainable cultivation of plantain could be explained by its ability for natural regeneration and the fact that most farmers use the plant to raise cocoa at the early stage because it provides shade for the tender plants. This implies that increased cocoa production could result into increased plantain production.

Table 5: Geometric growth index as a measure of sustainable crop production in Nigeria (1961 – 2000)

Crop	Yield Index	Land Index	Sustainability Index	Inference
Cereal	1.0126	1.0143	-0.0017	Unsustainable
Maize	1.0139	1.0275	-0.0136	Unsustainable
Rice	1.0133	1.0714	-0.0581	Unsustainable
Sorghum	1.0072	1.0092	-0.0020	Unsustainable
Millet	0.9986	1.0012	-0.0106	Unsustainable
Root and Tubers	1.0027	1.0407	-0.038	Unsustainable
Cassava	1.0011	1.0374	-0.0363	Unsustainable
Yam	1.0053	1.0471	-0.0418	Unsustainable
Potatoes	0.9848	1.0693	-0.0845	Unsustainable
Cocoa	1.0018	1.0016	0.0002	Sustainable
Kolanut	1.0001	0.9845	0.0156	Sustainable
Oil palm	1.0017	1.0022	-0.0005	Unsustainably
Vegetable & Melon	1.0112	1.0224	-0.0112	Unsustainable
Plantain	1.0136	1.0088	0.0048	Sustainable

Source: Computed from data from FAO Publications

4. Conclusion

Sustainability of agricultural system is paramount for ensuring food security of a nation. This objective is however far from being achieved in many developing countries due to rapid degradation of soil resources. The findings from this study have shown that crop production in Nigeria was more sustainable between 1961 and 1980. This study also found that the growth rates of yield are lower than that of land area in most of crops cultivated in Nigeria in recent time. The government needs to redefine research focus and priorities in order to meet the challenges of resource degradation. Many researches in Nigeria are wrongly focused or unclearly defined. Redefining research goals and priorities is imperative. More research is needed on the impact of human cropping activities on the environment especially in the Savannah zone that produces about 80% of grains and 95% of livestock products to satisfy the basic human needs of food. Sustainable agriculture as an integral component of sustainable economic development in Nigeria must be approached by research efforts geared towards broad based holistic goals that can be achieved through multi-disciplinary and system approaches that give due consideration and cognizance to the interactions between man, technology, environmental resources, economic and ecology. Integrating the goal of sustainable and regenerative agriculture is therefore a *sine qua non* for enhancement of resource productivity in the Nigerian agriculture.

References

1. Adegboye RO. Land tenure and land use pattern. A Final Report on Oyo State Feasibility Study of Statewide Agricultural Development Project. Federal Military Government of Nigeria/ FACU, 1986.
2. Barbier EB. The Economic Linkages Between Rural Poverty and Land Degradation: Some Evidence from Africa, *Agriculture, Ecosystems and Environment* 2000; 82 : 355 – 70.
3. Barbier EB. The Economics of Tropical Deforestation and Land Use: An Introduction to the Special Issue" *Land Economics* 2001; 77(2): 155-171.
4. Barbier EB, and Thompson, JR He Value of Water, Floodplain Versus Large Scale Irrigation Benefits in Northern Nigeria" *Ambio* 1998; 27 (6): 434-40.
5. ECA (Economic Commission for Africa) Africa: Demographic, Environmental and Agricultural Indicators. Addis Ababa: ECA. 1998.
6. Falusi AO. Agricultural Development and Food Production in Nigeria: Problem and Prospects". In: Shaib, B. N.O.Adedipe, A. Aliyu, and M.M. Jir (eds.) *Integrated Agricultural Production in Nigeria: Strategies and Mechanisms for Food Security*. Monograph No.5. Abuja: National Agricultural Research Project, 1997.
7. FAO.*Technical Background Document for the World Food Summit* Rome: FAO, 1997.
8. FAO. Forest Resources Assessment 1009: Survey of Tropical Forest Cover and Study of Change Processes. FAO Forestry Paper No. 130. Rome: FAO. 1997.
9. FAO (1998). *Rural Women and Food Security: Current Situation and Perspectives*. Rome.
11. FAO. Land and Water Constraints to Sustainable Agriculture, 2000. www.fao.org/waicent/faoinfo/agricult/agl/swlwpur/nigeria/e_bright.htm
12. FOS. *Poverty and Agricultural Sector in Nigeria: Poverty Incidence of Farmers by Region*. Nigeria: Federal Office of Statistics.. 1999.
13. Higgins GM. and Antoine J.. *Nigeria Resource, Potential, Population, and Soil Degradation*. Rome : FAO, 1991.
14. Monteith JL. "Can Sustainability Be Quantified?" *Indian Journal of Dryland Agricultural Resource Development* 1990; 5 (1&2): 1-5.
15. Nwosu AC. "Issues in African Rural Development" Arlington (USA): Winrock International Institute for Agricultural Development pp 196-217, 1991.
16. Pinstrup-Andensen P, Pandya-Lorch R and, Rosegrant MW. 'Global Food Security: A Review of the Challenges' In: Pinstrup-Andensen, P. and Pandya-Lorch, R (eds.) *The Unfinished Agenda*. Washington, D.C.: International Food policy Research Institute (IFPRI). (2001)
17. Pinstrup-Andensen, P. and Pandya-Lorch, R. 'Agricultural Growth Is the Key to Poverty Alleviation in Low-Income Developing Countries' In: Pinstrup-Andensen, P. and Pandya-Lorch, R (eds.) *The Unfinished Agenda*. Washington, D.C.: International Food policy Research Institute (IFPRI), 2001.
18. Pretty J. 'Farmer-Based Agroecological Technology' In: Pinstrup-Andensen, P. (ed.) *Appropriate Technology for Sustainable Food Technology* Focus 7 Policy Brief 2 of 9 Washington D.C.: International Food Policy Research Institute (IFPRI), 2001.
19. Reardon MJ. The Role of Tenure Security and Private Time Preference in Neotropical Deforestation. *Land Economics* 1998; 74 (May): 162-170.
20. Scherr SJ. and Yadav S. *Land Degradation in Developing World: Implications for Food , Agriculture and the Environment to 2020*. International Food Policy Research Institute, 1996.
21. WCED (World Commission on Environment and Development). *Our Common Future - The Brundtland Report*. Oxford : Oxford University Press. 1987.
22. World Bank). *Towards The Development of An Environmental Action Plan for Nigeria*. Washington D.C.: The World Bank. 1990a
23. World Bank *Nigeria Strategy for Food and Nutrition Security*. Main Report. Washington D. C.: The World Bank, 1990b.

10/13/2012

Mode of action of medicinal plants on diabetic disorders

Elahe Seyed Hosseyni[1♦], Hamed Haddad Kashani[2♦], Mohammad Hossein Asadi[3*]

[1]Research Center for Sciences and Biotechnology, Lavizan, Tehran. Iran
[2]Anatomical Sciences Research Center, Kashan University of Medical Sciences, Kashan, Iran
[3]Department of Anatomy, Baqiyatallah University of Medical Sciences
***Corresponding author:** Mohammad Hossein Asadi, Department of Anatomy, Baqiyatallah University of Medical Sciences. Asadi.mh@yahoo.com, Tel:09121241280.

Abstract: Diabetes mellitus is a systemic metabolic disease characterized by hyperglycemia, hyperlipedemia, hyperaminoacidemia, and hypoinsulinaemia it leads to decrease in both insulin secretion and insulin action, along with varying degrees of peripheral resistance to the action of insulin. The long-term effects of impaired glucose regulation can lead to permanent organ damage, such as cardiovascular disease, and disabilities. Nowadays, there is growing interest in medicinal herbs due to the side effects associated with the therapeutic agent for the treatment of diabetes mellitus. In addition therapeutic action of herbal medicines is due to the herbal ingredients mechanism, bioactive compounds of most of the plants have been isolated and identified. However, mechanisms of action of most plants and their products that used for lowering of blood glucose remain unknown. in this study by searching in different sources and references such as Pub Med, MEDLINE, CNKI, EMBASE, Wiley Inter Science, Elsevier data bases, tried to express mode of action some common medicinal herbs that have important role in lowering of blood glucose and diabetics recovery.
[Elahe Seyed Hosseyni, Hamed Haddad Kashani, Mohammad Hossein Asadi. **Mode of action of medicinal plants on diabetic disorders.** *Life Sci J* 2012;9(4):2776-2783]. (ISSN: 1097-8135). http://www.lifesciencesite.com. 409
409

Key words: Diabetic, Medicinal plant, Mechanism, Bioactive, Metabolism, Insulin.

Introduction:

Diabetes mellitus is a metabolic disorder characterized by failure of glucose homeostasis with disturbances of carbohydrate, fat and protein metabolism resulting defects in insulin secretion, insulin action, or both. Without enough insulin, body tissues, particularly, the liver, muscle and adipose tissues fail to take and utilize glucose from the blood circulation. This results in elevated blood glucose levels, a condition known as hyperglycemia. If blood glucose levels remain high over a long period of time, this can result in long-term damage of organs such as the kidneys, eyes, nerves, heart and blood vessels. Complications in some of these organs can lead to death [1-3].

Currently, type 2 diabetes mellitus, the most common type of diabetes mellitus, is managed by a combination of diet, exercise, oral hypoglycemic drugs and sometimes insulin injections [4]. However, synthetic oral hypoglycemic drugs, which are currently the main form of treatment for type 2 diabetes mellitus have been shown to have undesirable side effects and high secondary failure rates [4]. In addition, these drugs cannot be afforded by the majority of people living in rural communities of developing countries because of their high cost [4].

These limitations, of currently available antidiabetic pharmacological agents have prompted researchers all over the world to investigate alternative antidiabetic remedies. In particular, consideration is given to plants and herbs used by traditional healers and herbalists as antidiabetic remedies with the hope of discovering new natural products that can be used or developed into safe, inexpensive and effective antidiabetic remedies. For their hypoglycemic potential using experimental animal models of diabetes [5-7] as well clinical studies involving diabetic patients [8-10]. In addition, bioactive compounds of most of these plants have been isolated and identified [10, 11]. However, mechanisms of action whereby most of these plants and their products exert their blood glucose lowering effects on tissue or organs remain unknown.

Methods:

We searched for papers published in Pub Med, MEDLINE, CNKI, EMBASE, Wiley Inter Science, Elsevier data bases. In this context, a number of medicinal plants and herbs have been studied and validated assess without language limit by retrieving key words “Diabetic, Medicinal plant, Mechanism, Bioactive, Ingredient, Insulin, phytochemistry, complication, carbohydrate, metabolism,” to identify mechanism and mode of action of medicinal plants on diabetics disorders. These searches were conducted by two independent examiners. The last date of the search was January 28, 2012.

Results:

Type 2 diabetes mellitus; commonly known as non-insulin diabetes mellitus occurs in adult patients aged 40 years and above, is a polygenic disorder with obesity related insulin resistance playing a major role in its onset and progression. It is characterized by excessive hepatic glucose production, decreased insulin secretion from pancreatic beta cells, and insulin resistance in peripheral tissue such as muscle adipose and liver [12]. There are convincing data to indicate a genetic component associated with insulin resistance. Insulin resistance is a feature of the offspring of parents with type 2 diabetes. In Pima Indians, a group with a very high prevalence of insulin resistance and type 2 diabetes, the insulin resistance has been suggested to have a co-dominant mode of inheritance [13]. Insulin resistance is also caused by acquired factors such as obesity, sedentary life style, pregnancy, and hormone excess. During its early stage, insulin resistance is compensated for by hyperinsulinemia, thus preserving normal glucose tolerance. Deterioration into impaired glucose tolerance occurs where either insulin resistance increases or the insulin secretory responses decrease, or both [14].

Popularity of diabetes mellitus

Currently, the overall global prevalence of diabetes is estimated to be between 3.0% and 3.6% of the population, of which 90% is type 2 diabetes [15, 16] In this context, the prevalence of diabetes for all age groups worldwide was estimated to be 2.0% in 1997[15], 2.8% in 2000 [16] and 3.6% in 2010 [15] and was projected to be 4.4% (366 million people) in 2030 [16]. The prevalence of diabetes is reported to be higher in men than in women; however, there are more women than men with diabetes [16]. Population growth, urbanization, increasing prevalence of obesity and physical inactivity are thought to be the main factors responsible for the increasing prevalence of type 2 diabetes mellitus [16-18].

Complications of diabetes mellitus

Uncontrolled hyperglycemia in type2 diabetes leads to the development of both acute and long term complications [3]. Acute complications of diabetes mellitus include non ketotic hyperosmolar coma. Long term complications include cardiovascular diseases, hypertension, chronic renal failure, retinal damage, nerve damage, erectile dysfunction and macrovascular damage which may cause poor healing of wounds particularly of the feet and can lead to gangrene which may require amputation. Chronically elevated blood glucose levels lead to increase production of mitochondrial reactive oxygen species (ROS), which activate a number of metabolic pathways whose end products contribute to the development of long term complication of diabetes [3, 19]. These metabolic pathways activated by hyperglycemia-induced ROS include: the polyol pathway, formation of advanced glycation end product (AGE), hexosamine pathway and the protein kinase C (PKC) pathway [20-25].

Treatment of type 2 diabetes mellitus

The chronic hyperglycemia of diabetes can lead to health complications such as blindness, gangrene, kidney failure, heart attacks and strokes, which are devastating to the individual and very expensive to the health services [1, 26, 27] Available evidence indicates that diabetes related complications can be prevented or delayed by achieving tight glycemic control [28].Therefore, much effort has been devoted to the search and development of optimal therapeutic regimens for the management of diabetes. Currently, type 2 diabetes is controlled and managed by a combination of diet restriction, weight reduction programs and oral hypoglycemic drugs [4]; Orally administered hypo-glycemic agents (e.g. sulfonylureas, repaglinide, metformin, alpha glucosidase inhibitors and thiazolidinediones (TZDs) are used first together with dietary restriction and exercise programs [4]. When hyperglycemia becomes severe, patients are usually switched to insulin injections, with or without oral agents to improve insulin action [4] However, current anti-diabetic medications have toxic side effects including, but not limited to, nausea, diarrhea, and hypoglycemia at higher doses, liver problems, lactic acidosis and weight gain. These side effects prompt patients to stop taking these anti-diabetic medications. Furthermore, despite the intensive use of current anti-diabetic agents, many type 2 diabetic patients still exhibit poor glycemic control and some develop serious complications within six years of diagnosis [26]. Clearly, there is a need for new anti-diabetic agents.

Mode of action of hypoglycemic medicines

Oral hypoglycemia agents exert their glucose lowering effects via a variety of mechanisms. These mechanisms of action include reduction of hepatic glucose production, (metformin, a biguanide), enhancement of insulin secretion by pancreatic beta cells, improvement of insulin sensitivity and inhibition of intestinal glucose digestion and absorption (alpha glucosidase inhibitors). The use of these drugs is however, limited by the fact that they have adverse side effects, such as potential hypoglycemia (e.g. sulfonylurea), weight gain (meglitinides, sulfonylurea and thiazolidinesdiones), gastro-intestinal discomforts (alpha glucosidase inhibitors, and alpha amylase inhibitors) and lactoacidosis (metformin) [29] In addition to their potential side effects, many of the oral anti-diabetic agents have higher secondary failure rates [4].

Medicinal plants for diabetes

As is the case with other diseases, medicinal plants have been used since ancient times to treat and manage diabetes mellitus in traditional medical systems of many cultures throughout the world [30, 31]Currently, medicinal plants continue to play an important role in the management of diabetes mellitus, especially in developing countries, where many people do not have access to conventional antidiabetic therapies [11] [32]. In developed countries the use of antidiabetic herbal remedies is reported to have been declining since the introduction of insulin and synthetic oral hypoglycemic agents during the early part of the twentieth century. However, in recent years, there has been a resurgence of interest in medicinal plants with hypoglycemic potential in these countries. This renewed interest in herbal antidiabetic remedies in developed countries is believed to be motivated by several factors, including, the side effects, high secondary failure rates and the cost of conventional synthetic antidiabetic remedies [31]. Ethnopharmacological surveys indicate that more than 1200 plants are used in traditional medical systems for their alleged hypoglycemic activity [33].The hypoglycemic activity of a large number of these plants products has been evaluated and confirmed in animal models [6, 34] as well as in human beings [8-10] In some cases the bioactive principles have also been isolated and identified [5, 10, 11]. However, the mechanism of action of the most products, lower the blood glucose level, remain speculative.

Most studied antidiabetic medicinal plants

The most studied and commonly used medicinal plants whose blood glucose lowering effects have been tested and confirmed in different parts of the world include: Allium cepa (Onion), Allium sativum (Garlic), Aloe vera, Cinnamomum tamala, Coccinia indica, Gymnema sylvestre (Gurmar), Momordica charantia (Bitter Melon), Murrayi koningii, Ocimum sanctum, Panax (Asian) Ginseng, Trigonella foenum-graecum (Fenugreek), Pterocarpus marsupium (Indian Kino) and Syzigium cumini [35-43].

Bioactive constituents of antidiabetic medicinal plants

Ivorra et al [44] cited by Tanira, [45], studied the structure of 78 different compounds isolated from plants with attributed hypoglycaemic activity. They classified these compounds according to the following chemical groups: 1. Polysaccharides and proteins (59 com-pounds), 2. Steroids and terpenoids (7compounds), 3. Alkaloids (7compounds), 4. Flavonoids and related compounds (5 compounds). Similarly, Bailey and colleague [30] listed 29 compounds that contained 14 polysaccharides, 5 alkaloids 4 glycosides and 6 other compounds. Grover and colleague [11] reviewed 45 medicinal plants of India with confirmed antidiabetic potential. Of the 17 hypoglycemic principles isolated and identified in this review 5 compounds are amino acids and related compounds, 5 compounds are glycosides, and 3 compounds are phenolic (flavonoids) compounds. The remaining compounds are alkaloids (2 compounds), terpenoids (1 compoud) and polysaccharides (1compound). Bnouham [46, 47] also reviewed 178 with potential antidiabetic activity. The 56 hypoglycemic principles identified in this review belong to the following chemical groups: 1. Glycosides (mostly saponins) (24 compounds). 2. Phenolics (mostly flavonoids) (11 compounds) 3.Polysaccharides (9 compounds) 4.Terpernoids (5 compounds) 5.Amino acids and related compounds (4 compounds) 6.Alkaloids (3 compounds).

It can be concluded on the basis of these four studies that a variety of phytochemicals possess hypoglycemic activity. However, the majority of plants with blood glucose lowering activity appear to contain polysaccharides, glycosides and flavonoids. Another point of note in the above mentioned review studies is that a given plant and its product may possess more than one hypoglycemic principles which may act in synergy to exert a blood glucose lowering effect.

Mechanism of action of antidiabetic medicinal plants and their constituents

There are several possible mechanisms through which these herbs can act to control the blood glucose level [45]. The mechanisms of action can be related, generally, to the ability of the plant in question (or its active principle) to lower plasma glucose level by interfering with one or more of the processes involved in glucose homeostasis. The reported mechanisms whereby herbal antidiabetic remedies reduce blood glucose levels are more or less similar to those of the synthetic oral hypoglycemic drugs and are summarized as follows [45-48]: 1. Stimulation of insulin synthesis and secretion from pancreatic beta-cells. 2. Regeneration/revitalization of damaged pancreatic beta cells. 3. Improvement of insulin sensitivity (enhancement of glucose uptake by fat and muscle cells). 4. Mimicking the action of insulin (acting like insulin). 5. Alteration of the activity of some enzymes that are involved in glucose metabolism. 6. Slowing down the absorption of carbohydrates from the gut. 36medicinal plants and their products reviewed by Grover and colleagues [11]. They studied hypoglycemic action of the plants. 13altered the activities of hepatic enzymes involved in glucose metabolism (stimulation of glucokinase and glycogen synthase and inhibition of glycogen phosphorylase and glucose 6-phospatase), 11 stimulated insulin secretion from pancreatic beta cells,

4 decreased intestinal absorption of glucose, 3 increased insulin sensitivity, 3 regenerated or protected pancreatic beta-cells from damage and 2 acted like insulin. Similarly, of the 60 plants extracts reviewed by Bnouham and co-workers [46, 47] whose hypoglycemic mechanism of action have been studied, 20 stimulated insulin secretion from pancreatic beta cells, 11 altered the activities of hepatic enzymes involved in glucose metabolism, 11 decreased the intestinal absorption of glucose, 11increased insulin sensitivity, 4 regenerated or repaired pancreatic beta-cells and 3 acted like insulin. It can be concluded on the basis of the above mentioned reviews that the majority of antidiabetic medicinal plants exert their blood glucose lowering effect through stimulation of insulin release from pancreatic beta cells or through alteration of some hepatic enzymes involved in glucose metabolism. Another point of note in the above mentioned reviews is that a given plant or its product may exert its blood glucose lowering effect through a combination of more than one mechanism [11].

Investigation of the antidiabetic activity of plant substances.

To study antidiabetic potential of medicinal plants, Firstly, candidate plants are collected, extracted and screened for hypoglycemic activity using either in vitro or in vivo bioassay techniques. Secondly, active ingredients are isolated and identified from plants showing hypoglycemic effects during the screening tests. Thirdly, the blood glucose lowering mechanism of action of the crude plant extract and active ingredients is investigated. Fourthly, clinical trials are conducted on the crude plant extract or isolated active ingredients [30].

Monitoring of medicinal plants for antidiabetic activity

Candidate medicinal plant material (usually selected on the basis of information obtained from traditional healers and herbalist) are collected, dried, powdered and extracted with a suitable solvent (usually either water or alcohol) and screened for hypoglycemic activity. Screening tests commonly used to assess the antidiabetic/hypoglycemic activity of medicinal plants.

In vivo bioassay

In vivo bioassay screening tests for antidiabetic activity of medicinal plant extracts and other antidiabetic remedies are usually carried out in normal or diabetic animals in which diabetes has been induced either by chemical, dietary, surgical or genetic manipulations [49, 50] [51, 52]. By far the most commonly used animal models for screening plants for antidiabetic activity are the chemically (alloxan and streptozotocin) induced diabetic animal models [52]. Alloxan and streptozotocin exert their diabetogenic action when administered parenterally: intravenously, intraperitoneally or subcutaneously [52]. The dose of these agents required for inducing diabetes depends on the animal species, route of administration and nutritional status. According to the administered dose of these agents, syndromes similar to type 2 diabetes mellitus or glucose intolerance can be induced [53, 54]. In general, the majority of published studies which evaluated the antidiabetic activity of medicinal plants using alloxan or streptozotocin-induced animal models of diabetes report the amount of reduction of blood glucose that is always evaluated after a period of fasting following acute or chronic treatment with a specific natural product [11]. Comparative studies are carried out with non-diabetic and/or diabetic animal groups treated with known antidiabetic drugs. Glucose is measured by standard glucose-oxidase or dehydrogenase assays, mainly by means of commercial meters available everywhere [52, 55]. Animal models of diabetes appear to be more useful in screening plants for their antidiabetic activity than in vitro bioassay screening techniques, but ethical and practical considerations make it impossible to screen large numbers of samples [52].

In vitro cell based assays

Cell based assays commonly used to screen or evaluate the antidiabetic activity of medicinal plants belongs to a class of in vitro bioassays known as “mechanism based assay” [56, 57]. A mechanism-based bioassay differ from an ordinary cell culture bioassay in that it can provide a possible mechanism of action at the same time that the plant material is screened for biological activity[57]. Two different types of mechanism based in vitro bioassays are commonly used to assess the antidiabetic/hypoglycemic of medicinal plants and/or products: the insulin secretion stimulation [58, 59] and the glucose uptake biosasays [57] [60].

Insulin secretion stimulation bioassays

Insulin secretion stimulation bioassays in general, assess the ability of a plant extract or natural product to stimulate perfused pancreas, isolated pancreatic islets cells or clonal pancreatic beta cell–lines (e.g. BRIN-BD11 cells) to secrete insulin [61, 62] In a typical insulin secretion stimulation bioassay cells are seeded (at a specified density) usually in 24- or 96-microtitre well plates, and cultured overnight in a suitable buffer supplemented with glucose, 10% foetal calf serum and antibiotics. Following attachment of cell to the plates, cultured cells are washed several times and incubated in Krebs ringer buffer (KRB) containing 1 mM glucose in the presence or absence of plant extracts and other test agents. Positive and negative controls are also included in the well plates. Following incubation,

aliquots are removed from each well, centrifuged and assayed for insulin levels [61]. Plants whose antidiabetic mechanism of action has been evaluated this way include Medicago sativa.

Glucose uptake bioassays

These types of bioassays assess the ability of plant materials to enhance glucose uptake by insulin target cell-lines (e.g. C2C12 myocytes, 3T3-L1 preadipocytes and human Chang liver cells) [56, 63] [60]. A glucose uptake bioassay is generally performed by incubating cultured insulin target cells in a buffer containing glucose (radiolabeled (tritiated 2-deoxyglucose) or unlabelled) and insulin in the presence and absence of the candidate plant extract [57]. Following incubation, glucose in aliquots of the incubation media is measured by means of a scintillation counter or colorimetrically [64]. The difference between the initial and final glucose concentration equals the amount of glucose taken up by the cultured cells and provides a measure of the antidiabetic activity of the plant extract under evaluation [65] [60]. As with other cell based in vitro bioassays, mechanism based bioassays for the assessment of the antidiabetic activity of medicinal plants are generally faster and uses relatively small amounts of materials than the in vivo bioassays. However, antidiabetic/hypoglycemic activity might be missed, for example, where a metabolite rather than the parent substance is the active component [65]. Another disadvantage of these techniques is that only "acute" or immediate effects are measured, whilst effects that may only be apparent after chronic exposure to the antidiabetic compound are overlooked [65].

Sub-molecular enzyme inhibition-based assays

Some antidiabetic agents are known to exert their blood glucose lowering effects through inhibition of specific carbohydrate metabolizing enzymes. For this reason several researchers [66, 67] have investigated the ability of plant extracts to inhibit the activities of enzymes such as α-amylase, α-glucosidase, hexokinase (glucokinase) and glucose 6-phosphatase by means of in vitro sub-molecular enzyme inhibition assays. A typical in vitro enzyme inhibition based assay involves three distinct steps. Firstly, the enzyme is pre-incubated in an appropriate buffered solution with or without the test compound. In addition to the incubation buffer, the test solution may include numerous other reagents such as sulfhydryl compounds, metals, protein cofactors and stabilizing agents that are needed by the enzyme. This pre-incubation step allows a maximum opportunity for the enzyme to interact with the test substance before the reaction is initiated. The second stage is the initiation of the reaction. This is most often done by automated or manual addition of substrate to each tube or well. Finally, the reaction must be terminated if it is single-time point readout and the amount of the product formed or the loss of the substrate must be determined. Stopping the reaction can be achieved by a variety of ways depending upon the particular enzyme. One general way is to denature the enzyme by addition of a denaturing agent, for example trichloroacetic acid or a rapid increase in temperature. If a metal ion is required for the activity of the enzyme, the reaction may be stopped by addition of a chelating agent such as EDTA to sequester the metal ion. Once the reaction is stopped, absorption readings are made against a blank by means of a spectrophotometer.

Investigation of the mechanism of action of antidiabetic plant extracts

As described an antidiabetic agent may exert its blood glucose lowering effect by stimulating insulin secretion from pancreatic beta-cells, enhancing glucose uptake by fat and muscle cells, altering the activity of some enzymes that are involved in glucose metabolism or slowing down the absorption of sugars from the gut [29, 47, 68, 69].

Effect on insulin secretion

In most published studies, investigation of the effect of medicinal plant extract on insulin secretion in vivo has involved the use of streptozotocin or alloxan induced animal models of diabetes [70] [5, 6, 71, 72]. Both alloxan and streptozotocin causes destruction of pancreatic beta cells resulting in reduced insulin secretion [52, 73]. In streptozotocin and alloxan induced animal models of diabetes, insulin is markedly depleted but not absent [52, 74, 75]. For this reasons these animal models have been widely used to study the effect of antidiabetic remedies on insulin secretion in vivo.

In order to investigate the effect of a plant extract on insulin secretion in vivo, the majority of published studies have divided normal animal and diabetic animals into at least five groups: normal control rats, normal rats treated with plant extract, diabetic control; diabetic rats treated with plant extract and diabetic rats treated with a conventional insulin secretory [5, 71, 76, 77]. Experimental animals are then treated with the plant extract for a given period of time while control groups receive vehicle during the experimental period. At the end of the experimental period blood is withdrawn for the measurement of plasma insulin. A significant increase in the plasma insulin level of experimental rats compared to those of control rats would suggest the insulinotropic effect of the plant extract, whereas a significant increase in the plasma insulin level of extract treated diabetic animal compared with the diabetic control but no difference between the plasma levels of extract treated normal animal and normal control would suggest a

regenerative effect of the plant extract on pancreatic beta cells [46, 47, 71, 78-79].

Inhibition or activation of carbohydrate metabolizing enzymes

It has been establish that some antidiabetic remedies, for example, metformin exert its blood glucose effects by inhibiting endogenous glucose production by the liver through the process of gluconeogenesis and glycogenolysis [79-80]. For this reason, as part of efforts to find out the possible mode of action of antidiabetic remedies, several researchers have investigated the effect of plant extracts on the activities of gluconeogenic enzymes: glucose 6-phosphatase, fructose 1,6-bisphosphatase; the glycogenolytic enzyme; glycogen phosphorylase and hepatic glucokinase. In order to investigate the effect of medicinal plant extract on key enzymes involved in glucose homeostasis in vivo, the study design used are similar to the one describe above for the study the effect of plant extract on stimulation of insulin except that at the end of the feeding period blood and selected tissues are also collected for the measurement of the activity of selected enzymes in plasma or tissue homogenates in vitro [69, 81, 82].

Conclusion:

Diabetes is one of the most prevalent chronic diseases throughout the world, affecting more than 300million people worldwide. For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. Herbs are used to manage diabetes and their complications. Therefore, treating diabetes mellitus with plant derived compounds which are accessible and do not require laborious pharmaceutical synthesis seems highly attractive. In this review article, hypoglycemic mechanism of medicinal plants was considered. Scientists working the field of pharmacology and therapeutics to develop evidence-based alternative medicine to cure different kinds of diabetes in man and animals. Isolation & identification of active constituents of plants, preparation of standardized dose & dosage regimen can play a significant role in improving the hypoglycemic action. Herbal therapy for diabetes has been followed all over the World successfully. Herbs are used to manage diabetes and their complications. A large number of plants, screened for their anti diabetic effect, have yielded certain interesting leads as mentioned above, however more laboratorial work is needed to specify the mechanism of medicinal plant and their anti diabetic actions.

***Corresponding author:** Mohammad Hossein Asadi, Department of Anatomy, Baqiyatallah University of Medical Sciences. Asadi.mh@yahoo.com

♦**First Authors:** Hamed Haddad Kashani and Elahe Seyed Hosseini

References:

1. Hirch, I.B., Glycemic control and complications of diabetes mellitus. West J Med, 1995. 162(5): p. 430-8.
2. Brownlee, M., Biochemistry and molecular cell biology of diabetic complications. Nature, 2001. 414(6865): p. 813-20.
3. Weiss, J.S. and B.E. Sumpio, Review of prevalence and outcome of vascular disease in patients with diabetes mellitus. Eur J Vasc Endovasc Surg, 2006. 31(2): p. 143-50.
4. Bailey, C.J., Potential new treatments for type 2 diabetes. Trends Pharmacol Sci, 2000. 21(7): p. 259-65.
5. Kesari, A.N., R.K. Gupta, and G. Watal, Hypoglycemic effects of Murraya koenigii on normal and alloxan-diabetic rabbits. J Ethnopharmacol, 2005. 97(2): p. 247-51.
6. Kesari, A.N., et al., Hypoglycemic and antihyperglycemic activity of Aegle marmelos seed extract in normal and diabetic rats. J Ethnopharmacol, 2006. 107(3): p. 374-9.
7. Ruzaidi, A., et al., The effect of Malaysian cocoa extract on glucose levels and lipid profiles in diabetic rats. J Ethnopharmacol, 2005. 98(1-2): p. 55-60.
8. Jaouhari, J.T., et al., Hypoglycaemic response to Zygophyllum gaetulum extracts in patients with non-insulin-dependent diabetes mellitus. J Ethnopharmacol, 1999. 64(3): p. 211-7.
9. Herrera-Arellano, A., et al., Clinical trial of Cecropia obtusifolia and Marrubium vulgare leaf extracts on blood glucose and serum lipids in type 2 diabetics. Phytomedicine, 2004. 11(7-8): p. 561-6.
10. Jayawardena, M.H., et al., A double blind randomised placebo controlled cross over study of a herbal preparation containing Salacia reticulata in the treatment of type 2 diabetes. J Ethnopharmacol, 2005. 97(2): p. 215-8.
11. Grover, J.K., S. Yadav, and V. Vats, Medicinal plants of India with anti-diabetic potential. J Ethnopharmacol, 2002. 81(1): p. 81-100.
12. Ahmed, I. and B. Goldstein, Diabetes mellitus. Clin Dermatol, 2006. 24(4): p. 237-46.
13. Evans, J.L., et al., Oxidative stress and stress-activated signaling pathways: a unifying hypothesis of type 2 diabetes. Endocr Rev, 2002. 23(5): p. 599-622.
14. DeFronzo, R.A., Pathogenesis of type 2 diabetes mellitus. Med Clin North Am, 2004. 88(4): p. 787-835, ix.
15. Amos, A.F., D.J. McCarty, and P. Zimmet, The rising global burden of diabetes and its complications: estimates and projections to the year 2010. Diabet Med, 1997. 14 Suppl 5: p. S1-85.
16. Wild, S., et al., Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care, 2004. 27(5): p. 1047-53.

17. He, K., et al., Evaluation of antidiabetic potential of selected traditional Chinese medicines in STZ-induced diabetic mice. J Ethnopharmacol, 2011. 137(3): p. 1135-42.
18. Dhanabal, S.P., et al., Hypoglycemic effect of ethanolic extract of Musa sapientum on alloxan induced diabetes mellitus in rats and its relation with antioxidant potential. J Herb Pharmacother, 2005. 5(2): p. 7-19.
19. Xue, W., et al., Trigonella foenum graecum seed extract protects kidney function and morphology in diabetic rats via its antioxidant activity. Nutr Res. 31(7): p. 555-62.
20. Zheng, X.K., et al., Anti-diabetic activity and potential mechanism of total flavonoids of Selaginella tamariscina (Beauv.) Spring in rats induced by high fat diet and low dose STZ. J Ethnopharmacol. 137(1): p. 662-8.
21. Paul, S., T.K. Bandyopadhyay, and A. Bhattacharyya, Immunomodulatory effect of leaf extract of Murraya koenigii in diabetic mice. Immunopharmacol Immunotoxicol. 33(4): p. 691-9.
22. Paul, S., T.K. Bandyopadhyay, and A. Bhattacharyya, Immunomodulatory effect of leaf extract of Murraya koenigii in diabetic mice. Immunopharmacol Immunotoxicol, 2011. 33(4): p. 691-9.
23. Xue, W., et al., Trigonella foenum graecum seed extract protects kidney function and morphology in diabetic rats via its antioxidant activity. Nutr Res, 2011. 31(7): p. 555-62.
24. Zheng, X.K., et al., Anti-diabetic activity and potential mechanism of total flavonoids of Selaginella tamariscina (Beauv.) Spring in rats induced by high fat diet and low dose STZ. J Ethnopharmacol, 2011. 137(1): p. 662-8.
25. Nathan, D.M., Long-term complications of diabetes mellitus. N Engl J Med, 1993. 328(23): p. 1676-85.
26. Clark, C.M., Jr. and D.A. Lee, Prevention and treatment of the complications of diabetes mellitus. N Engl J Med, 1995. 332(18): p. 1210-7.
27. Stratton, I.M., et al., Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ, 2000. 321(7258): p. 405-12.
28. Cheng, A.Y. and I.G. Fantus, Oral antihyperglycemic therapy for type 2 diabetes mellitus. CMAJ, 2005. 172(2): p. 213-26.
29. Bailey, C.J. and C. Day, Traditional plant medicines as treatments for diabetes. Diabetes Care, 1989. 12(8): p. 553-64.
30. Gurib-Fakim, A., Medicinal plants: traditions of yesterday and drugs of tomorrow. Mol Aspects Med, 2006. 27(1): p. 1-93.
31. Balde, N.M., et al., Herbal medicine and treatment of diabetes in Africa: an example from Guinea. Diabetes Metab, 2006. 32(2): p. 171-5.
32. Dey, L., A.S. Attele, and C.S. Yuan, Alternative therapies for type 2 diabetes. Altern Med Rev, 2002. 7(1): p. 45-58.
33. Gupta, R., B. Gabrielsen, and S.M. Ferguson, Nature's medicines: traditional knowledge and intellectual property management. Case studies from the National Institutes of Health (NIH), USA. Curr Drug Discov Technol, 2005. 2(4): p. 203-19.
34. Herrera, C., et al., Hypoglycemic and antihyperglycemic effect of Witheringia solanacea in normal and alloxan-induced hyperglycemic rats. J Ethnopharmacol. 133(2): p. 907-10.
35. Kasabri, V., F.U. Afifi, and I. Hamdan, In vitro and in vivo acute antihyperglycemic effects of five selected indigenous plants from Jordan used in traditional medicine. J Ethnopharmacol. 133(2): p. 888-96.
36. Cekic, V., et al., Hypoglycaemic action of stevioside and small a, Cyrillic barley and brewer's yeast based preparation in the experimental model on mice. Bosn J Basic Med Sci. 11(1): p. 11-6.
37. Park, C.H., et al., The effects of corni fructus extract and its fractions against alpha-glucosidase inhibitory activities in vitro and sucrose tolerance in normal rats. Am J Chin Med. 39(2): p. 367-80.
38. Davis, P.A. and W. Yokoyama, Cinnamon intake lowers fasting blood glucose: meta-analysis. J Med Food. 14(9): p. 884-9.
39. Cekic, V., et al., Hypoglycaemic action of stevioside and small a, Cyrillic barley and brewer's yeast based preparation in the experimental model on mice. Bosn J Basic Med Sci, 2011. 11(1): p. 11-6.
40. Herrera, C., et al., Hypoglycemic and antihyperglycemic effect of Witheringia solanacea in normal and alloxan-induced hyperglycemic rats. J Ethnopharmacol, 2011. 133(2): p. 907-10.
41. Kasabri, V., F.U. Afifi, and I. Hamdan, In vitro and in vivo acute antihyperglycemic effects of five selected indigenous plants from Jordan used in traditional medicine. J Ethnopharmacol, 2011. 133(2): p. 888-96.
42. Park, C.H., et al., The effects of corni fructus extract and its fractions against alpha-glucosidase inhibitory activities in vitro and sucrose tolerance in normal rats. Am J Chin Med, 2011. 39(2): p. 367-80.
43. Ivorra, M.D., M. Paya, and A. Villar, A review of natural products and plants as potential antidiabetic drugs. J Ethnopharmacol, 1989. 27(3): p. 243-75.
44. Tanira, M.O., et al., Antimicrobial and phytochemical screening of medicinal plants of the United Arab Emirates. J Ethnopharmacol, 1994. 41(3): p. 201-5.
45. Bnouham, M., et al., Antidiabetic effect of some medicinal plants of Oriental Morocco in neonatal non-insulin-dependent diabetes mellitus rats. Hum Exp Toxicol. 29(10): p. 865-71.
46. Bnouham, M., et al., Antihyperglycemic activity of Arbutus unedo, Ammoides pusilla and Thymelaea hirsuta. Pharmazie, 2007. 62(8): p. 630-2.
47. Bastaki, W., et al., Primary hepatic carcinoid tumor. Med Princ Pract, 2005. 14(4): p. 288-91.
48. Rees, D.A. and J.C. Alcolado, Animal models of diabetes mellitus. Diabet Med, 2005. 22(4): p. 359-70.
49. Masiello, P., Animal models of type 2 diabetes with reduced pancreatic beta-cell mass. Int J Biochem Cell Biol, 2006. 38(5-6): p. 873-93.
50. Srinivasan, K. and P. Ramarao, Animal models in type 2 diabetes research: an overview. Indian J Med Res, 2007. 125(3): p. 451-72.

51. Frode, T.S. and Y.S. Medeiros, Animal models to test drugs with potential antidiabetic activity. J Ethnopharmacol, 2008. 115(2): p. 173-83.
52. Mythili, M.D., et al., Effect of streptozotocin on the ultrastructure of rat pancreatic islets. Microsc Res Tech, 2004. 63(5): p. 274-81.
53. Federiuk, I.F., et al., Induction of type-1 diabetes mellitus in laboratory rats by use of alloxan: route of administration, pitfalls, and insulin treatment. Comp Med, 2004. 54(3): p. 252-7.
54. Matsui, T., et al., alpha-Glucosidase inhibitory profile of catechins and theaflavins. J Agric Food Chem, 2007. 55(1): p. 99-105.
55. Soumyanath, A., et al., UV irradiation affects melanocyte stimulatory activity and protein binding of piperine. Photochem Photobiol, 2006. 82(6): p. 1541-8.
56. Benjamin, B.D. and N.B. Mulchandani, Studies in biosynthesis of secondary constituents in tissue cultures of Tylophora indica. Planta Med, 1973. 23(4): p. 394-7.
57. Gray, A.M. and P.R. Flatt, Pancreatic and extra-pancreatic effects of the traditional anti-diabetic plant, Medicago sativa (lucerne). Br J Nutr, 1997. 78(2): p. 325-34.
58. Gray, A.M. and P.R. Flatt, Insulin-secreting activity of the traditional antidiabetic plant Viscum album (mistletoe). J Endocrinol, 1999. 160(3): p. 409-14.
59. van de Venter, M., et al., Antidiabetic screening and scoring of 11 plants traditionally used in South Africa. J Ethnopharmacol, 2008. 119(1): p. 81-6.
60. McClenaghan, N.H., P.R. Flatt, and C.J. Bailey, Insulin-releasing action of the novel antidiabetic agent BTS 67 582. Br J Pharmacol, 1998. 123(3): p. 400-4.
61. Hannan, J.M., et al., Soluble dietary fibre fraction of Trigonella foenum-graecum (fenugreek) seed improves glucose homeostasis in animal models of type 1 and type 2 diabetes by delaying carbohydrate digestion and absorption, and enhancing insulin action. Br J Nutr, 2007. 97(3): p. 514-21.
62. Brush, J., et al., The effect of Echinacea purpurea, Astragalus membranaceus and Glycyrrhiza glabra on CD69 expression and immune cell activation in humans. Phytother Res, 2006. 20(8): p. 687-95.
63. Frost, S.C. and M.D. Lane, Evidence for the involvement of vicinal sulfhydryl groups in insulin-activated hexose transport by 3T3-L1 adipocytes. J Biol Chem, 1985. 260(5): p. 2646-52.
64. Soumyanath, A., et al., Centella asiatica accelerates nerve regeneration upon oral administration and contains multiple active fractions increasing neurite elongation in-vitro. J Pharm Pharmacol, 2005. 57(9): p. 1221-9.
65. Ali, H., P.J. Houghton, and A. Soumyanath, alpha-Amylase inhibitory activity of some Malaysian plants used to treat diabetes; with particular reference to Phyllanthus amarus. J Ethnopharmacol, 2006. 107(3): p. 449-55.
66. Bhandari, M.R., et al., Alpha-glucosidase inhibitor from Chinese aloes. Fitoterapia, 2008. 79(6): p. 456-7.
67. Patel, M.B. and S.H. Mishra, Hypoglycemic activity of C-glycosyl flavonoid from Enicostemma hyssopifolium. Pharm Biol, 2011. 49(4): p. 383-91.
68. 70.Sheela, C.G., K. Kumud, and K.T. Augusti, Anti-diabetic effects of onion and garlic sulfoxide amino acids in rats. Planta Med, 1995. 61(4): p. 356-7.
69. 71.Chattopadhyay, R.R., Possible mechanism of antihyperglycemic effect of Azadirachta indica leaf extract: part V. J Ethnopharmacol, 1999. 67(3): p. 373-6.
70. 72.Eidi, A., M. Eidi, and E. Esmaeili, Antidiabetic effect of garlic (Allium sativum L.) in normal and streptozotocin-induced diabetic rats. Phytomedicine, 2006. 13(9-10): p. 624-9.
71. 73.Szkudelski, T., The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. Physiol Res, 2001. 50(6): p. 537-46.
72. 74.Pushparaj, P.N., B.K. Tan, and C.H. Tan, The mechanism of hypoglycemic action of the semi-purified fractions of Averrhoa bilimbi in streptozotocin-diabetic rats. Life Sci, 2001. 70(5): p. 535-47.
73. 75.Walde, S.S., et al., Molecular target structures in alloxan-induced diabetes in mice. Life Sci, 2002. 71(14): p. 1681-94.
74. 76.Pari, L. and M.A. Satheesh, Effect of pterostilbene on hepatic key enzymes of glucose metabolism in streptozotocin- and nicotinamide-induced diabetic rats. Life Sci, 2006. 79(7): p. 641-5.
75. 77.Balamurugan, R., V. Duraipandiyan, and S. Ignacimuthu, Antidiabetic activity of gamma-sitosterol isolated from Lippia nodiflora L. in streptozotocin induced diabetic rats. Eur J Pharmacol. 667(1-3): p. 410-8.
76. 78.Kusano, S. and H. Abe, Antidiabetic activity of white skinned sweet potato (Ipomoea batatas L.) in obese Zucker fatty rats. Biol Pharm Bull, 2000. 23(1): p. 23-6.
77. 79.Bnouham, M., et al., Antidiabetic and antihypertensive effect of a polyphenol rich-fraction of Thymeleae hirsuta L. in a model of neonatal streptozotocin-induced diabetic and L-NAME hypertensive rats. J Diabetes, 2012.
78. 80.Bastaki, S.M., et al., Effects of streptozotocin-induced long-term diabetes on parietal cell function and morphology in rats. Mol Cell Biochem, 2010. 341(1-2): p. 43-50.
79. 81.Andrade-Cetto, A., Inhibition of gluconeogenesis by Malmea depressa root. J Ethnopharmacol, 2011. 137(1): p. 930-3.
80. 82.Zhen, Z., et al., Anti-diabetic effects of a Coptis chinensis containing new traditional Chinese medicine formula in type 2 diabetic rats. Am J Chin Med, 2011. 39(1): p. 53-63.

Protecting Effect of Antioxidants (Antox) on the Dentate Gyrus of Aged Male Albino Rat

[1]Mohammed. H. Mohammed and [2]Mostafa A. Abouelnaga

[1]Department of Anatomy and Embryology, Faculty of Medicine, Assiut University and
[2]Faculty of Medicine, AL- Azhar University– Damietia branch

Abstract: Introduction: Aging has been defined as a time-related loss of the capacity of cells to maintain their functions. A primary cause of the aging process has been claimed to be the reduced antioxidant defense.**Aim of the study:** This study aims to elucidate the histological features of the dentate gyrus in male albino rats during aging process and to investigate the important protective role of antioxidant (Antox) on the aging of the dentate gyrus of adult male albino rats. **Material and methods :**41 male adult albino rats were used and were classified into three groups; Control adult group (3-6 months), Control aged group which was further classified into three subgroups aged 12, 18, and 24 months, respectively and Antox -treated aged group which was also classified into three subgroups aged 12,18 and 24 months. The treated animals received Antox dissolved in water at a dose level of 3.4 mg/kg body weight 3 times weekly for 3 months starting at 9,15 and 21months for the three age subgroups respectively. Sections of hippocampus were prepared were prepared for light and electron microscope examinations. **Results:** With light and electron microscope, there was a progressive increase in the appearance of dark neurons with advancing age in addition to a noticeable neuronal loss and a decrease in the frequency of appearance of neurons in the control aged groups. Senile changes such as the accumulation of lipofuscinin the neuronal perikarya and changes in the nucleus, mitochondria, rough reticulum, and *Golgi* apparatus were observed in the control group. Also, membrane-bound organelle-free areas were observed. Degenerated neurons, with shrunken nuclei and ill-defined few cytoplasmic organelles, were observed with advancing age. After the treatment with Antox, the senile changes were less when compared with the control aged group. It was also noticed that, the Antoximproving age - associated histological changes were best especially at the middle age (12 months) rather than that of the early old age (18 months) and the oldest age (24 months), mostly due to the irreversible degenerative changes which had occurred at older age groups prior to the treatment with Antox.**Conclusion:** The present study showed that the age - associated histological changes may be the basis for the age associated functional changes of the gyrusof the hippocampal formation, which may be manifest in elderly people by disturbances in motor coordination and declines.The present study also demonstrates the effectiveness of the combination antioxidants (Antox) in reducing the age-related histological changes in the dentate gyrus of the hippocampal formation. So, it is recommended to investigate its use in age-related neurodegenerative

[Mohammed. H. Mohammed **Protecting Effect of Antioxidants (Antox) On the Dentate Gyrus of Aged Male Albino Rat.** *Life Sci J* 2012;9(4):2784-2795]. (ISSN: 1097-8135). http://www.lifesciencesite.com. 410

Key Words: Dentate Gyrus, Aging, Antox.

1. Introduction

The dentate gyrus (DG) is a simple cortical region that is an integral portion of the larger functional brain system called the hippocampal formation **(Kempermann, 2002).** The hippocampus is a neural structure in the medial temporal lobe that has a distinctive curved S shape. The hippocampal formation is defined as the complex of six structures: Gyrusdentatus, hippocampus proprius, subiculumproprium, presubiculum, parasubiculum and area entorhinalis **(Andersen et *al.*, 2000).**

The DG consists of three layers: the outer molecular layer, the middle granule cell layer and the inner polymorphic layer (hilus). The principal neurons of the DG are the granule cells, which have most of the features typical of small neurons. They are organized compactly and form an inferior and superior blade in the rat DG **(Laatsch and Cowan, 1966)**. The hilar cells resemble the morphology of the spiny pyramidal neuron **(Seroogy*et al.*, 1983**). Experimental studies proved that the hippocampus has a very important role in the process of learning and in a wide range of memory types particularly in spatial memory **(El Falougy and Benuska, 2006).**

The hippocampal dentate gyrus was reported to be one of the few regions of the mammalian brain where neurogenesis continue to occur throughout adulthood. The neurogenesis in the dentate gyrus was thought to play an important role in hippocampus-dependent learning and memory **(Gao, *et al.*, 2007, and Li, *et al.*, 2008).** Hence, DG is thought to contribute to new memories as well as other functional roles **(Saab *et al.*, 2009)**. Aging is characterized by a general decline in physiological function that leads to morbidity and mortality **(Miyoshi, *et al.*, 2006).**

Hippocampal circuitry is particularly vulnerable to aging and neurodegenerative conditions

(Chohan*et al.*, 2009). Normal aging brings with it changes in dopaminergic and memory functions **(Morcom*et al.*, 2010).** Moreover, aging is the greatest environmental risk factor for the sporadic cases of Alzheimer's disease (AD) which is progressive neurodegenerative disorder characterized by a progressive memory loss and cognitive decline **(Caselli, *et al.*, 2006).**

The antioxidants are either reactive chemicals such as Antox or specialized enzymes as catalase. The body produces enzymatic antioxidants but cannot make the antioxidant chemicals (e.g. Antox, C and flavonoids), that protect the sites in the body that the enzymatic antioxidants cannot reach **(Hagga*et al*,. 2006; Mosad*et al.*, 2007)** mentioned that beta carotene (a carotenoid metabolic precursor to vitamin A), Antox, vitamin C and selenium are involved in the overall cellular antioxidant defense mechanism.

Antioxidents nutrients, as ascorbic acid, tocopherol, B-carotene, etc., are considered to give protection against oxidative damage induced by different toxicants and reduce the activity of free radical-induced reactions **(McCall and Balz, 1999)**. Antox is an antioxidant drug composed of selenium, vitamin A acetate, ascorbic acid and vitamin E. Antox was used in therapy of different liver diseases **(Wastone*t al.*, 1999, Hamooda, *et al.*,2003,Zhong and Lemasters, 2004 and Oz *et al.*, 2004).**

The aim of the study

The goal of the present study is to elucidate the histological features of the dentate gyrus in male albino rats during aging process and to investigate the important protective role of antioxidant (Antox) on the aging of the dentate gyrus of adult male albino rats.

2. Material and Methods

Material:

A total number of 41 male albino rats (average weight 200-250 gm) were used in this study. The animals were isolated in clean properly ventilated cages in the animal house of AssiutUniversity under normal conditions with an appropriate temperature, normal light and dark cycle and free access to food and water.

The animals were divided into 3 groups:

Group I (Control adult group): This group includes 5 male rats aged 3-6 months.

Group II (Control aged group):This group includes 18 male rats that were equally divided according to their age (Shettyand Turner, 1999) and its corresponding human age (Flood, et al., 1987) into three subgroups:

Subgroup II a: 12 months-aged control animals were used representing the middle age group which corresponds to the age of fifties in human.

Subgroup II b: 18 months-aged control animals were used representing the early old age group that corresponds to the age of seventies in human.

Subgroup II c: 24 months-aged control animals were used representing the oldest old age group that corresponds to the age of nineties in human.

Subgroup III (Antox-treated aged group): This group includes 18 male rats that were equally divided into three subgroups:

Subgroup III a 12 months-aged Antox-treated animals,

Subgroup III b: 18 months-aged Antox-treated animals,

Subgroup III c: 24 months-aged Antox-treated animals.

Drug dosage and administration:

The treated animals received Antox dissolved in water at a dose level of 3.4 mg/kg body weight 3 times weekly for 3 months starting at 9,15 and 21months for the three age subgroups respectively. Antox tablets composed of selenium, medicinal yeast, ascorbic acid, vitamin A acetate and vitamin E (Hawazen and Maisaa,2007).

Methods:

Tissue Preparation

Each animal was anaesthetized with ether, its heart was exposed, and saline solution was perfused through the left ventricle until the coming fluid was blood-free. Then perfusion was done with Bouin's fixative for light microscopy, and with cold 4% gluteraldhyde in a buffered cacodylate solution pH 7.4 for electron microscopy. The cranial cavity was opened; the brain was carefully dissected out and left immersed in the fixative and undisturbed for one hour. Then, the right cerebral hemisphere was sectioned coronallyfor studying the right dentate gyrus of the hippocampal formation.

For light microscopy, paraffin sections (5-7µm) of tissue specimens were prepared and stained with Harris haematoxylin and eosin according toDrury and Wallington (1980). Semithin sections (0.5-lµm) of the specimens fixed in 4% gluteraldhyde were stained with toluidine blue (Gupta, 1983) and were examined with light microscope. Subsequently, thin sections (500-800A) were obtained for the selected areas in semithin sections, contrasted with uranyl acetate and lead citrate (Reynolds, 1963), and studied with the transmission electron microscope, JEOL (J.E.M.- 100 CXI 1) and photographed at 80 K.V. in Assiut University Electron Microscope Unit.

3. Results

A- With light Microscope:

Group I (Control adult group): Plate 1

The haematoxylin and eosin stained sections of the dentate gyrus of control adult male albino rats show that the dentate gyrus forms a distinctive V-shaped structure that surrounds the free border of the Amon's horn (Plate 1, Fig. 1). The dentate gyrus consists of three layers, an outer molecular layer, a

central granule cell layer, and an inner polymorphic layer (Plate 1, Fig. 2). The molecular layer is formed mainly of nerve fibers and few nerve cells. The granule cell layer contains the perikarya of granule cells, which are densely packed with little or no intervening tissue. The nuclei of granule cells are rounded or oval in shape and pale basophilic in stain. Their nucleoli are densely stained basophilic and usually peripherally located. A thin rim of cytoplasm is surrounding the nucleus of granule cells (Plate 1, Fig. 3).

The semithin sections stained with toluidine blue confirm that the dentate gyrus is formed of three layers, the outer molecular layer, the granule cell layer and the inner polymorphic layer (Plate 1, Fig. 4). The outer molecular layer consists mainly of nerve fibers together with few scattered cells. The middle granule cell layer shows dense packing of the granule bodies with little intervening tissue. The granule cells usually assume liar or polyhedral shape. Their nuclei appear pale, rounded or ovoid in with single dense peripheral nucleoli and finely dispersed chromatin. Nuclei are surrounded by thin run of pale staining cytoplasm (Plate 1, Fig.5). The inner polymorphic layer shows a variety of cells of different types. These cells include large pyramidal neurons, few displaced granule and some glial cells (Plate 1, Fig. 6).

Group II (Control aged group):Plate 2

The haematoxylin and eosin-stained sections of the dentate gyrus of the control 12 months - aged male albino rats show some changes in the shape and staining intensity of granule neurons mainly in the deeper parts of the granule cell layer. The cell bodies of these neurons assume irregular profiles with irregular outline and show increase staining intensity. Their nuclei are irregular in shape and deeply stained with no visible nucleoli. The more superficial neurons show normal shape and staining intensity with rounded pale nuclei and visible dense nucleoli (Plate 2, Fig. 1).

For control 18 months – aged group, the heamatoxylin and eosin – stained sections, the granule cell layer of dentate gyrus of male albino rats shows that many granule cell bodies appear darkly stained with irregular outline. Their nuclei are irregular, deeply stained and surrounded by thin rim of deeply stained cytoplasm. Some of the granule cell bodies appear relatively normal shape and staining intensity (Plate 2, Fig. 2).

For control 24 months – aged group, the heamatoxylin and eosin – stained sections in the dentate gyrus of male albino rats show that the most of the granule neurons appear darkly stained with irregular outline and deeply stained nuclei and cytoplasm. Empty spaces are observed among the granule cell bodies (Plate 2, Fig.3).

The semithin sections of the dentate gyrus of control 12 months – aged group show deeply stained granule cell bodies especially in the more basal parts granule cell layer. The nuclei of these neurons appear darkly stained with hardly visible deeply stained nucleoli and surrounded by thin rim of stained cytoplasm, which shows small vacuoles. Other granule cell bodies show pale stained, clear, vacuolated cytoplasm and their nuclei relatively normal in shape and staining intensity. The remaining cells show more or less normal shape and staining intensity of their nuclei and cytoplasm (Plate 2, Fig. 4).

For control 18 months – aged group, the semithin sections of the dentate gyrusshow that the granule cell layer contains many darkly stained granule cell bodies having irregular outlines. The nuclei of these dark cells appear darkly stained with hardly visible, darkly stained nucleoli. Their cytoplasm is darkly stained forms thin rim around the nuclei. Some of the granule neurons show relatively normal staining of their nuclei, while, their cytoplasm contains 56 pale vacuolated areas (Plate 2, Fig. 5).

For control 24 months – aged group, the semithin sections of the dentate gyrusshow that the granule cell layer is mainly formed of the darkly stained granule cells which have deeply stained irregular nuclei surrounded by thin rim of darkly stained cytoplasm. Few of the granule cells appear pale stained. Their nuclei are relatively normal in staining intensity. Their cytoplasm appears pale vacuolated (Plate 2, Fig.6).

Group III (Antox treated aged group): Plate 3

The haematoxylin and eosin-stained sections in the dentate gyrus of Antox-treated 12 months-aged group, animals show that most of the granule cell bodies in the granule cell layer are almost of normal shape and staining intensity. They have rounded pale nuclei with visible dense nucleoli and surrounded by thin rim of cytoplasm. Only few granule cell bodies in the basal part of the granule cell layer appear darkly stained with deeply stained nuclei and cytoplasm (Plate 3, Fig. 1).

For treated 18months-aged group, the haematoxylin and eosin stain, sections in the dentate gyrus of Antox-treated male albino rats show that many granule ells are relatively normal in shape and staining intensity. They have rounded or oval pale nuclei with visible dense nucleoli and surrounded by thin layer of cytoplasm. Few granule neurons, located basely in the granule cell layer, appear darkly stained with irregular outline. These dark cells are comparatively much less frequent than those observed m the control of the same age group (Plate 3, Fig. 2).

For treated 24 months-aged group, the haematoxylin and eosin-stained sections in the dentate gyrus of Antox-treated male albino rats show that some of the granule cell bodies have rounded or

oval large pale nuclei with visible dense nucleoli and surrounded by pale staining cytoplasm. The other granule cell bodies appear darkly stained nuclei and cytoplasm. No empty spaces are observed among the granule cells in comparison with the control group of the same age (Plate 3, Fig. 3).

In semithin sections of the dentate gyrus stained with toluidine blue, the granule cell layer of 12 months-aged group, is mainly formed of pale staining cells. These cells show rounded or oval pale nuclei with visible dense nucleoli and surrounded by pale staining cytoplasm which are more or less similar to those of the control adult age group. Only few granule cell bodies appear darkly stained and have irregular outline, deeply stained nuclei and thin rim darkly stained cytoplasm. These dark cells are observed in the basal part the granule cell layer and are less than those observed in the control 12 months-aged animals (Plate 3, Fig. 4).

For treated 18 months-aged group, semithin sections in the dentate gyrus stained with toluidine blue confirm that many granule cell bodies have large oval or rounded pale nuclei with visible dense nucleoli and surrounded by pale staining cytoplasm. Small pale vacuolated areas are observed infrequently in the cytoplasm of these pale staining granule cells. Few granule cells appear darkly stained and are comparatively much less frequent than those served in the control of the same age group (Plate 3, Fig. 5).

For treated 24 months-aged group, the semithin sections in the dentate gyrus of this group stained with toluidine blue show that some of the granule cell bodies are much similar to those of the control adult age group. Some granule cells have relatively normal nuclei surrounded by lightly stained, vacuolated cytoplasm, and other granule cells are darkly stained with irregular outline and deeply stained nuclei and cytoplasm. The frequency of these dark granule cells is muchless in comparison with the control group of the same age (Plate 3, Fig. 6).

B- With Electron Microscope:

Group I (Control adult group): Plate 4

The dentate gyrus shows the detailed fine structure of its three layers. The molecular layer is formed mainly of unmyelinated nerve and few myelinated fibers having variable size and containing neurofibrils and mitochondria. Few displaced granule cells are seen especially in the inner half of the molecular layer near to the granule cell layer. They resemble all the features of the ordinary granule cells; their nucleus is large and nearly rounded with finely dispersed chromatin and dense nucleolus. Scattered glial cells are seen in this layer with small nuclei containing dense clumps of chromatin and surrounded by scanty amount of cytoplasm (Plate 4, Fig. 1).

Also, the granule cell layer shows the characteristic close packing of cell bodies of the granule neurons with little intervening tissue. The cell bodies of the granule neurons appear nearly circular or polygonal in shape. Their nuclei are oval rounded with uniformly dispersed chromatin and single electron dense peripheral nucleoli. The cytoplasm forms a narrow rim around the nucleus and contains cisternae and vesicles of Golgi apparatus, mitochondria, ribosomes and few short cisternae of rER (Plate 4, Fig. 2).

In the polymorphic layer, the most striking feature is the presence of large numbers of myelinated nerve fibers especially immediately beneath granule cell layer. Also, unmyelinated nerve fibers can be seen in this layer. Few g1ial cells are also observed with small nucleus containing clumps of dense chromatin and surrounded by scanty amount of cytoplasm (Plate 4, Fig. 3).

Group II (Control aged group): Plate 4

The dentate gyrus of control 12 months – aged male albino rats shows that some of the granule cell bodies are more electron dense in their cytoplasm and nuclei. Their nuclei appear indented or irregular in shape. Their cytoplasm shows dilated short segments of rER. Some of the granule neurons show relatively normal shape and electron density of their nuclei, but the cytoplasm of these neurons contains accumulations of lipofuscin pigment, membrane-bound vacuoles and few dilated rER segments. In the cytoplasm of both the dark and pale granule cells, some mitochondria appear distorted (Plate 4, Fig. 4).

The dentate gyrus of control 18 months – aged male albino rats shows that many granule neurons are irregular in outline and their cytoplasm and nuclei appear dark. The cytoplasm of these cells show distorted Golgi cisternae, distorted mitochondria and dilated rER cisternae. Some of the dark granule neurons appear degenerated with dark homogenous (amalgamated) nuclei and few distorted cytoplasmic organelles. Some of the granule neurons show relatively normal electron density of their nuclei. Some lipofuscinpigment bodies, dilated rER segments and membrane- bound vacuoles are present The neuropil between the granule cell bodies shows many organelles – free areas (Plate 4, Fig. 5).

The dentate gyrus of control 24 months – aged male albino rats shows that most of the granule neurons appear dark (more electron dense) with irregular outline, markedly electron dense nuclei, no visible nucleoli. The cytoplasm of these cells show distorted Golgi cisternae, distorted mitochondria and fragmented short segments of rER and lipofuscin pigment. Few of the granule cells have relatively normal electron density of their nuclei with wide organelle – free areas and marked distortion of the mitochondria in their cytoplasm (Plate 4, Fig. 6).

Group III (Antox treated aged group): Plate 5

The dentate gyrus of Antox-treated 12 months-aged male albino shows that most of the granule cells appear relatively similar to those control adult group. They contain large rounded pale nuclei having dispersed chromatin and electron dense nucleoli. The nuclei of these are surrounded by thin rim of cytoplasm that shows relatively electron density and normal appearance of the neuronal organelles mitochondria, andrER. No membrane-bound or organelle-free areas are observed in their cytoplasm (Plate 5**,** Fig. 1).

The dentate gyrus of Antox-treated 18 months-aged male albino rats shows that many granule neurons have large rounded pale nuclei with finely dispersed chromatin. The cytoplasm of these neurons is of normal electron density and shows normal appearance of most neuronal organelles. Some of the granule cells show dilated rER cisternae with little or no distortion of the mitochondria (Plate 5, Fig. 2). Infrequently, small organelle-free areas are served in the cytoplasm of few granule cells. Only few granule cells appear dark electron dense similar to those in the control group of the same age (Plate 5, Fig. 3).

The dentate gyrus of Antox-treated 24 months-aged male albino rats showed that some of the granule cells had rounded or oval pale nuclei with finely dispersed chromatin and electron-dense nucleoli. The cytoplasm neurons appeared relatively of normal electron density with more normal neuronal organelles. The cytoplasm of other granule cells dilated rER segments, small lipofuscin pigment, some mitochondria and organelle-free areas. Some of the neurons appeared dark with irregular outline and more electron- dense nuclei and cytoplasm (Plate 5, Fig. 4).

4. Discussion

Dentate gyrus is a subregion of the hippocampus that is crucial in cognitive functions such as learning and memory (Tashiro *et al.,* 2007). Brain aging is the key risk factor for the development of cognitive impairment and the development of age related degenerative pathologies (Brayne, 2007). The dentate gyrus is differentially vulnerable to the aging process (Small *et al.,* 2004).

In the present study, male albino rats were utilized to avoid the female hormonal effect. That was supported by previous investigator who suggested that estrogen enhanced cell proliferation during proestrus resulted in more immature neurons in the hippocampal formation of females compared with males and present the possibility that these new cells exert an important influence on hippocampal function (Tanapat*et al.,*1999 and 2001).

In the current study, by studying the dentate gyrus of control aged animals, dark neurons appeared in the granule cell layer which increased in frequency progressively with increasing age. These dark granule neurons appeared shrunken with irregular outline and increased staining intensity, dilated perinuclear cisterna and rER cisternae, together with distorted mitochondria and *Golgi* cisternae in their dark electron dense cytoplasm. These age-associated nuclear alterations **are in** agreement with the s**tudies** of **Radak, *et al.,* (2006)** who **found** an increase of oxidative DNA damage in neurons of regions involved in neurodegenerative diseases, such as Alzheimer's disease, which is suggestive of an accelerated aging process in specific populations of neurons.

The progressive accumulation of mitochondrial dysfunction has been proposed to contribute to the neuronal death and dysfunction with aging. The decline in neuronal metabolism is reported to be a constant alteration in the old brain as a whole, and discrete zones of the CNS are particularly disposed to develop alterations in neuronal metabolic efficiency with aging, including the hippocampal formation. In addition, there was a noticeable accumulation of lipofuscin pigment in the granule neurons of the dentate gyrus of aged animals which increased progressively with advancing age. The age - related accumulation of lipofuscin pigment bodies observed in the present study is in accord of several experimental studies which demonstrated that the most persistent age-related cytological change is the deposition of lipofuscin pigment bodies m the neurons of the hippocampal formation which increases in size and complexity with increasing age **(Sushma, *et al.,* 2011).**

The organelle-free areas observed in the present study are in agreement with the studies of **Sushma, *et al.,* (2011**) who described extreme cytoplasmic vacuolation in the aged hippocampal cells and reported that these vacuolated cells may be regarded as the initial stages of necrotic cell death. A more progressive increase in neuronal cell death by apoptosis has been reported in neurodegenerative disorders, such as Alzheimer's disease **(Ivins, *et al.,* 2000).**

It has been reported that when loss of neurons occurs asin sequence of aging, the healthy neurons in the same area can assume parallel functions to maintain functional stability and, later on, as loss of neurons progresses over the compensatory mechanisms of the surviving neurons, the function is definitely disturbed. It is reasonable, to consider that the changes occurring in the histological structure of the dentate gyrus during aging may be mediated by damage after decline of the antioxidant defense system **(Small *et al.,* 2004).**

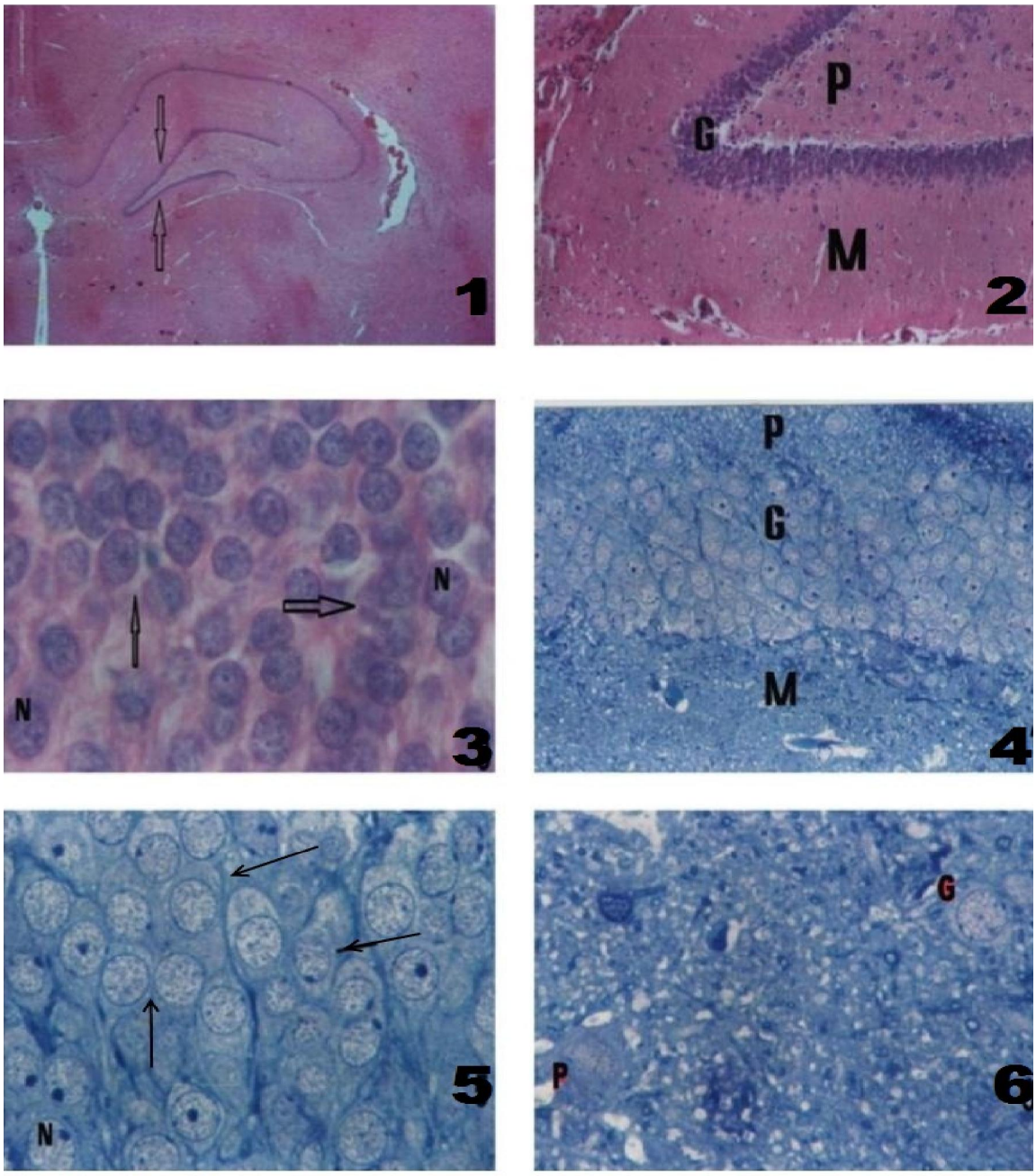


PLATE 1

Fig. 1: A photomicrograph of a section in the hippocampal formation of the control adult group showing; the V –shaped dentate gyrus (arrows) H.&E. X 100

Fig. 2: A photomicrograph of a section in dentate gyrus of the control adult group showing; the outer molecular layer (M), the middle granular layer (G) and the inner polymorphic layer (P). H.&E. X 400

Fig. 3: A photomicrograph of a section in dentate gyrus of the control adult group showing; the close packing of granule cells(arrows) and their large, pale rounded nuclei (N). H.&E. X1000

Fig. 4: A photomicrograph of a semithin section in dentate gyrus of the control adult group showing; the outer molecular layer (M), the middle granular layer (G) and the inner polymorphic layer (P). Toluidine blue X400

Fig. 5: A photomicrograph of a semithin section in dentate gyrus of the control adult group showing; the densely packed granule cells(arrows) with rounded paledense nuclei and thin rim of cytoplasm around the nuclei (N).Toluidine blue X1000

Fig. 6: A photomicrograph of a semithin section in dentate gyrus of the control adult group showing; apart of the polymorphic layer with scattered pyramidal cells (P),granule cells (G) and nerve fibers in between. Toluidine blue X1000

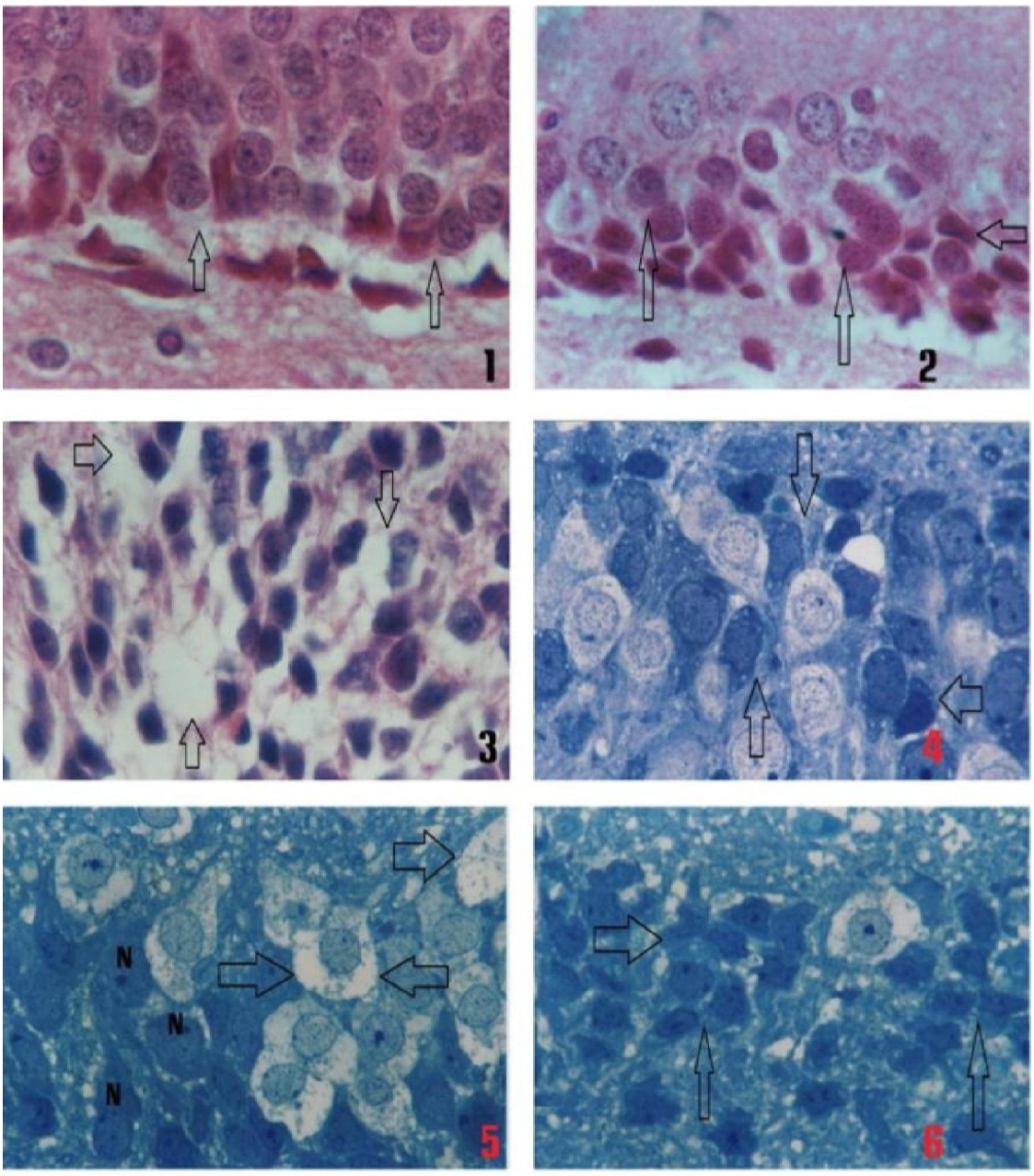


PLATE 2

Fig. 1: A photomicrograph of a section in dentate gyrus of the control 12 months - aged group showing; the intense staining of granule cell bodies in the deeper parts of the granular cell layer (arrows). H.&E. X 1000

Fig. 2: A photomicrograph of a section in dentate gyrus of the control 18 months- aged group showing; many granule cells with darkly stained nucleus and cytoplasm (arrows). H.&E. X 1000

Fig. 3: A photomicrograph of a section in dentate gyrus of the control 24 months - aged group showing; dark staining of most neurons in the granule cell layer and large empty spaces among granule cell bodies (arrows). H.&E. X1000

Fig. 4: A photomicrograph of a semithin section in dentate gyrus of the control 12 months - aged group showing; some granule cell bodies appear darkly stained with irregular outlines (arrows). Toluidine blue X1000

Fig. 5: A photomicrograph of a semithin section in dentate gyrus of the control 18 months - aged group showing; some granule cell bodies appear darkly stained with irregular outlines (N) and large vacuolated areas(arrows). Toluidine blue X1000

Fig. 6: A photomicrograph of a semithin section in dentate gyrus of the control 24 months - aged group showing; most of the granule cell bodies appear darkly stained with irregular outlines (arrows). Toluidine blue X1000

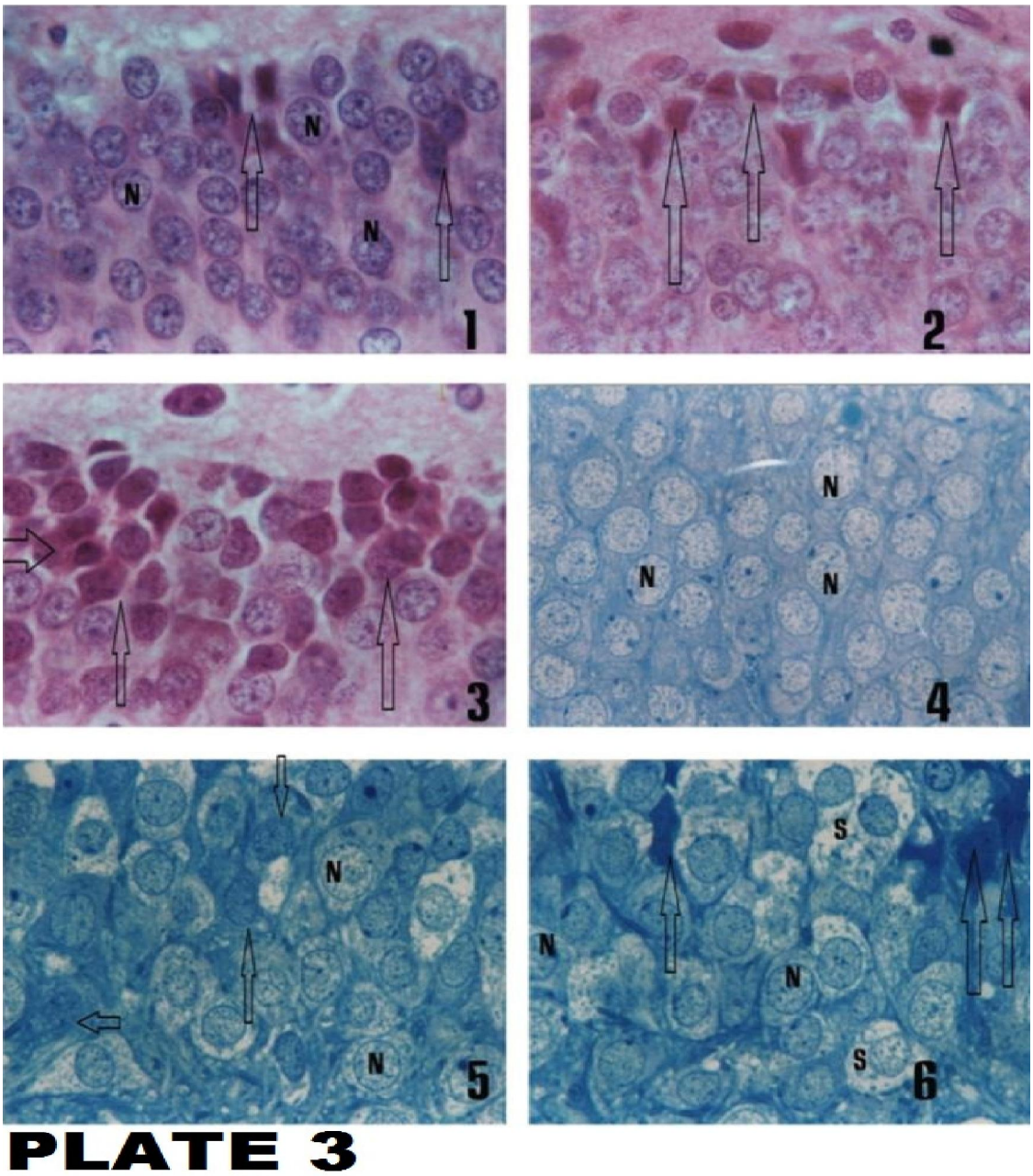


PLATE 3

Fig. 1: A photomicrograph of a section in dentate gyrus of the Antox treated 12 months – aged group showing; the normal appearance of most granule cells (N) with few deeply stained irregular granule cells (arrows). H. & E. X 1000

Fig. 2: A photomicrograph of a section in dentate gyrus of the Antox treated 18 months – aged group showing; the normal appearance of many granule cells with few stained irregular granule cells (arrows). H.&E. X 1000

Fig. 3: A photomicrograph of a section in dentate gyrus of the Antox treated 24 months – aged group showing; less empty spaces appear among granule cell bodies as compared with the control group of the same age group. H. & E. X1000

Fig. 4: A photomicrograph of a semithin section in dentate gyrus of the Antox treated 12 months – aged group showing; most of the granule cells have rounded pale nuclei with dense nucleoli much similar to the control group of the same age group.Toluidine blue X1000

Fig. 5: A photomicrograph of a semithin section in dentate gyrus of the Antox treated 18 months – aged group showing; many of the granule cells have rounded pale nuclei with dense nucleoli surrounded by pale cytoplasm. Few granule cells appear more darkly stained. Toluidine blue X1000

Fig. 6: A photomicrograph of a semithin section in dentate gyrus of the Antox treated 24 months – aged group showing; some of the granule cell bodies appear with rounded nuclei, empty spaces appear among granule cell bodies (arrows) and some darkly stained with irregular outlines granule cells. Toluidine blue X1000

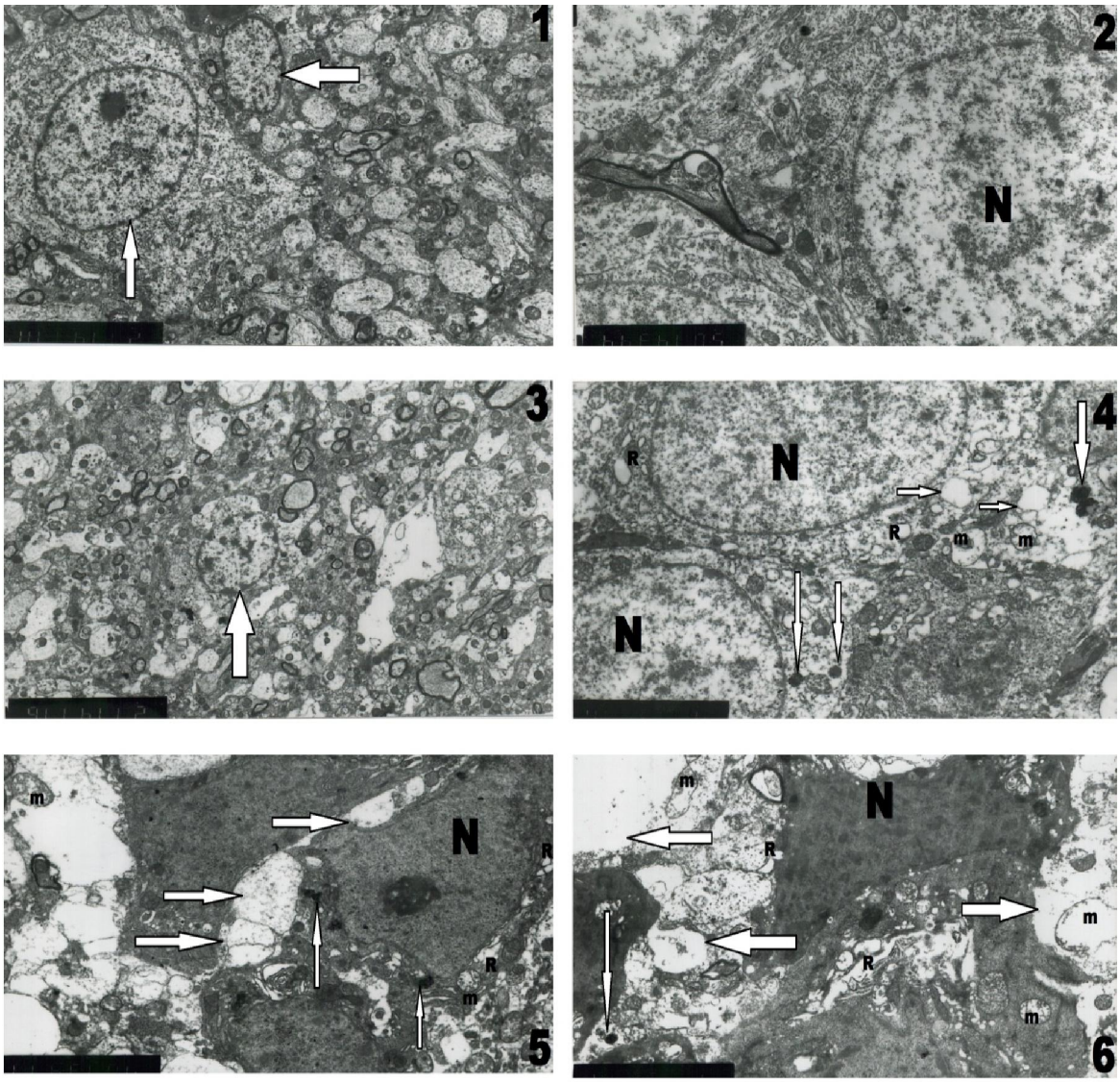


PLATE 4

Fig. 1: An electron micrograph of a section in dentate gyrus of the control adult group showing; a part of the molecular layer in which a displaced granule cell (left vertical arrow) seen the molecular layer. Beside it, a glial cell of smaller nucleus with scanty cytoplasm could be seen (right horizontal arrow). (X 2700).

Fig. 2: An electron micrograph of a section in dentate gyrus of the control adult group showing; a part of the granule cell layer in which the granule cells have pale rounded nuclei with finely dispersed chromatin (N). (X 5000).

Fig. 3: An electron micrograph of a section in dentate gyrus of the control adult group showing; a part of the polymorphic layer in which numerous nerve fibers. A glial cell is also seen (arrow). (X 2700).

Fig. 4: An electron micrograph of a section in dentate gyrus of the control 12 months - aged group showing; a part of the granular cell layer in which there is different electron density of granule cell bodies(N), lipofuscin pigment (vertical arrows), vacuoles (horizontal arrows), dilated short segments of rER (R) and distorted mitochondria (m). (X 4000).

Fig. 5: An electron micrograph of a section in dentate gyrus of the control 18 months - aged group showing; a part of the granular cell layer in which there is dark granule cell bodies (N), dilated short segments of rER (R), lipofuscin pigment (vertical arrows) and distorted mitochondria (m) and organelle - free areas among the granule cell bodies (horizontal arrows). (X 4000).

Fig. 6: An electron micrograph of a section in dentate gyrus of the control 24 months - aged group showing; a part of the granular cell layer in which there is marked increase in electron density of granule cells(N), dilated short segments of rER (R), lipofuscin pigment in their cytoplasm (vertical arrow) and distorted mitochondria (m)and many organelle - free areas among the granule cell bodies (horizontal arrows). (X5000).

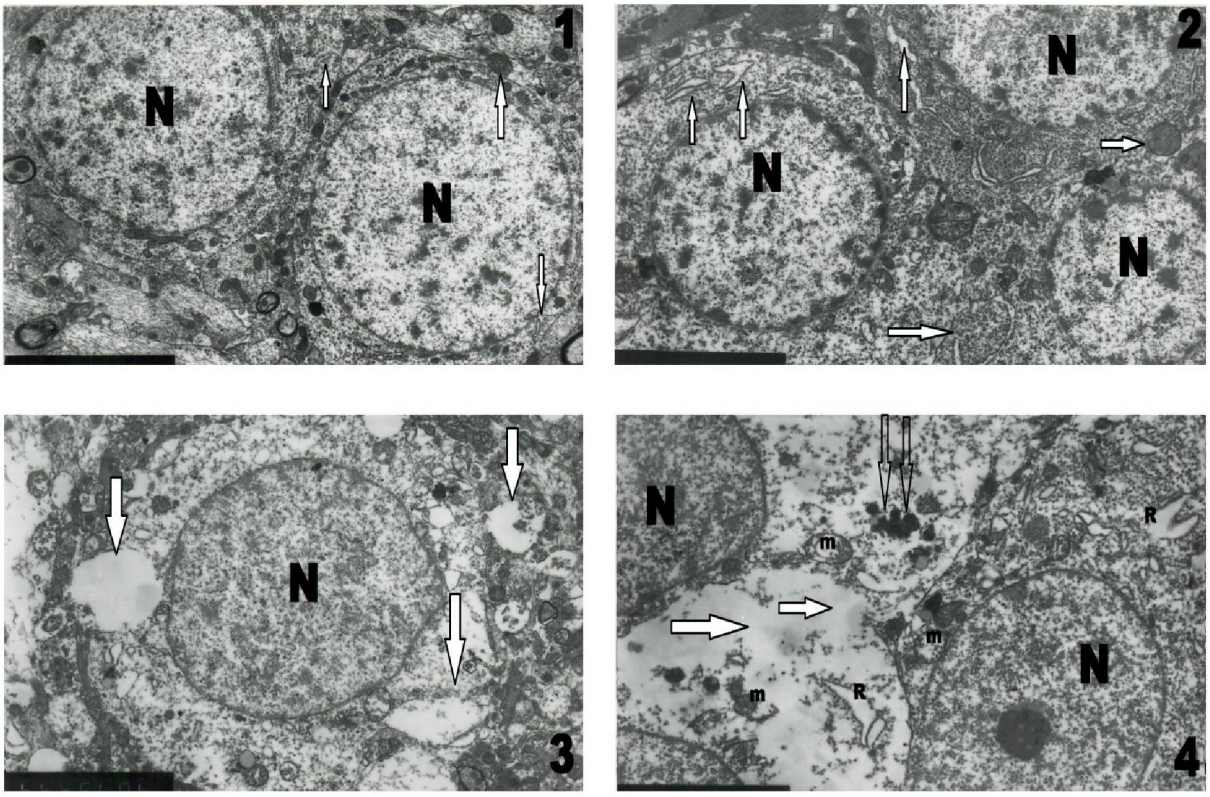


PLATE 5

Fig. 1: An electron micrograph of a section in dentate gyrus of the Antox treated 12 months – aged group showing; a relatively normal shape and electron density of nuclei of granule cells (N)and normal appearance of neuronal organelles (arrows). (X 4000).

Fig. 2: An electron micrograph of a section in dentate gyrus of the Antox treated 18 months – aged group showing; some of granule cells nuclei (N), dilated rER cisternae (vertical arrows) but little distortion of mitochondria (horizontal arrows). (X 4000).

Fig. 3: An electron micrograph of a section in dentate gyrus of the Antox treated 18 months – aged group showing; small organelle – free areas in the cytoplasm of granule cells (arrows). (X 4000).

Fig. 4: An electron micrograph of a section in dentate gyrus of the Antox treated 24 months – aged group showing; some of granule cells nuclei (N), dilated rER cisternae (R), lipofuscin pigment (vertical arrows) distortion of mitochondria (m) and organelle – free areas in the cytoplasm of granule cells (horizontal arrows). (X 4000).

Hawazenet and Maisaa, (2007)studied the effect of Antox on kidney of albino rats. They found that the antioxidant Antox led to an improvement in both histological and biochemical alteration of rats induced by toxic herbicide paraquat**. Sonali*et al.*,(2006)** stated that, the ameliorative potential of selenium revealed a positive role of selenium, especially when Se preceded As_2O_3 treatment in either *in vitro* or *in vivo*.

The noticeable reduction in the age-associated histological changes which was observed in the treated animals was less compared with those of the control aged animals. This observation reflects the protective effect of Antox against the free radical attack of mitochondrial membranes and mitochondrial DNA. These results correlates with that made by **Amal and Mona,(2009)** who reported that rats treated with Antox revealed an improvement in histopathological alteration after 3 weeks and 6 weeks. This proved the effectiveness of Antox that attributed to its antioxidant properties.

The present study showed that the protective effect of Antox against all these age-associated histological changes was noticeable in all age groups of treated animals, but to a varying degree with more protection being observed at the younger age groups. It is also noticeable that the preventive **effect of antioxidant** on age-associated histological changes was obvious **but this** prevention varied in degree according to the age group. Thus, **the** preventive

effect of antioxidants was best in the middle age group, **which** restored histological structure much similar to the adult group. The prevention was less in the early old group so that not all the neurons restored the normal shape and staining intensity with normal ultrastructure. Furthermore, in the oldest group, still some of the neurons showed some degenerative changes. These observations show a positive correlation between better restoration of neuronal structure and earlier treatment with antioxidants. This can be explained by that, at middle age, there were early reversible changes before the administration of antioxidants which can restore these changes and prevent the occurrence of any other degenerative changes. But, later in early old and oldest old groups, more irreversible degenerative changes had developed before the administration of antioxidants **(Murray and Lynch, 1998 a&b)**.

The incomplete prevention of all degenerative changes in older age groups by Antox may be due to the contribution of otherfactors, besides oxidative damage, to the aging process as the process ofaging is known to be a multifactorial process. Therefore, neuroendocrine factors, immunological factors, or vascular factors can contribute toa varying degree in the aging process. However, the marked noticeable improvement in age-associated histological degenerative changes as compared with the control of the same ages, signify the high contribution of tree radical-mediated oxidative damage to be the major causative factor of brain aging. Therefore, antioxidant therapies are being promoted to enhance mental functions and delay cognitive losses with aging. An increasing number of physicians are also recommending antioxidant therapies, for subjects with Alzheimer's disease and other neurodegenerative disorders (Von Arnim***et al.,*** **2012)**.

Conclusion

The present study showed that the age - associated histological changes may be the basis for the age associated functional changes of the dentate gyrusof the hippocampal formation, which may be manifest in elderlypeople by disturbances in motor coordination and declines. The present study also demonstrates the effectiveness of the combination antioxidants (Antox) in reducing the age-related histological changes in the dentate gyrus of the hippocampal formation. So, it is recommended to investigate its use in age-related neurodegenerative disorders human, for improvement of learning and memory during aging.

Corresponding authors
Mohammed. H. Mohammed
Department of Anatomy and Embryology, Faculty of Medicine, Assiut University.

References:

1. Amal E.Aand Mona H. M.(2009): Protective effect of some antioxidants on the brain of adult male albino rats, *Rattusrattus*, exposed to heavy metals. Bioscience Research, 6(1): 12-19, 2009
2. Andersen P., Soleng A.F. and Raastad M. (2000): The hippocampal lamella hypothesis revisited. Brain Res. Dec 15;886(1-2):165-171.
3. Brayne C. (2007): The elephant in the room - Healthy brains in later life, epidemiology and public health. Nat.Rev.Neurosci. ;8(3):233-239.
4. aselli R.J., Beach T.G., Yaari R. and Reiman E.M. (2006): Alzheimer's disease a century later. J.Clin.Psychiatry Nov;67(11):1784-1800.
5. Chohan M.O., Li B., Blanchard J., Tung Y.C., Heaney A.T., Rabe A., Iqbal K. and GrundkeIqbal I. (2009): Enhancement of dentate gyrus neurogenesis, dendritic and synaptic plasticity and memory by a neurotrophic peptide. Neurobiol.Aging (Article in press).
6. Drury R. A. B. and Wallington E. A. (1980): Carleton's Histological Technique, 4th ed. London, New York,Toronto: Oxford University Press.
7. El Falougy H. and Benuska J. (2006): History, anatomical nomenclature, comparative anatomy and functions of the hippocampal formation. Bratisl.Lek.Listy; 107(4):103-106.
8. Flood D.G., Guaranaccia M., and Coleman P.D.(1987): Dendritic extent in human CA2-3 hippocampal pyramidal neurons in normal aging and senile dementia. Brain Res.: 409:88-96.
9. Gao X Arlotta P, Macklis JD and Chen J. (2007): Conditional knock-out of β-catenin in postnatal-born dentate gyrus granule neurons results in dendritic malformation. J. Neurosci; 27(52):14317-14325.
10. Gupta O.P. (1983): A least-squares approach to depth determination from gravity data: Geophysics; 48: 357-360.
11. Haggag W.M., A.L. Kansoh and Aly A.M. (2006): Proteases from *Talaromycesflavus* and *Trichodermaharzianum*: Purification, characterization and antifungal activity against brown spot disease on faba bean. Plant Pathol. Bull., 15: 231-239.
12. Hamooda H., A. baalash K. Saad and Emara A. (2003): oxidative stress; a hallmark of cadmium induced toxicity in different tissues, Drug Metabolism Rev., 35(1): 231-237.
13. Hawazen A. Lamfon and Maisaa M. Al-Rawi, (2007) : Effect of antox on paraquat-induced histological and biochemical changes in kidney of albino rats. Journal of Applied Sciences 3 (10): 988 – 993).
14. Ivins J.K, Yurchenco P.D and Lander A.D (2000): Regulation of neurite outgrowth by integrin activation. J Neurosci 20:6551–6560.
15. Kempermann G. (2002): Why new neurons? Possible functions for adult hippocampal neurogenesis. J.Neurosci. Feb 1;22(3):635-638.
16. Laatsch R.H. and Cowan W.M. (1966): Electron microscopic studies of the dentate gyrus of the rat. I.

Normal structure with special reference to synaptic organization. J.Comp.Neurol. Nov;128(3):359-395.
17. Li B., Yamamori H., Tatebayashi Y., ShafitZagardo B., Tanimukai H., Chen S., Iqbal K. and GrundkeIqbal I. (2008): Failure of neuronal maturation in Alzheimer disease dentate gyrus. J.Neuropathol.Exp.Neurol. ;67(1):78-84.
18. McCall M.R. and Balz F. (1999). Can antioxidant vitamins materially reduce oxidative damage in humans? Free Rad. Biol. Med., 26: 1034-1053.
19. Miyoshi N., Oubrahim H., Chock P.B. and Stadtman E.R. (2006): Age-dependent cell death and the role of ATP in hydrogen peroxide-induced apoptosis and necrosis. Proc.Natl.Acad. Sci.U.S.A. Feb 7;103(6):1727-1731.
20. Morcom A.M, Bullmore E.T, Huppert F.A, Lennox B., Praseedom A.,Linnington H. and Fletcher P.C. (2010): Memory encoding and dopamine in the aging brain: A psychopharmacological neuroimaging study. Cerebral Cortex; 20(3):743-757. Neuroimaging study. Cerebral Cortex; 20(3):743-757.
21. Mosad S. M., El- Sayed H.M, El-Kannishy A.M, Ghanem A.A, El-Biomy A.A, and Al –Diasty A.M.(2007): Lens cadmium, lead and serum vitamin c, e & b-carotene in cataractous smoking patients. Mansoura J. Forensic Med. Clin. Toxicol. Vol. XV, No. 1, Jan. 2007.
22. Murray C. and Lynch M.A. (1998a): Analysis of the mechanism by which dietary supplementation with vitamin E and vitamin C restores ability of aged animals to sustain long-term potentiation in dentate gyrus. J BiolChem 273:12161–12168.
23. Murray C. and Lynch M.A. (1998b): Evidence that increased hippocampal expression of the cytokine, IL-1b, is a common trigger for age- and stress-induced impairments in long-term potentiation. J Neurosci 18:2974 –2981.
24. Oz, H.S., C.J. McClain, H.T. Nagasawa, M.B. Ray, W.J. deVilliers and Chen T(2004): Diverse antioxidants protect against acetaminophen hepatotoxicity. J. Biochem. Mol. Toxicol., 18(6): 361-368.
25. Radak Z., Toldy A., Szabo Z., Siamilis S., Nyakas C., Silye G., Jakus J. and Goto,S. (2006): The effects of training and detraining on memory, neurotrophins and oxidative stress markers in rat brain.Neurochemistry International 49 (2006) 387–392.
26. Saab B.J, Georgiou J., Nath A, Lee F.J.S., Wang M., Michalon A., Liu F., Mansuy I.M. and Roder J.C.(2009): NCS-1 in the dentate gyrus promotes exploration, synaptic plasticity and rapid acquisition of spatial memory. Neuron; 63(5):643-656.
27. Seroogy K.B, Seress L. and Ribak C.E. (1983): Ultrastructure of commissural neurons of the hilar region in the hippocampal dentate gyrus. Exp.Neurol. Dec;82(3):594-608.
28. Shetty A.K and Turner D.A. (1999): Aging impairs axonal sprouting response of dentate granule cells following target loss and partial deafferentation. J Comp Neurol 414:238 –254.
29. Small S.A., Chawla M.K., Buonocore M., Rapp P.R. and Barnes C.A. (2004): Imaging correlates of brain function in monkeys and rats isolates a hippocampal subregion differentially vulnerable to aging. Proc. Natl. Acad. Sci. U.S.A. May 4; 101(18):7181-7186. Coated by Pereira AC, Huddleston DE, Brickman AM, Sosunov AA, Hen R, McKhann GM, Sloan R, Gage FH, Brown TR and Small SA. (2007): An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. Proc. Nat. Acad.Sci. U.S.A.; 104 (13): 5638 -5643.
30. Sonali R., Asamanja C. and Shelley B. (2006). Arsenic—induced changes in optic tectalhistoachitecture and acetylcholinesterase-acetylcholine rofile in channapunctuatus amelioration by selenium. Comparative. Biochemistry and Physiology Part C: Toxicology & Pharmacology, 144 (1).
31. Sushma N.J, Priyanka S. and Jayantha K. R. (2011): Neuroprotective role of Melatonin against aluminum-induced oxidative stress in the hippocampus of mouse brain. Journal of Applied Pharmaceutical Science 01 (10); 2011: 126-133.
32. Tanapat P., Hastings N.B., Reeves A.J. and Gould E. (1999): Estrogen stimulates a transient increase in the number of new neurons in the dentate gyrus of the adult female rat. J.Neurosci. Jul 15;19(14):5792-5801.
33. Tanapat P., Hastings N.B., Rydel T.A., Galea L.A. and Gould E. (2001): Exposureto fox odor inhibits cell proliferation in the hippocampus of adult rats via an adrenal hormone-dependent mechanism. J Comp Neurol437:496–504.
34. Tashiro A., Makino H. and Gage F.H. (2007): Experience specific functional modification of the dentate gyrus through adult neurogenesis: A critical period during an immature stage. J.Neurosci.27 (12):3252-3259.
35. Von Arnim CA, Herbolsheimer F, Nikolaus T, Peter R, Biesalski HK, Ludolph AC, Riepe M, Nagel G.(2012): Dietary Antioxidants and Dementia in a Population-Based Case-Control Study among Older People in South Germany. J Alzheimers Dis. Jan 1;31(4):717-24.
36. Waston J.P., Jones D.E., James O.F, Cann P.A. and Bramble M.G. (1999): Oral antioxidant therepy for the treatment of primary biliary cirrhosis: a pilot study. J. GastroenterolHepatol., 14(10): 1034-1040.
37. Zhong Z. and Lemasters J.J. (2004): Role of free radicals in failure of fatty liver grafts caused by ethanol. Alcohol, 34(1): 49-58.

10/11/2012

Evaluation of C- reactive protein as a probable factor for cancer diagnosis

Safinaz Elshabrawy[1], Alyaa Farid[2], Mohamed El- Beddini[1], Ahmed Osman[2], Somaya El- Deeb[2]

Hematology Department, National Cancer Institute, Cairo University[1]
Zoology Department, Faculty of Science, Cairo University, Cairo, Egypt[2]
alyaafarid@yahoo.com

Abstract: C- reactive protein (CRP) is a definitive marker of inflammation produced and synthesized in the liver in response of interleukin-6 (IL-6). It was studied in 10 healthy individuals and 97 patients with different types of diseases including kidney failure (KF), cardiovascular disease (CVD), hepatocellular carcinoma (HCC), Non-Hodgkin lymphoma (NHL), lung cancer (L.C), colon and bladder carcinoma (C.C), ovary and cervix carcinoma (O.C) and breast cancer (B.C). Routine blood tests were assayed for the 107 studied cases such as some liver enzymes (aspartate aminotransferase (AST) and alanine aminotransferase (ALT)), some kidney function factors (urea and creatinine) and some tumor markers (alfafeto protein (AFP), carcinoembroyonic antigen (CEA), cancer antigens 19.9 (CA19.9), 15.3 (CA15.3) and 125 (CA125) pecific to the different studied types of cancers. This study examined the relationship between circulating levels of CRP and various parameters of blood analysis in addition to the level of various tumor markers. It was found that CRP is associated with both KF and CVD cases. The studied specific tumor markers were significantly high in HCC (AFP), NHL (CEA), L.C (CEA) and B.C (CA15.3) studied cases ($P<0.05$) but it showed no significance in the C.C (CA19.9) and O.C (CA125) studied cases. It was evident that CRP levels are closely related to CA19.9 and CA125 tumor markers in case of C.C and O.C, respectively.
[Safinaz Elshabrawy. **Evaluation of C- reactive protein as a probable factor for cancer diagnosis.** *Life Sci J* 2012;9(4):2796-2803] (ISSN:1097-8135). http://www.lifesciencesite.com. 411

Key words: C- reactive protein, acute phase proteins, inflammation, cancer, tumor markers.

1. Introduction

Cancer is one of the diseases which was found to be a major leading cause of death worldwide due to the late diagnosis of the disease. Hence, the early diagnosis of cancer plays a very important role in the management and the cure of the disease. The prognosis for many types of cancer is still poor for management and cure of the disease, so it has been of interest to find other parameters which could be more sensitive and could help in the early detection of cancer (Yasuda, 2006; Chang *et al.,* 2010).

C-reactive protein (CRP) is an acute phase protein synthesized by hepatocytes in the liver in response to interleukin-6 (IL-6) cytokine induction according to inflammatory process as a result of a host immune response. Although CRP is a nonspecific inflammatory marker associated with inflammatory diseases, it was flashed on to be an important marker for the early detection of abnormal conditions causing inflammatory action including, cancer, autoimmune diseases such as systemic lupus erythromatosus (SLE) (Szalai, 2004), kidney failure (KF) (Fox *et al.,* 2010; Hung *et al.,* 2011) and cardiovascular diseases (CVD) (Khreiss*et al.,* 2005).

Many common cancers develop as a consequence of years of chronic inflammation (Moss and Blaser, 2005). Chronic activation of the immune system by parasitic, viral and bacterial infections is associated with tumours at several sites (Il'yasova *et al.,* 2005), on the other hand, noninfectious chronic inflammation is also associated with several types of cancer (Hussain *et al.,* 2003).

The first findings of the association of the elevated levels of CRP with advanced cancer diseases were reported in 1985 (Zielinski *et al.,* 1985). CRP levels were investigated to might be a future prognostic biomarker in different malignancies such as Hodgkin lymphoma (Wieland *et al.,* 2003), colorectal cancer (Mazhar and Ngan, 2006) and ovarian cancer (McSorley *et al.,* 2007).

The aim of the present study is to investigate the role of the CRP as a probable factor for the early detection and diagnosis of some different types of cancer introducing another sensitive parameter for the early diagnosis of cancer that could help in the disease management and cure.

2. Material and Methods

1. The studied cases:

The total number of all studied cases was 107 individuals. The number per case was determined according to the availability. The individuals were chosen from National Cancer Institute (NCI) and Nasser Institute for research and treatment Hospital (NIH). A complete clinical history for each individual (age, sex and pathological examination) was obtained from the statistical department in NCI and NIH. According to the clinical history of each individual, the studied cases (males and females) were classified according to the clinical, pathological and radiological findings as follows (Table 1): Ten healthy individuals from both

sexes reported as free form any disease, 15 individuals were diagnosed as suffering from kidney failure (KF) disease, 9 individuals were diagnosed as having cardiovascular disease (CVD), 21 individuals having hepatocellular carcinoma (HCC), 9 individuals with lung cancer (L.C), 9 individuals with Non-Hodgkin lymphoma (NHL), 9 individuals with colon and/or urinary bladder cancer (C.C), 12 individuals (females) with breast cancer (B.C) and 13 individuals (females) with ovary and/or cervix cancer (O.C).

Table 1: Number of studied cases according to their clinical, pathological and radiological findings.

Studied cases	No. of individual
Healthy individuals (HI)	10
Kidney failure (KF) cases	15
Cardiovascular disease (CVD) cases	9
Hepatocellular carcinoma (HCC) cases	21
Lung cancer (L.C) cases	9
Non-Hodgkin lymphoma (NHL) cases	9
Colon and bladder cancer (C.C) cases	9
Breast cancer (B.C) cases	12
Ovary and cervix cancer (O.C) cases	13

2. Sample collection:

Venous blood samples were withdrawn in plain vacutainer tubes, two tubes of about 5 ml for each individual. Blood tubes were allowed to stand for 30 minutes (min) in water bath to clot then centrifuged at 3000 rpm for 5 min. The sera were collected and stored at -20 ^{O}C until use.

3. Parameters assessed:

3.1. C- reactive protein (CRP) assay:

CRP was measured according to nephlometric methods of analysis involving the reaction of CRP with the antibody bound to latex particle forming insoluble complexes (Okamura *et al.,* 1990; Ward *et al.,* 1999). The measurement of CRP was done using Minineph^{TM} Human C- reactive protein kit (The binding sit group Ltd, Birmingham, UK).

3.2. Assay of liver enzymes (aspartate aminotransferase (AST), alanine aminotransferase (ALT)):

AST and ALT were measured by kinetic method according to the International Federation of Clinical Chemistry (IFCC) (Bergmeyer *et al.,* 1986).

3.3. Assay of urea:

Urea was measured by urease-UV fixed rate (enzymatic method) (Tiffany *et al.,* 1972; Tietz, 1990).

3.4. Assay of creatinine:

Creatinine was measured by buffered kinetic Jaffé reaction without depolarization method (Bowers and Wong, 1980).

3.5. Assay of Lactate dehydrogenase (LDH):

LDH was measured by optimized test according to German Society of Clinical Chemistry (DGKC) (Recommendation of the German society of clinical chemistry, 1972).

3.6. Assay of creatine kinase (CK).

Creatine phosphokinase was measured by optimized UV- test according to IFCC and German Society of Clinical chemistry (DGKC) (Schumann *et al.,* 2002; Recommendations of the German society for clinical chemistry, 1977).

AST, ALT, urea, creatinine, LDH and CK were programmed to the automated Bechman system (Bechmansynchron CX®9 clinical system (Marca REG, USA)) according to the application sheets provided with the kits (Diasys diagnostic systems kits (GmbH, Germany)).

3.7. Assay for tumor markers:

Measured tumor markers:

Carcinoembryonic antigen (CEA): A follow up marker for various carcinomas (Lokich *et al.,* 1978; Khoo *et al.,* 1979).

Alfa-fetoprotein (AFP): A marker for HCC (Waldmann and Mclntire, 1974).

Cancer antigen 19.9 (CA 19.9): A colorectal, pancreatic and gastrointestinal tumor marker (Herlyn *et al.,* 1982).

Cancer antigen 15.3 (CA 15.3): Breast tumor marker (Gion *et al.,* 1991).

Cancer antigen 125 (CA 125): Ovarian tumor marker (Crombach *et al.,* 1985).

Tumor markers measurement is based on the Microparticle Enzyme Immunoassay (MEIA) technology (Gold and Freedman, 1964; US Department of Health and Human Services, 2007). Tumor markers kit (Abbott Diagnostics division kits (Finisklin business park, Sligo, Ireland)) was defined on the AxSYM automated analyzer system (Abbott AxSYM © system automated immunoassay analyzer (Abbott laboratories diagnostics division, Abbott park, IL6, Germany)) by the bar code specialized for the kit. Reaction vessels and matrix cells were loaded to the automated system preparing for the run.

4. Statistical analysis:

Collected data was analyzed by ANOVA test (analysis of variance test) using the statistical analysis systems (SAS) (2010) SAS program ver.9.1, SAS institute incorporation, cary, NC25713USA. The mean, frequency and standard error of the measured variables were calculated using the F-test and the data represented as mean±standard error with 95% confidence intervals. The significance of the studied parameters CRP, AST, ALT, urea and creatinine are reported as $P < 0.05$ referred as significant, $P< 0.01$ referred as highly significant and $P < 0.001$ referred as extremely significant. The relation between different tumor markers and the studied parameter CRP was measured using Pearson correlation coefficient for calculation the correlation coefficient factor r.

3. Results

Comparison of the mean level of each parameter assayed in all studied cases:

1. C- reactive protein (CRP):

The mean concentration level of the parameter of interest, the CRP, showed a high significant increase in all studied cases when compared with the HI cases but the highest mean concentration level of CRP was shown for patients with O.C (143.51 ± 41.2) followed by patients with CVD (128.75 ± 21.83), and the increased mean concentration level of CRP was shown to be associated with all cancer cases studied (HCC: 20.23 ± 4.73, L.C: 61.08 ± 19.59, NHL: 31.45 ±14.30, C.C: 29.14 ± 8.32, B.C: 15.02 ±4.34 and O.C: 143.51 ±41.2) which were significantly higher than those of the HI cases (Table 2).

2. Aspartate amino transferase

The mean level of the liver enzyme AST was shown to be significantly higher in patients with CVD (205.8 ± 69.03 U/l) and patients with HCC (57.53 ± 7.89 U/l), while it showed no significant difference in the other studied cases when compared with the HI cases. This indicates an association of the increased level of the AST with CVD and HCC diseases rather than the other studied diseases (KF, L.C, NHL, C.C, B.C and O.C) which showed no significant difference of the AST (Table 2).

3. Alanine amino transferase

The mean concentration level of ALT was shown to be significantly associated with patients with CVD syndromes (84.33 ± 36.99 U/l) and no significant association with the other studied cases (Table 2).

4. Urea and creatinine.

The kidney function parameters were assayed, the urea mean levels (132.80 ±9.67 and 109.22 ±16.19 mg/dl respectively) were shown to be associated with only the KF cases and CVD cases while these two parameters showed no significant association with the other studied diseases (HCC, L.C, NHL, C.C, B.C and O.C). Creatinine mean levels were also shown to be associated with KF and CVD patients but not associated with the other studied cases (HCC, L.C, NHL, C.C, B.C and O.C) (Table 2).

Table 2: Comparison of the mean level of each parameter in all studied cases.

Parameter	Cases studied								
	HI	KF	CVD	HCC	L.C	NHL	C.C	B.C	O.C
CRP (mg/L)	1.77 ±0.27	52.14 ±10.31***	128.74 ±21.83***	20.23 ±4.73**	61.08 ±19.59**	31.45 ±14.30*	29.14 ±8.32**	15.02 ±4.34*	143.51 ±41.20**
AST (U/l)	29.20 ±2.77	28.87 ±2.51	205.83 ±69.03**	57.52* ±7.89	27.44 ±2.52	29.77 ±1.99	28.66 ±3.07	29.41 ±3.42	34.67 ±5.44
ALT (U/l)	22.20 ±3.72	22.46 ±2.22	84.33* ±36.69	46.94 ±8.55	22.44 ±2.35	21.88 ±1.18	20.75 ±1.75	23.67 ±3.64	29.58 ±7.41
Urea (mg/dl)	31.60 ±3.16	132.80*** ±9.67	109.22*** ±16.19	34.04 ±2.36	28.66 ±4.01	34.33 ±2.68	33.44 ±4.02	27.33 ±2.54	40.00 ±9.93
Creatinine (mg/dl)	0.76 ±0.04	4.90*** ±0.63	3.03* ±0.85	0.89 ±0.04	0.84 ±0.07	0.76 ±0.04	0.81 ±0.04	0.71 ±0.04	1.13 ±0.25

CRP: C-reactive protein.
KF: kidney failure.
NHL:Non-Hodgkin lymphoma.
AST: Aspartate aminotransferase.
CVD: Cardiovascular disease.
C.C: Colon and bladder cancer.
ALT: Alanine aminotransferase.
HCC: Hepatocellular carcinoma.
B.C: Breast cancer.
HI: Healthy individuals.
L.C: Lung cancer.
O.C: Ovary and cervix cancer.
Significant: *P<0.05.
Highly significant: **P<0.01.
Extremly significant: ***P<0.001
Data are represented as mean ±standard error.

Relation between levels of C-reactive protein and various tumor markers:

The level of CRP for each case was compared with the levels of the different tumor markers in the different studied cases.

1. Hepatocellular carcinoma cases:

In the HCC cases (N=11), the CRP levels were shown not to be associated with the AFP tumor marker levels but it may be associated with the malignancy. The correlation coefficient value "r" studying the relation between the CRP and the AFP (r=-0.34) showed a weak reverse relationship between the levels of CRP and levels of AFP in patients with HCC (Fig. 1).

2. Lung cancer cases:

The increased CRP levels were also not associated with the levels of the tumor marker CEA which was shown to be within the normal range (up to 3.5 ng/ml) for patients (N=7) with L.C. So there was a weak reverse relationship between the CRP and the CEA (r= -0.48) in patients with L.C (Fig. 2).

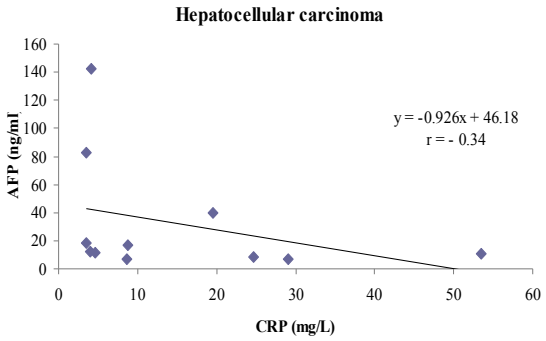


Figure1: The reverse relationship between C-reactive protein and alpha feto protein (AFP) tumor marker in patients with hepatocellular carcinoma.

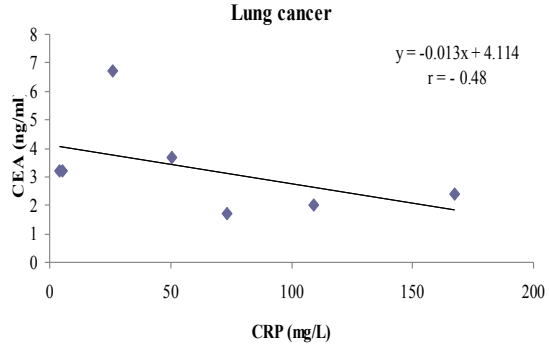


Figure 2: The reverse relationship between C-reactive protein and carcinoembroyinc antigen in patients with lung cancer.

4.3. Non-Hodgkin lymphoma cases:

The weak reverse relationship between the increased levels of CRP and CEA (r= -0.6) was revealed in NHL cases (N=7) (Fig. 3) where no association has been found between the CRP and CEA levels for the individuals studied in this case.

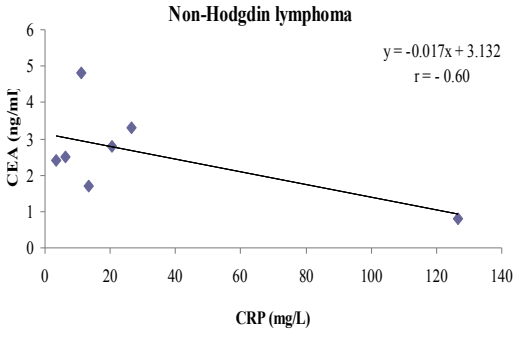


Figure 3: The reverse relationship between C-reactive protein and carcinoembryonic antigen in patients with non-Hodgkin lymphoma.

4.4. Colon and bladder cancer cases:

An association may have appeared between levels of CRP and CA19.9 tumor marker for the C.C cases (N=6). This association was supported by the strong proportional relationship revealed by the correlation coefficient factor r= 0.77 (Fig. 4).

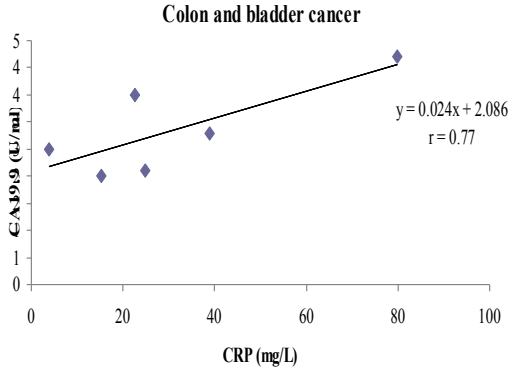


Figure 4: The proportional relationship between C-reactive protein (CRP) and cancer antigen 19.9 in patients with colon and bladder cancer.

4.5. Breast cancer cases:

In B.C cases (N=10), the CRP levels were also not related to the CA15.3 levels showing no association between the CRP and the tumor marker but there may be an association between the CRP and the breast malignancy. The studied correlation coefficient factor of the CRP and CA15.3 (r= -0.55) showed a weak reverse relationship between CRP and tumor marker CA15.3 levels (Fig.5).

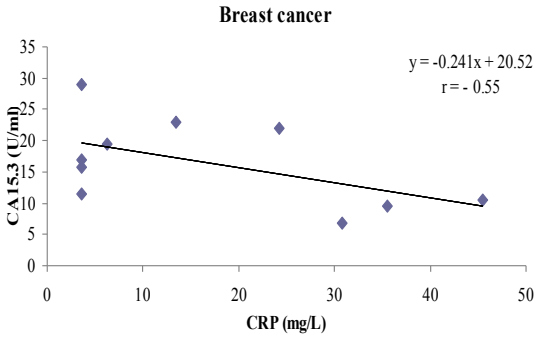


Figure 5: The reverse relationship between C-reactive protein and cancer antigen 15.3 in patients with breast cancer.

4.6. Ovary and cervix cases:

A proportional relationship has also been found between the CRP and CA125 levels for patients with O.C (N=9) (r= 0.48) but it is a weak relationship (Fig.

6), this is because the CRP levels were not associated with the levels of the CA125 demonstrating another evidence of non-association between the CRP levels and the level of the tumormarker but it may be associated with malignancy.

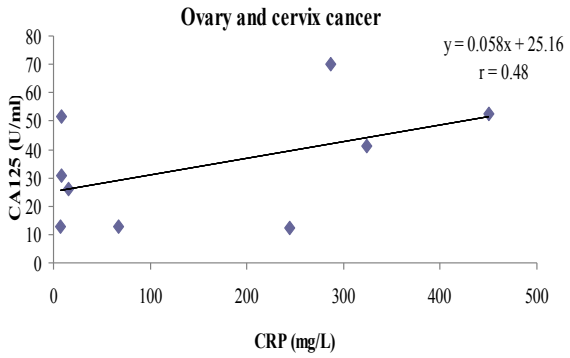


Figure 6: The proportional relationship between C-reactive protein and cancer antigen 125 in patients with ovary and cervix cancer.

4. Discussion:

Many of the common cancers are preceded by years of chronic inflammation. Tumor progression is always followed by development of acute phase protein response, that is chronic malignant disease involve changes in protein metabolism which result in production of acute phase proteins as a kind of immune response such as the production of CRP (Weinstein *et al.,* 1984; Stamatiadis *et al.,* 1992; Chung and Chang, 2003).

CRP is not only a marker of inflammation, it was also shown as a marker of activation of the immune system (Nauta *et al.,* 2003; Manfredi *et al.,* 2008).

Elevated levels of CRP were shown to be a predictive factor for different inflammatory diseases and infections and a predictive factor for increased risk of coronary events (Hage and Szalai, 2007), SLE (Szalai, 2004) and cancer risk (Allin *et al.,* 2009; Williams and Muddiman 2009) .

In the present study, there was a significant increase of CRP (P<0.0001) in patients with KF and this is in agreement with the study of Abraham and his colleagues, as they studied the levels of high sensitivity C-reactive protein (HsCRP) in Indian patients with CKD. They reported that the high HsCRP levels in Indian CKD patients indicate the high prevalence of inflammation in non-dialysis patients (Abraham *et al.,* 2009). The increased levels of CRP in the present study for the KF patients were also in accordance with the elevated concentrations of CRP in a heterogeneous population studied by Lobo and others, who stated that the elevated concentrations of serum CRP on ICU admission are correlated with an increased risk of organ failure and death (Lobo *et al.,* 2003).

The CRP levels in patients with CVD, during this study showed a significant increase (P<0.0001) and this was in agreement with Galante and others since, they found that CRP levels were higher in patients with aortic valvular stenosis than in controls (p = 0.0001) (Galante *et al.,* 2001).

Levels of AST, ALT, urea and creatinine in the present study also showed significant increase (P=0.0045, 0.0439, 0.0001 and 0.021, respectively) in CVD patients. The significant association of urea in CVD patient in this study was in accordance with Ostfeld and his coworkers who stated that elevated serum blood urea nitrogen (BUN) on admission was associated with an increased burden of coronary artery disease (CAD) on cardiac characterization during index hospitalization in patients who are presented with symptoms of unstable angina and without known cardiovascular disease suggesting that an elevated serum BUN in these subjects may predict a larger burden of CAD on cardiac characterization independent of creatinine clearance (Ostfeld *et al.,* 2010). Further study is warranted to explore this association. In addition in earlier studies it was documented that CRP is a strong, independent predictor of future myocardial infarction and stroke among apparently healthy asymptomatic men (Ridker *et al.,* 1997; 1998).

On the other hand elevated levels of CRP showed no association with the AFP during the study of the correlation between the CRP and AFP and this was demonstrated by the weak reverse correlation coefficient factor resulting from that correlation study (r=-0.34). This finding is in agreement with that of Lee and others since they found that the CRP levels correlated poorly with their corresponding AFP levels (r=0.0513). Although it was shown that CRP and AFP are not correlated, these markers seem to complement each other as out of 104 patients with HCC, CRP and AFP detected 78% and 80%, respectively (Lee *et al.,* 1989).

While AST was shown to be associated with HCC as its level significantly increases (P=0.0172). ALT was not statistically significantly different (P=0.051) but can be associated with the hepatic malignancy. The significant difference of CRP levels in HCC shows significant association of the elevated levels of CRP with the HCC. Thus, the significance of the elevated levels of CRP in patients with HCC cannot be neglected but it points to a new factor which may play a role in the early detection and diagnosis of the disease.

The current study showed an association of CRP levels with LC patients. CRP levels were shown to be

significantly increased (P <0.01) in patient with LC. These results are in accordance to those shown by Chaturvedi and his colleagues, since they stated that elevated CRP levels are associated with subsequently increased LC risk, suggesting an etiologic role for chronic pulmonary inflammation in lung carcinogenesis (Chaturvedi *et al.,* 2010).

The levels of the tumor marker CEA and levels of CRP in patients with LC in this study were shown not to be correlated and not associated and this was proved by the weak reverse correlation (r value -0.48) that appeared during this study.

As CRP levels were shown to be significantly increased in patients with LC (P=0.0036) while the other measured routine blood tests AST(P=0.6484), ALT (P =0.9533), urea (P=0.5700) and creatinine (P=0.3591) showed no significant association. The significantly elevated levels of CRP in this work also agreed with different studies on LC cases (Trichopoulos *et al.,* 2006; Allin *et al.,* 2009).

The present study showed significantly increased levels of CRP levels in patients with NHL (P < 0.05). That significant increase was also shown by Yildirim, and his colleagues, during their study when they measured the levels of ferritin and CRP in patients with NHL before and after treatment and they found a significant decrease in levels of ferritin and CRP following treatment when compared to pre-treatment measurement concluding that serum ferritin and CRP parameters may be used as tumor markers and may be indicators in the efficacy evaluation of treatment in NHL (Yildirim, *et al.,* 2009).

The correlation coefficient factor r (r=-0.60) studied for the correlation between the CRP and CEA in patients with NHL showed strong reverse relationship giving evidence of the probability that CRP can be used as a predictive factor for the presence of NHL in the absence of the role of the tumor marker CEA. Such a correlation was not available in previous reports.

The blood levels of AST, ALT, urea and creatinine showed no significant association in patients with NHL in the current work. Such a correlation was also not available in previous reports.

A strong proportional relationship (r=0.77) was found during the study of the relation between the CRP and the CA19.9 with CC. This was concurring with a previous study (Wong *et al.,* 2007), as they reported that CRP was associated with larger metastases size and elevated CA 19.9 level exploring the important role of CRP in the evaluation, detection and follow up of colon and bladder cancer

On the other hand, routine blood tests in the present study didn't show any significant association (AST, ALT, urea and creatinine). Pitifully there is no relevant information in the literature in case of CC patients with high CRP levels.

The correlation coefficient factor studied for the relationship between CRP and CA15.3 in B.C cases showed to be poorly correlated (r=-0.55) proving that the CRP is not associated with the tumor marker but may be with the malignancy. Such a correlation was not available in previous reports.

The studied CRP levels in patients with OC in the present study were shown to be significantly higher than that in HI cases. These results concur with the documented results of McSorley and others, who stated that ovarian cancer risk was positively associated with increasing CRP concentrations. They also proved that the risk of developing ovarian cancer among women in the highest third of the distribution of CRP compared with those in the lowest third produced evidence of and increasing risk with increasing concentration of CRP (McSorley *et al.,* 2007).

This present study showed weak proportional correlation between the CRP and CA125 (r=0.48) this is in correspondence with McSorley and others study who showed no correlation between CRP and CA125 (r=-0.02) (McSorley *et al.,* 2007) and Hefler's and coworkers study who found that serum CRP was not significantly correlated with serum CA 125 (r= 0.02) (Hefler *et al.,* 2008).

In conclusion, the present results suggest that (a) CRP levels are a more consistent indicator of cancer risk than some tumor markers, (b) the association between cancer incidence and CRP as an inflammatory marker may be tumor type specific (c) increased level of CRP may show a stronger association with risk of cancer incidence, recurrence, and death.

Corresponding author
Safinaz Elshabraw
Hematology Department, National Cancer Institute, Cairo University[1]
alyaafarid@yahoo.com

References

1. Abraham G, Sundaram V, Sundaram V, Mathew M, Leslie N and Sathiah V (2009): C-Reactive protein, a valuable predictable marker in chronic kidney disease. *Saudi J Kidney Dis Transpl;* 20(5):811-815.
2. Allin KH, Bojesen SE and Nordestgaard BG (2009): Baseline C-reactive protein is associated with incident cancer and survival in patients with cancer. *J Clin Oncol;* 27: 2217-2224.
3. Bergmeyer HU, Horder M and Rej R (1986): Approved recommendation (1985) on IFCC methods for the measurement of catalytic concentration of enzymes part 3. IFCC method for alanine

aminotransferase (L-alanine; 2-oxoglutarate aminotransferase, EC 2.6.1.2). *J Clin Chem Clin Biochem;* 24:481-495.
4. Bowers LD and Wong ET (1980): Kinetic serum creatinine assays. II. A critical evaluation and review. *Clin Chem;* 26:555-61.
5. Chang C, Sun1 C, Pai H, Wang W, Hsieh C, Kuo L and Wang C (2010): Preoperative serum C-reactive protein and gastric cancer; clinical-pathological correlation and prognostic significance. *Chang Gung Med J;* 33:301-12.
6. Chaturvedi AK, Caporaso NE, Katki HA, Wong H, Chatterjee N, Pine NR, Chanock SJ, Goedert JJ and Engels EA (2010): C-Reactive protein and risk of lung cancer. *J Clin Oncol;* 28:2719-2726
7. Chung YC and Chang YF (2003): Serum C-reactive protein correlates with survival in colorectal cancer patients but is not an independent prognostic indicator. *Eur J Gastroenterol Hepatol;* 15(4):369-73.
8. Crombach G, Zippel HH and Wrz H (1985): Clinical significance of cancer antigen 125 (CA 125) in ovarian cancer. *Cancer Detect Prev;* 8:135.
9. Fox ER, Benjamin EJ, Sarpong DF, Nagarajarao H, Taylor JK, Steffes MW, Salahudeen AK, Flessner MF, Akylbekova EL, Fox CS, Garrison RJ and Taylor HA (2010): The relation of C- reactive protein to chronic kidney disease in African Americans: the Jakson Heart study. *BMC Nephrology;* 11: 1-7.
10. Galante A, Pietroiusti A, Vellini M, Piccolo P, Possati G, De Bonis M, Grillo RL, Fontana C and Favalli C (2001): C-reactive protein is increased in patients with degenerative aortic valvular stenosis. *J Am Coll Cardiol;* 38:1078-82.
11. Gion M, Mione R and Nascimbe O (1991): The tumor associated antigen CA 15.3 in primary breast cancer. Evaluation of 667 cases. *Br J Cancer;* 63:809-813.
12. Gold P and Freedman SO (1964): Demonstration of /tumor-specific antigens in human Colonic Carcinomata by immunological Tolerance and absorption techniques. *J Exp Med;* 121:439.
13. Hage FG and Szalai AJ (2007): C-reactive protein gene polymorphisms, C-reactive protein blood levels, and cardiovascular disease risk. *J Am Coll Cardiol;* 50:1115-22.
14. Hefler LA, Concin N, Hofstetter G, Marth C, Mustea A, Sehouli J, Zeillinger R, Leipold H, Lass H, Grimm C, Tempfer CB and Reinthaller A (2008): Serum C - reactive protein as independent prognostic variable in patients with ovarian cancer. *Clin Cancer Res;* 14:710-714.
15. Herlyn M, Sears HF, Steplewski Z and Koprowski H (1982): Monoclonal antibody detection of a circulating tumor associated antigen. I. Presence of antigen in sera of patients with colorectal, gastric and pancreatic carcinoma. *J Clin Immunol;* 2:135-40.
16. Hung AM, Ikizler TA, Griffin MR, Glenn K, Greevy RA, Grijalva CG, Siew ED and CrawfordDC (2011): CRP polymorphisms and chronic kidney disease in the third national health and nutrition examination survey. *BMC Med Genet;* 12: 65.
17. Hussain SP, Hofseth LJ and Harris CC (2003): Radical causes of cancer. *Nat Rev Cancer;* 3: 276–85.
18. Il'yasova D, Colbert LH, Harris TB, Newman AB, Bauer DC, Satterfield S and Kritchevsky SB (2005): Circulation levels of inflammatory markers and cancer risk in the health aging and body composition Cohort. *Cancer Epidemiol Biomarkers Prev;* 14(10): 2413-8.
19. Khoo SK, Whitaker S, Jones J and Mackay W (1979): Predictive value of serial carcinoembryonic antigen levels in long-term follow-up of ovarian cancer. *Cancer;* 43:2471.
20. Khreiss T, Jozsef L, Potempa LA and Filep JG (2005): Loss of pentameric symmetry in C - reactive protein induces interleukin-8 secretion through peroxynitrite signaling in human neutrophils. *Circ Res;* 97:690-697.
21. Lee F, Lee S, Tsai Y, Wu J, Lai K, and Lo K (1989): Serum C - reactive protein as a serum marker for the diagnosis of hepatocellular Carcinoma. *Cancer;* 63: 1567-1571.
22. Lobo SM, Lobo FR, Bota DP, Lopes-Ferreira F, Soliman HM, Mélot C and Vincent J (2003): C-Reactive protein levels correlate with mortality and organ failure in critically ill patients. *Chest;* 123: 2043-2049.
23. Lokich JJ, Zamcheck N and Lowenstein M (1978): Sequential carcinoembryonic antigen levels in the therapy of metastatic breast cancer. *Ann Intern Med;* 39:902.
24. Manfredi AA, Rovere-Querini P, Bottazzi B, Garlanda C and Mantovani A (2008): Pentraxins, humoral innate immunity and tissue injury. *Curr Opinion in Immunol;* 20: 538-544.
25. Mazhar D and Ngan S (2006): C-reactive protein and colorectal cancer. *Q J Med;* 99:555–559.
26. McSorley MA, Alberg AJ, Allen DS, Allen NE, Brinton LA, Dorgan JF, Pollak M, Tao Y and Helzlsouer KJ (2007): C-reactive protein concentrations and subsequent ovarian cancer risk. *Obstet Gynecol;* 109(4):933-41.
27. Moss DW and HendersonAR (1999): Clinical enzymology in: Tietz textbook of clinical chemistry. 3rd ed. BurtisCA and Ashwood ER, editors.Philadelphia: W.B Saunders Company; 617-621.
28. Nauta AJ, Daha MR, Van Kooten C and Roos A (2003): Reconition and clearance of apoptotic cells: A role for complement and pentraxins. *Trens Immunol;* 24: 148- 154.

29. Okamura JM, Miyagi JM, Terada K and Hokama Y (1990): Potential clinical applications of C-reactive protein. *J Clin Lab-Analysis;* 4: 231-235.
30. Ostfeld R, Spinelli M, Mookherjee D, Holtzman D, Shoyeb A, Schaefer M, Kawano T, Doddamani S, Spevack D, Duc Y (2010): The association of blood urea nitrogen levels and coronary artery disease. *EJBM;* 3-7.
31. Recommendations of the German society for clinical chemistry (1977): Standardization of methods for the estimation of enzyme activities in biological fluids: standard method for the determination of creatinekinase acitivty. *J Clin Chem Clin Biochem;* 15:255-60.
32. Ridker PM, Cushman M, Stampfer MJ, Tracy RP and Hennekens CH (1997): Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. *N Engl J Med;* 336: 973–9.
33. Ridker PM, Glynn RJ and Hennekens CH (1998): C-reactive protein adds to the predictive value of total and HDL cholesterol in determining risk of first myocardial infarction. *Circulation;* 97:2007–11.
34. Schumann G, Bonora R, Ceriotte F and Férard G (2002): IFCC primary reference procedure for the measurement of catalytic activity concentrations of enzymes at 37 ˚C. Part 5: Reference procedure for catalytic concentration of creatine kinase. *Clin Chem Lab Med;* 40:635-42.
35. Stamatiodis AP, Manouras AJ, Triantos GN, Katergiannakis VA and Apostolidis NS (1992): Combination of serum carcinoembryonicanigen and C-reactive protein a useful test in preoperative staging of colorectal cancer. *Eur J Surg Oncol;* 18:41-3.
36. Szalai AJ (2004): C- reactive protein (CRP) and autoimmune disease: Facts and conjectures. *Clin Dev Immunol;* 11: 221-226.
37. Tietz NW, Ed (1990): Clinical guide to laboratory tests. 2nd ed, P566. Philadelphia: WB Saunders.
38. Tiffay TO, Jansen JM, Burtis CA, Overtion JB and SCOTT CD (1972): Enzymatic kinetic rate and end point analysis of substrate, by use of a GeMSAEC fast analyzer. *Clin Chem;* 18:829-840.
39. Trichopoulos D, Psaltopoulou T, Orfanos P, Trichopoulou A and Boffetta P (2006): Plasma C-reactive protein and risk of cancer: A prospective study from Greece. *Cancer Epidemiol Biomarkers Prev;* 15(2): 381-4.
40. US department of health and human services (2007): Biosafety in microbiological and biomedical laboratories, 5th ed. Washington, DC: US Government printing office.
41. Waldmann TA and Mclntire KR (1974): The use of a radioimmunoassay for Alpha-fetoprotein in the diagnosis of malignancy. *Cancer;* 34:1510-5.
42. Ward AM, Riches PG, Fifield R and Smith AM (1999): SAS Protein reference Units: Handbook of Clinical Immunochemistry, 6th ed, pp 109-111. A Milford Ward Publ. PRU Publications, Sheffield, UK NEQAS for Immunology and Immunochemistry.
43. Weinstein PS, Skinner M and Sipe JD (1984): Acute phase proteins or tumor markers: The role of SAA, CRP and CEA as indicators of metastasis in a broad spectrum of neoplastic disease. *Scand J Immunol;* 19: 193-19.
44. Wieland A, Kerbl R, Berghold A, Schwinger W, Mann G, and Urban C (2003): C - reactive protein (CRP) as tumor marker in pediatric and adolescent patients with hodgkin disease. *Med Pediatr Oncol;* 41:21–25.
45. Williams DK and Muddiman C (2009): Absolute quantification of C- Reactive protein in human plasma derived from patients with epithelial ovarian cancer utilizing protein cleavage Isotope dilution mass spectrometry. *J. Proteome Res;* 8(2):1085-1090.
46. Wong VK, Malik HZ, Hamady ZZ, Al-Mukhtar A, Gomez D, Prasad KR, Toogood GJ and Lodge JP (2007): C-reactive protein as a predictor of prognosis following curativeresection for colorectal liver metastases. *British Journal of Cancer;* 96: 222–225.
47. Yasuda K (2006): Early gastric cancer: Diagnosis, treatment techniques and outcomes. *Eur J Gastro enterol Hepatol;* 18:839–845.
48. Yildirim R, Gundogdu M, Erdem F, Kiki I and Bilici M (2009): The levels of serum C- Reactive protein, beta 2 microglobulin, ferritin, lactate dehydrogenase and some specific proteins in patients with non-Hodgkin's lymphoma before and after treatment. *EAJM;* 41:165-168.
49. Zielinski CC, Preis P, Aiginger P and Eibl MM (1985): Acute-phase-proteins and parameters of humoral immunity in patients with advanced Hodgkin's disease. *J Cancer Res Clin Oncol;* 110: 65–70.

10/10/2012

Autogenous Transplantation of Maxillary And Mandibular Molars

Maha Negm[1], Sameh Seif[2], Khaled El Hayes[3], Galal Beheiri [4]

[1] Demonstrator at Oral & Maxillofacial Surgery department, Faculty of Oral & Dental medicine, Cairo University.
[2] Lecturer at Oral & Maxillofacial Surgery department, Faculty of Oral & Dental membranemedicine, Cairo University.
[3] Professor at Oral & Maxillofacial Surgery department, Faculty of Oral & Dental medicine, Cairo University.
[4] Professor at Oral & Maxillofacial Surgery department, Faculty of Oral & Dental medicine, Cairo University.
Corresponding Author: maha-negm7@hotmail.com

Abstract: ***Objectives:*** To evaluate the validity and reliability of the autogenous transplantation of maxillary or mandibular molars. ***Methods:*** Ten patients received either a mandibular or maxillary third molar to replace a non restorable mandibular first or second molar. The clinical parameters were mobility and probing pocket depth. Radiographic assessment of progress of root development, periapical or periodontal radiolucencies, root resorption and ankylosis, was done by using digital panoramic radiographs with1:1 magnification correction. All clinical parameters and panoramic radiographs were taken at 2, 4, 6 and 9 months postoperatively. ***Results:*** The pocket depth readings and teeth mobility showed statistical significant decrease throughout the study. Regarding the radiographic results, no root resorption or ankylosis and 80% of patients had root development with no observed radiolucencies. ***Conclusion:*** The transplantation of developing molars in growing adults is a viable and reliable treatment option.
[Maha Negm, Sameh Seif, Khaled El Hayes, Galal Beheiri. **Autogenous Transplantation of Maxillary And Mandibular Molars.** *Life Sci J* 2012;9(4):2804-2812] (ISSN:1097-8135). http://www.lifesciencesite.com. 412

Keywords: autogenous transplantation, third molars, immature root.

1.INTRODUCTION

A significant number of patients have premature loss of their first and second molars because of dental caries and/or dental crowding. As a result; ridge resorption, malfunction, over eruption of opposing tooth, loss of space, temporomandibular disorder, etc..... may occur ***(Reich 2008)***. Removable partial denture and fixed partial denture are the options to solve these problems but they have their own disadvantages and limitations ***(Reich 2008)***. In planning the treatment for such cases, clinicians should make patients aware of other alternatives, including dental implants and transplantation of teeth ***(Cohen et al.,(1995)***. Auto-transplantation is a viable option for replacing a missing tooth when a donor tooth is available ***(Thomas et al., (1998);Lee et al.,(2001); Kim et al.,(2005); Teixeira et al.,(2006)***. Tooth auto-transplantation offers one of the fastest and most economically feasible means of replacing missing teeth ***(Cohen et al.,. 1995)***. While there are many reasons for auto-transplanting teeth, tooth loss as a result of dental caries is the most common indication, especially when mandibular first molars are involved. First molar erupt early and are often heavily restored. Auto-transplantation in this situation involves the removal of a third molar, which may then be transferred to the site of an unrestorable first molar ***(Clokie et al. ,(2001); Mejàre et al., (2004)***.

Teeth most commonly used for autotransplantation are premolars, canines, incisors (especially supplemental teeth) and third molars ***(Natiella et al., 1970)***. In theory, although any tooth may be transplanted, the donor tooth should be of limited value in the dentition, e.g. a premolar in a crowded arch, or a supplemental incisor ***(Thomas et al., 1998)***.

Zachrisson et al., (2004) found that after transplantation of partly formed rooted teeth, root growth continued, and the teeth maintained their capacity for functional adaptation. Endodontic treatment was usually not necessary. The optimal time for autotransplantation of premolars to maxillary anterior region was when the root development has reached two thirds to three fourths of the final root length. The prognosis for complete periodontal healing at this stage of root development was better than 90%. ***Reich et al., (2008)*** reported that after transplantation of 42 molar teeth with mean follow up 19 months transplants remained asymptomatic and functioning. No infection, ankylosis, loss of the transplant, or root resorption has been noted. In addition, endodontic therapy has not been necessary on any transplanted teeth. Auto-transplantation is a technique-sensitive procedure. A traumatic surgical technique preserves bone and periodontal support. Minimal handling of the transplant is required to protect the Hertwig's root sheath and pulpal tissue. A traumatic surgical removal of the third molar is essential, preserving the root sheath and apical

portion of the developing tooth bud. Adequate exposure and preparation of the recipient site are performed. Stabilization of the transplanted third molar is performed with suture material in a crossover fashion to prevent up-and-down movement of the transplant. Splinting with composite or wire banding isn't advised. Excessive time or rigid splinting of the transplanted tooth will adversely affect its healing ***(Tsurumachi & Kakehashi (2007); Reich(2008)***.The biological course of autotransplantated teeth is influenced by a number of preoperative, peroperative and postoperative conditions, which are recognized as prognostic factors. For example, age of the patient, developmental stage of the graft, the type of tooth transplanted, surgical trauma during graft removal and the extraoral storage of the transplanted tooth during surgery as concluded by ***Schwartz et al., (1985)***. The goal of this study is to highlight the evidence-based principles for successful autotransplantation; evaluating viability, reliability, lack of discomfort and complications, and stable occlusion of autogenous transplantation.

2.PATIENTS AND METHODS

2.1.Patients:

Ten female patients ranging from 16 to 20 years with a mean of 17.9 years were selected from the outpatient clinic of Oral and Maxillofacial Department, Faculty of Oral and Dental Medicine, Cairo University**.** Patients had non-restorable badly decayed lower first or second molar teeth requiring extraction and replacement with teeth (Figures 1 & 2).

2.2.Methods:

2.2.1.Operation:

**** Pre-operative assessment***

All patients fulfilled the following criteria:

- Non-restorable mandibular 1st or 2nd molar (Extracted tooth).
- Caries-free retrievable maxillary or mandibular 3rd molar (Auto-transplanted tooth).
- Recipient site having adequate bone support with sufficient alveolar bone support in all dimensions and adequate attached keratinized tissue (healthy periodontium).
- The sacrificed tooth was not lost due to terminal periodontal disease and/or acute inflammatory process.

**** Surgical procedure:***

Co-amoxiclav antibiotic prophylaxis was given preoperatively. After local anesthesia, non-surgical a traumatic extraction of the non restorable teeth were done using extraction forceps, or elevators in case of remaining roots. Adequate exposure and preparation of the recipient socket were performed with low-speed hand piece and surgical burs.

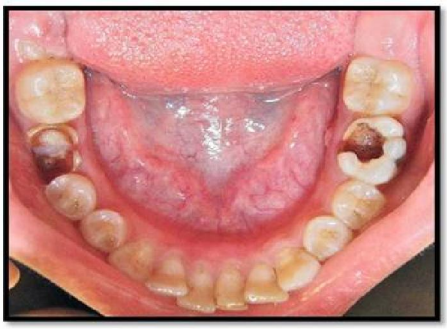


Figure 1: Preoperative photograph showing badly decayed non restorable lower left 1st molar.

Figure 2: Preoperative panoramic radiograph showing periapical & periodontal radiolucencies related to lower left 1st molar.

Copious irrigation with normal saline was used throughout the procedure. Trimming of the inter-radicular bone using bone rongeur was required to create a 4-wall surgically prepared bony socket. Additional removal of bone beyond the apex to ensure an apical cushion or tension-free zone where the root buds could be positioned without threat of compression. This apical preparation also allowed for the transplant to be positioned at/or slightly below the occlusal plane so as to avoid premature occlusal contacts. A traumatic extraction, avoiding disruption of the root sheath and root buds of the donor tooth. The auto-transplants were immediately transferred to the recipient site and seated in place with firm finger pressure. Care was taken to avoid any premature occlusal interference. The ideal position was considered to be 1 to 2 mm infra-occlusion allowing complete root development and eruption of the transplants. Stabilization of the transplants was achieved by 3/0 black silk **"Basket suture"**.

Postoperative antibiotic, analgesic and mouth wash were prescribed. Patients were strictly instructed not to masticate on the transplanted tooth. All patients were placed on a full liquid diet for 48 hours and then advanced to a pureed diet for 2 weeks. A soft diet was recommended for another 2 weeks.

Follow up visits:

Suture removal of donor and recipient sites were performed 2 weeks postoperatively. The patients were followed up for 2, 4, 6 and 9 months both clinically (Pocket depth and mobility) and radiographically (progress of root development, periapical or periodontal radiolucencies, root resorption and ankylosis).

2.2.2.10-mm Visual Analogue Scale questionnaire:

All patients examined at the last follow up visit (9 months) were asked to fill out a questionnaire that included six questions. Anamnestic perceptions of the transplantation procedure (two questions) and the present status of the transplanted tooth (four questions) were recorded on a 0 to 10-mm visual analogue scale (VAS). The patients indicated their opinion by marking a mark along the VAS; 0 was entirely positive and 10 was entirely negative.

2.2.3.Statistical Analysis:

Statistical analysis was performed using SPSS (Statistical package for social sciences) version 15, Echosoft corp., U.S.A. Unless otherwise specified, data were represented as mean ± standard deviation. Repeated measures analysis of variance (ANOVA) test was used to compare numeric variables within the studied group of patients. For categorical data, non-parametric ANOVA (Friedman's test) was performed to detect significant changes within the studied group of patients. Post Hoc test was done to identify the different group if ANOVA test was positive. In all tests, result was considered statistically significant if the *P*-value was less than 0.05.

3.RESULTS

3.1. Clinical assessment:

Clinical examination of teeth and soft tissues were performed on regular bases at 2, 4, 6 and 9 months' intervals. Tooth discoloration, premature contacts, occlusion, signs of infection and gingival color and contour were assessed during the examination. No positive findings were detected except for two patients (figures 5 to 8).

3.1.1.Pocket depth:

At 2 months, the minimum pocket depth was 3.50 mm and the maximum was 5 mm with mean of 4.25 mm. At 4 months, pocket depth started at 3.17 mm and ended at 4.67 mm with mean of 3.78 mm. On the other hand, a reduction was noticed at 6 months follow up visit ranging from 2.50 mm to 4.17 mm and mean of 3.25 mm. Further reduction at 9 months was detected with minimum of 2.17 mm, maximum of 4.17 mm and mean of 2.71 mm. ANOVA test showed statistical significant decrease ($P = 0.001$) in pocket depth throughout the follow up period (Figure 3).

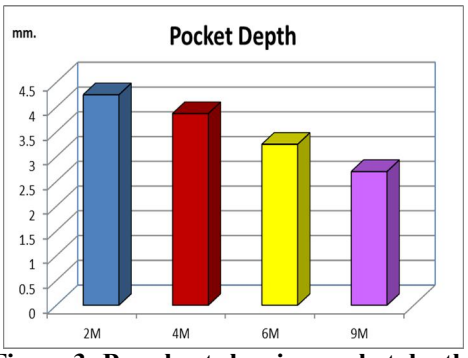


Figure 3: Bar chart showing pocket depths throughout the follow up period.

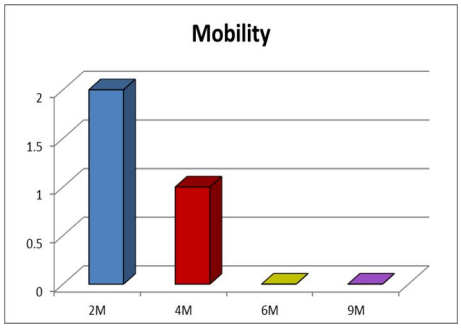


Figure 4: Bar chart showing mobility grades throughout the follow up period.

Figure 5: Two weeks follow up photographs of lower left 3rd molar transplant.

Figure 6: Nine months follow.

Figure 7: Two weeks follow up.

Figure 8: Nine months follow.

Since the ANOVA test was positive, Post Hoc test was done to determine the significant group of patients. In relation to 2nd month readings, the reduction at 4 months was not statistically significant $P = 0.274$ but at 6 and 9 months the reduction was significant $P = 0.002$ and 0.001 respectively. On the other hand, in comparison to 4th month readings, the decrease at 6 months was not statistically significant $P = 0.182$ but at 9 months the decrease was significant $P = 0.004$. Furthermore, 6 months readings compared to 9 months was not statistically significant $P = 0.286$.

3.1.2.Mobility:

Grade II mobility was noted at 2 months interval in all the studied cases. At 4 months, 90% of patients showed grade I, which was the minimum and the remaining 10% had grade II mobility that was the maximum with range and mode 1. On the other hand, a reduction was detected at 6 months follow up where 60% of the patients showed no mobility which was the minimum, 30 % had grade I and 10 % grade II that was the maximum with range 2 and mode 0. At 9 months, further improvement was noticed, 70% of the cases had grade 0 which was the minimum, 20% showed grade I and the remaining 10% were still grade II that was the maximum with range 2 and mode 0. Friedman test result showed statistical significant decrease ($P = .001$) in mobility throughout the follow up period (Figure 4).

Since the Friedman test was positive, Post Hoc test was done to determine the significant group of patients. There was a statistical significant change at 4 months, 6 months and 9 months compared to 2nd month grades($P = 0.001$) in all cases. On the other hand there was no statistical significant difference in mobility ($P > 0.05$) at 6 and 9 months when compared to 4 and 6 months intervals.

3.2.Radiographic assessment:

At the end of follow up period, radiographic assessment revealed that 8 patients (80%) had root development while the remaining 20% showed arrested root development. On the other hand, only 20% of cases had periapical or periodontal radiolucency while 80 % showed no radiolucencies. Neither of the patients had root resorption nor ankylosis (Figures 9 to 12).

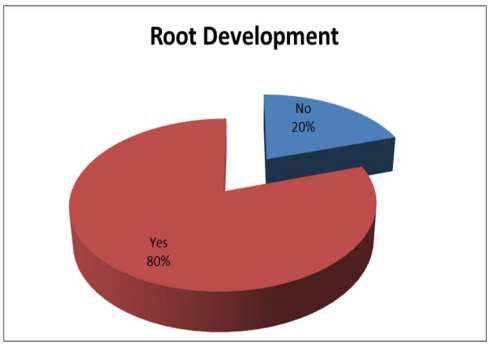


Figure 9: Pie chart showing root development of the transplants at the end of the follow up period.

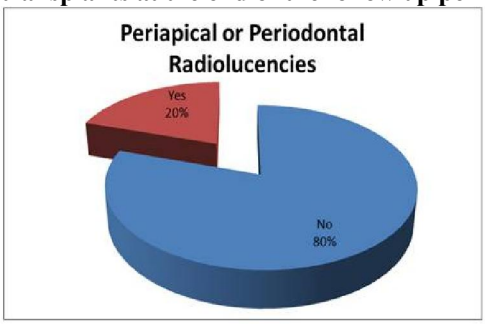


Figure 10: Pie chart showing periapical or periodontal radiolucencies of the trasnplants at the end of the follow up period.

Figure 12: Nine months postoperative radiograph of lower left 3rd molar transplant.

Figure 11: Two weeks postoperative radiograph of lower left 3rd molar transplant.

3.3. ***10-mm Visual analogue scale questionnaire:***

The patients received the autotransplantation as a somewhat painful procedure. Their decision to do transplantation was easy. Patients perceived the transplanted teeth quite different than others but they considered it to fit nicely in the dental arch. They didn't remember the original position of the transplants. Furthermore, patients had taken no particular measures to care for the auto-transplanted teeth.

4.DISCUSSION

Implant technology has taken great strides in recent years in terms of predictability, in both success rate &aesthetic result. Comparison between auto-transplantation & implantation as treatment options in replacing missing teeth seems inevitable. One major advantage of transplantation is its applicability in the management of patients before puberty growth has finished. Implants will not grow with growing patients and result in infra-occlusion as it becomes ankylosed to the alveolar bone. The beauty of transplanted teeth is that they are biological and able to erupt in harmony with adjacent teeth and growing jaws ***(Eddie 2009)***.

While there are many reasons for auto-transplantating teeth, tooth loss as a result of dental caries is the most common indication, especially when mandibular first molars are involved. First molars erupt early and are often heavily restored. Auto-transplantation in this situation involves the removal of a third molar, which may then be transferred to the site of an unrestorable first molar ***(Leffingwell 1980, Clokie et al., 2001, Reich 2008)***.In the present study, ten immature third molar teeth were autotransplanted as a replacement for unrestorable first or second molar teeth.

In the current study, all the patients were female with an age ranging from 16 to 20 years. Sex and age seem to have no effect on the final outcome. However, because immature teeth are usually covered by a thick follicle or periodontal ligament, which enables extraction of the transplanted tooth with minimal force, there are fewer chances of damaging the ligament during the procedure. That was in agreement with ***Cohen et al., (1995)*** who chose the patients having 15 years to 19 years and found that those patients are more appropriate candidates for third molar transplant.

The root length of the transplants in the present study was two-thirds root formation based on the study of ***Andreasen et al., (1990d*)** who reported that this was the ideal length. The main advantage of the open apex of the transplanted tooth with intact Hertwig epithelial root sheath allows healing and regeneration of the pulpal tissue and therefore saving subsequent root canal procedures. ***Andreasen et al,. (1990a & b)*** stated that the correlation between root length at the time of transplantation and vitality was: the more open the root apex the better the re-innervation. They found that teeth with incomplete and complete root formation showed 96 and 15 percent pulpal healing respectively. This discrepancy reflects the potential for revascularzation in teeth with open and closed apices. Furthermore, ***Skoglund et al., (1978)*** stated that the revascularization of the pulp appeared to occur mainly by in growth of newly vessels. In some instances, however, anastomoses seemed to form pre-existing vessels in the pulp.

Auto-transplantation is a technique-sensitive procedure as reported by ***Andreasen et al., (1988)***. So an atraumatic surgical technique was adopted in the current study following ***Kristerson & Andreasen (1984); Andreasen et al., (1990a);Cohen (1995) ;Teixeira et al., (2006)*** to preserve bone and periodontal support. Otherwise root growth may be compromised, leading to ankylosis or root resorption and attachment loss as stated by ***Slagsvold & Bjercke (1974) ;Nethander (1998)***. Furthermore, additional removal of bone beyond the apex at the recipient site was done to ensure an apical cushion or tension-free zone where the root buds could be positioned without threat of compression. This apical preparation also allowed for the transplant to be positioned at/or slightly below the occlusal plane so as to avoid premature occlusal contacts. Trimming of the interradicular bone using bone rongeur was required

to create a 4-wall surgically prepared bony socket to reduce lateral forces. This was in accordance with ***Bauss et al. (2002) and Reich (2008)***. Close contact of the autotransplanted tooth with the alveolar bone of the recipient site was assured as it is believed that this might provide better blood supply and adequate nutrition to the periodontal ligament cells, thereby increasing the number of viable cells as stated by ***Kallu et al., (2005)***. All the transplants were placed just slightly below the occlusal level to prevent postoperative traumatic occlusion as stated by ***Thomas et al., (1998)***; ***Clokie (2001) ;Bauss et al. (2009).*** Extra oral storage time if exceeding half an hour has an adverse influence on the results ***(Andreasen et al., 1970)***. Since the graft tooth was extracted immediately before grafting, injury to the periodontal membrane was minimal. This technique was applied in the present study, as it is likely to improve the clinical course after autotransplantation of teeth and avoid desiccation, which was confirmed by ***Kristerson & Andreasen (1984); Andreasen et al., (1990a&d) ; Honda et al., (2010)***.

A "basket suture" that runs across the occlusal surface of the transplant was selected as a type of splinting in the current study. That was in agreement with ***Bauss et al., (2002)*** who compared between rigid fixation and suture splinting "basket suture" for a total of 76 transplanted germs of third molars. Then they found that the significant increases in ankylosis and pulp necrosis were the factors for the less favorable results of the rigidly fixed teeth. Also ***Sagne & Thilander (1990)*** advised using flexible splinting where this allows for some physiological movement of the transplants functional stimuli assist healing. It's suggested that this movement stimulates periodontal ligament cellular activity and bone repair Two weeks of fixation period was adopted in the present study following ***Andreasen et al., (1990a & c); Lundberg & Isaksson (1996); Marcusson & Lilja-Karlander (1996); Frenken et al., (1998) ;Czochrowska et al., (2000)***. Furthermore, ***Pogrel (1987)*** concluded that rigid long-term fixation of the transplanted teeth had adverse effects on the periodontal and pulpal healing of the tooth.

The survival rate in the present study is 100%, as after transplantation of ten molar teeth with nine months follow-up, all transplants remained present. Also, the success rate is 80%, as eight out of the ten transplants fulfilled the success criteria; transplantation was defined successful if the tooth was still present without evidence of abnormal mobility, pathological pockets, root resorption or periapical radiolucencies. This was in agreement with ***Reich et al., (2008)*** who had a success rate of 95.5% where the transplants remained asymptomatic and functioning. As well as, no infection, ankylosis, loss of the transplant, or root resorption has been noted. In addition, endodontic therapy has not been necessary on any transplanted teeth.

In the follow-up period subsequent to tooth trasnplanatation, clinical measurements obtained through probing pocket depths and tooth mobility tests, were used to evaluate the healing process (***Altonen et al., (1978); Bauss et al.,(2004); Czochrowska et al., (2002) ; Mejàre et al., (2004)***. Since it is controversial, vitality test was not performed in the current study. Commonly, the vitality of the tooth is determined by means of cold or electrical tests, or both ***(Andreasen et al. (1970);Bolton (1974)***. As the so-called "vitality test" is a test of neurologic function of the pulp, it has been argued that it is possible for the transplant to have an intact blood supply without being re-enervated i.e. without having a nerve supply. Such a transplant would register non-vital to a vitality tester. The regeneration of a nerve supply to the pulps of that autograft may not have developed to the degree necessary for it to react to electrical stimulus at the time it was tested. Thus, the importance of a positive reaction to a cold or an electrical stimulus is a matter of controversy ***(Guralnick & Shulman 1962).***

The statistical significant decrease in pocket depth throughout the follow up period may be explained by the osteoinducing potential of the periodontal ligament cells resulting in bone regeneration between gap of the walls of socket and transplanted tooth. This is a welcome phenomenon that was observed clinically and confirmed with radiographs in the current study. This was in agreement with ***Eddie (2009)*** who found that genetically the periodontal ligament cells could differentiate into fibroblasts, cementoblasts and osteoblasts thus explaining this osteoinducing phenomenon. Furthermore, Pulp regeneration can be expected in immature replanted teeth. The optimal reattachment of periodontal ligament occurred within two weeks after autotransplantation between the periodontal ligament connective tissues of the root surface and the recipient socket wall ***(Tsukiboshi 2002)***.

The initial increase of mobility followed by reduction was observed in the present study. This was in accordance to ***Wally et al., (1979)*** who attributed the reduction in the mobility in their study to improved occlusal relationship and reduction in inflammation. Similarly, ***Cary et al., (1979)*** confirmed that mobility increased initially after surgery and decreased later on and attributed this to the healing of the periodontal ligament and bone surrounding the transplanted tooth.

In the current study continued root growth was noticed in 80% of the cases.

This was in line with results of a study conducted by ***Zachrisson et al.,(2004)*** where the authors found that after transplantation of partly formed rooted teeth when the root development has reached two thirds to three fourths of the final root length, root growth continued, and the teeth maintained their capacity for functional adaptation. Also, endodontic treatment was usually not necessary. Furthermore, the prognosis for complete periodontal healing at stage of root development was better than 90%. On the other hand, the time when the root completes its development after transplantation has not been examined, and an answer to this question will have an impact on prognostic assessment and clinical protocols for post-surgery follow-up (***Myrlund et al,. 2004)***.

All the recipient sites in the present study had sufficient bony support in all dimensions and sufficient keratinized mucosa to enhance post-operative stability in agreement to ***Teixeira et al., (2006)***, except for two cases. Distal bone resorption with furcation involvement and periapical radiolucency were seen in one case, which could be explained as a consequence of long standing chronic infection preoperatively. No improvement was noticed in the following radiographic follow up. This was correlated to the clinical findings, which determined increased pocket depths at the 6th month follow up interval. This patient missed some of the follow up visits and then recalled at the 6th month follow up visit and reported the presence of premature contact in the transplant. On the other hand, the other patient showed improvement in bone.

Bone resorption and increased pocket depth were detected in one case in the current study, where ***Bauss & Kiliaridis (2009)*** concluded that incorrect positioning with absence of occlusal and interproximal contacts are frequent findings in transplanted teeth. Incongruity between recipient site and root morphology of the transplanted might the cause of the transplant failure tooth. Moreover, the mesial and distal surfaces of the transplanted tooth and the adjacent teeth should be in contact with each other. If an interproximal space existed between the transplant and one of the adjacent teeth, then this will lead to food impaction and trauma to the interproximal gingival tissues leads to irritation, inflammation and even pocket formation ***(Bauss et al., (2002)***.

No root resorption was noted throughout the follow up period of the current study. The perquisite for periodontal regeneration is the survival of the majority of cells from the periodontal ligament, which are in competition with osteoblasts and osteoclasts from the alveolar bone. If the latter are predominant, root resorption starts and there is a poor prognosis as stated by ***Negri et al.,(2008) and Harzer et al., (2009)***. The final position of the donor tooth, within the recipient socket, influences periodontal healing. The donor tooth should be placed so that one to two mm of width of the periodontal ligament stays above the bone crest to achieve an ideal biologic width. Otherwise, apical migration of epithelium may occur and result in vertical bone resorption (too deep placement) or long connective tissue attachment (too shallow placement) as concluded by ***(Tsukiboshi 2001)***.

No ankylosis was determined until the end of the current study. ***Berude et al,. (1988)*** stated that replacement resorption (ankylosis) usually occurs and is secondary to cemental or periodontal ligament damage. It is unpredictable and usually irreversible. ***Mine et al., (2005)*** suggested that occlusal stimuli promoted the regeneration of the periodontal ligaments and prevented dentoalveolar ankylosis, whereas excessive initial force might cause severe root and bone resorption.

5.REFRENCES

1. **Altonen M., Haavikko K. and Malmstrom M (1978)**Evaluation of auto-transplantation of completely developed maxillary canines, *International Journal of Oral Surgery,* **7,** 434-441.
2. **Andreasen J. O., Hjørting-Hansen E. and Jølst O. (1970)** A clinical and radiographic study of 76 auto-transplanted third molars,*Scandinavian Journal of Dental Research,* 78, 512-523.
3. **Andreasen J. O., Kristerson L. and Andreasen F. M. (1988)** Damage of the Hertwig's epithelial root sheath: effect upon growth after auto-transplantation of teeth in monkeys,*Endodontics and Dental Traumatology,* 4, 145-151.
4. **Andreasen J. O., Paulsen H. U. Yu Z. and Bayer T. (1990d)** A long-term study of 370 auto-transplanted premolars. Part IV. Root development subsequent to transplantation, *European Journal of Orthodontics,* 12**,** 38-50.
5. **Andreasen J. O., Paulsen H. U. Yu Z. and Schwartz O. (1990c)** A long-term study of 370 auto-transplanted premolars. Part III. Periodontal healing subsequent to transplantation, *European Journal of Orthodontics,* 12, 25-37.
6. **Andreasen J. O., Paulsen H. U., Yu Z., Ahlquist R., Bayer T. and Schwartz O. (1990a)** long-term study of 370 auto-transplanted premolars. Part I. Surgical procedures and standardized techniques for

monitoring pulp healing, *European Journal of Orthodontics,* 12, 3-13.

7. **Andreasen J. O., Paulsen H. U., Yu Z., Bayer T. and Schwartz O. (1990b)**A long-term study of 370 autotransplanted premolars. Part II. Tooth survival and pulp healing subsequent to transplantation, *European Journal of Orthodontics,* 12**,** 14-24.
8. **Bauss O, Schilke R., Fenske C., Engelke W. and Kiliaridis S. (2002)** Autotransplantation of immature third molars: influence of different splinting methods and fixation periods,*Dental Traumatology,* 18, 332-328.
9. **Bauss O. and Kiliaridis S**. **(2009)** Evaluation of tooth position. Occlusion and interproximal contacts after transplantation of immature third molars, *European Journal of Orthodontics,* 31**,** 121-128.
10. **Bauss O., Engelke C., Fenske C., Schilke R. and Schwestka-polly R. (2004)** Auto-transplantation of immature third molars into edentulous and atrophied jaw sections, *International Journal of Oral and Maxillofacial Surgery*, 33, 558 -563.
11. **Berude J. A., Hicks M. L., Sauber J. J. and Li S-H. (1988)** Resorption after physiological and rigid splinting of replanted permanent incisors in monkeys, *Journal of Endodontics,* 14, 592-600.
12. **Bolton R. (1974)**Autogenous transplantation and replantation of teeth: report on 60 treated patients, *British Journal of Oral Surgery,* **12,** 147-165.
13. **Cary G., Herbert S., Ceib P. and William F. (1979)** The effect of splinting on tooth mobility II: After osseous surgery,*Journal of Clinical Periodontology,* 6, 317-333.
14. **Clokie C. M., Yau D. M. and Chano L. (2001)** Autogenous tooth transplantation: an alternative to dental implant placement, *Journal of the Canadian Dental Association,* 67, 92-96.
15. **Cohen A. S., Shen T. C. and Pogrel M. A. (1995)** Transplanting teeth successfully: autografts and allografts that work, *Journal of the American Dental Association*, 126, 481-485.
16. **Czochrowska E. M., Stenvik A., Album B. and Zachirsson B. U. (2000)** Auto-transplantation of premolars to replace maxillary incisors: a comparison with natural incisors, *American Journal of Orthodontics and Dentofacial Orthopedics,* 118**,** 592-600.
17. **Czochrowska E. M., Stenvik A., Bjerke B. and ZachirssonB.U.(2002)** Outcome of tooth transplantation: Survival and success rates 17-41 years post-treatment, *American Journal of Orthodontics and Dentofacial Orthopedics,* 121, 110-119.
18. **Eddie C. Y. (2009)** Tooth auto-transplantation as treatment option, *Dental Bulletin*, **14,** 21-24.
19. **Frenken J. W. F. H., Baart J. A. and Jovanovic A. (1998)** Auto-transplantation of premolars. A retrospective study, *International Journal of Oral and Maxillofacial Surgery,* 27, 181-185.
20. **Guralink W. C. and Shulman L. B. (1962)** Tooth transplantation, *Dental Clinics of North America,* **7,** 499-511.
21. **Harzer W., Rüger D. and Tausche E. (2009)** Auto-transplantation of first premolar to replace a maxillary incisor -3D- volume tomography for evaluation of the periodontal space,
22. *Dental Traumatology,* 25, 233-237.
23. **Honda M., Uehara H., Uehara T., Honda K., Kawashima S. and Yonehara Y. (2010)** Use of a tooth replica graft tooth for evaluation before auto-transplantation of a tooth. A CAD/ CAM model produced using dental-cone-beam computed tomography, *Oral Maxillofacial Surgery,* 9, 1016-1019.
24. **Kallu R., Vinkier F., Politis C., Mwalili S. and Willems G. (2005)** Tooth transplantations: a descriptive retrospective study,*International Journal of Oral and Maxillofacial Surgery,* 34**,** 745-755.
25. **Kim E., Jung J. Y., Cha I. H., Kum K. T. and Lee S. J. (2005)** Evaluation of the prognosis and causes of failure in 182 cases of autogenous tooth transplantation,*Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics,* 100**,** 112-119.
26. **Kristerson L. and Andreasen J. O. (1984)** Autotransplantation and replantation of tooth germs in monkeys, *International Journal of Oral Surgery,*13**,** 324-333.
27. **Kristerson L. and Andreasen J. O. (1984)**
28. Influence of root development on periodontal and pulpal healing after replantation of incisors in monkeys, *International Journal of Oral Syrgery,* 13, 313-323.
29. **Lee S. J., Jung I.Y., Lee C.Y., Choi S. Y. and Kum K. Y. (2001)** Clinical application of computer-aided rapid prototyping for tooth transplantation, *Dental Traumatology,* 17, 114-119.
30. **Leffingwell C. M. (1980)**Autogenous tooth transplantation: a therapeutic alternative.*Journal of Dental Surgery,* 56**,** 22-26.
31. **Lundberg T. and IsakssonS. (1996)** A clinical follow-up study of 278 auto-transplanted teeth, *British Journal of Oral and Maxillofacial Surgery,* 34, 181-185.

32. Marcusson K. A. M. and Lilja-Karlander E. K. (1996) Auto-transplantation of premolars and molars in patients with tooth aplasia, *Journal of Dentistry,* **24,** 355-358.

33. **Mejàre B., Wannfors K., and Jansson L. (2004)** A prospective study on transplantation of third molars with complete root formation, *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics,* **97,** 231-238.

34. Mine K., Kanno Z., Muramoto T. and Soma K. (2005) Occlusal forces promote periodontal healing of transplanted teeth and prevent dento-alveolar ankylosis: An experimental study in rats, *The Angle Orthodontist,* **75,** 637-644.

35. Myrlund S., Stermer E. M., Album B. and Stenvik A. (2004) Root length in transplanted premolars,*Acta Odontologica Scandinivia,* 62, 132-136.

36. Natiella J. R., Armittage J. E. and Grenee G. W. (1970) The replantation and transplantion of teeth,*Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics,* 29, 397-419.

37. Negri M. R., Panzarini S. R., Poi W. R., Sonoda C. K., Gilinelli J. L. and Saito C. T. M. H. (2008) Analysis of the healing process in delayed tooth replantation after root canal filling with calcium hydroxide, Sealapex, Endofill : A microscopic study in rats, *Dental Traumatology,* 24**,** 645-650.

38. Nethander G. (1998) Autogenous free tooth transplantation by the two-stage operation technique. An analysis of treatment factors, *Acta Odontologica Scandinivia,* 56**,** 110-115.

39. Pogrel M. A. (1987) Evaluation of over 400 autogenous tooth transplants,*Journal of Oral and Maxillofacial Surgery,* 45, 205-211.

40. Reich P. P. (2008) Autogenous transplantation of maxillary and mandibular molars,*Journal of Oral Maxillofacial Surgery,* 66, 2314-2317.

41. Schwartz O., Bergmann P. and Klausen B. (1985) Auto-transplantation of human teeth. A life table analysis of prognostic factors, *International Journal of Oral Surgery,* 14**,** 245-258.

42. Skoglund A., Tronstad L. and Wallenius K. (1978) A microangiographic study of changes in replanted and auto-transplanted teeth of young dogs, *Oral Surgery,* 45, 17-28.

43. **Slagsvold O. and Bjercke B. (1974)** Auto-transplantation of premolars with partly formed roots: a radiographic study of root growth, *American Journal of Orthodontics,* 66**,** 355-366.

44. Teixeira C. S., Pasternak B., Vansan L. P. and Sousa-Neto M. D. (2006) Autogenous transplantation of teeth with complete root formation: two case reports, *International endodontic journal,* 39**,** 977- 985.

45. Thomas S., Turner S. R. and Sandy J. R. (1998) Auto-transplantation of Teeth: Is There a Role? *British Journal of Orthodontics,* 25**,** 275-282.

46. Tsukiboshi M (2002) Autotransplantation of teeth: requirements of predictable success, *Dental Traumatology,* 18**,** 157-180.

47. Tsukiboshi M. (2001) Autotransplantation of teeth,*Chicago: Quintessence Publishing Co, Inc:* 2001.

48. **Tsurumachi T. and Kakehashi Y. (2007)** Auto-transplantation of maxillary third molar to replace a maxillary premolar with vertical root fracture. *International endodontic journal,* 40, 970-978.

49. **Wally K., Herert S. and Ceib P. (1979)** The effect of splinting on tooth mobility I: During therapy, *Journal of Clinical Periodontology,* 6, 45-58.

50. **Zachirson B., Stenvik A. and Haanæs H. R. (2004)** Management of missing maxillary anterior teeth with emphasis on autotransplantation, *American Journal of Orthodontics and Dentofacail Orthopedics,* 126, 284-288.

11/10/2012

Molavi's anthropological pedagogic orientations in order to improve objectives of high and primary schools' education in Iran

Maryam Saif Naraghi[1], Marzieh Kahnooji[2] (Corresponding author), Ali Shariatmadari[3], Ezatollah Naderi[4]

[1.] Professor of Tehran Islamic Azad University, science and research branch
[2.] PhD student of philosophy of education, Tehran Islamic Azad University, science and research branch
[3.] Professor of Tehran Islamic Azad University, science and research branch
[4.] Professor of Tehran Islamic Azad University, science and research branch

Abstract: The aim of this study is to investigate Molavi's anthropological pedagogic orientations in order to improve objectives of high and primary schools' education in Iran. In this regard, five components of anthropological basics have been studied from Molavi's point of view and they are wisdom, responsibility, determinism and authority, nature and spirit. The methodology of the present study is descriptive and it is an applied research. Statistical population includes works of Molavi and other experts (about Molavi's thoughts). Data were gathered by interviewing with professionals in this field, note taking on cards from library information. In this direction, strategies have been suggested to develop above mentioned basics and their application can shift educational settings from external knowledge transfer to knowledge production (creativity).
[Maryam Saif Naraghi, Marzieh Kahnooji, Ali Shariatmadari, Ezatollah Naderi. **Molavi's anthropological pedagogic orientations in order to improve objectives of high and primary schools' education in Iran**. *Life Sci J* 2012;9(4):2813-2821] (ISSN:1097-8135). http://www.lifesciencesite.com. 413

Keywords: anthropology, pedagogy, wisdom, responsibility, authority and determinism, nature and spirit.

Introduction

All elements of Education system including objectives, principles, factors and obstacles of pedagogy testify human status so it is necessary to know human being and his being aspects (Beheshti, 2008:45-46).

Anthropology has been originated from two Greek words of Anthropos meaning human and Logos meaning study and cognition. Anthropology means the ways of studying human being and deals with all human aspects such as social behavior, language, roles, arts and so on (Askari Khanghah and Kamali, 2007:13). There are different views regarding anthropology. According to Quran's perspective anthropological basics are spirit, body, spiritual validity, eternity, wisdom, authority, socialization, ambition, greatness, desire for perfection (Beheshti, 2007: 86-162). Sobhani (2010:24-34) defines anthropological basics as boy, spirit, nature, authority, responsibility, greatness, intellectual life.

Safavi (2009:49-103) said : from Molavi's point of view, anthropology is responsibility, familiarizing with secrets and being realities, spirit, body, wisdom, believing in resurrection and prevention of concupiscence.

Beheshti et al (volume 2, 2000:187-210) stated: from Molavi's point of view, anthropology is spirit, wisdom, responsibility, determinism and authority, effectiveness and being affected.

In present research, five foundations of anthropological basics have been investigated from Molavi's point of view including wisdom, responsibility, determinism and authority, nature, spirit. Then pedagogical orientations of each basis have been studied with their goals in different academic periods (high and primary schools) (the studied system is based on new educational system for a 6 year primary and high schools).

General Objective:

1- Studying pedagogical orientations of Molavi's anthropological basics in order to improve objectives of high and primary schools' education in Iran

Specific Goals

1- Studying pedagogic orientations of wisdom training in order to improve objectives of high and primary schools' education in Iran

2- Studying pedagogic orientations of responsibility training in order to improve objectives of high and primary schools' education in Iran

3- Studying pedagogic orientations of determinism and authority training in order to improve objectives of high and primary schools' education in Iran

4- Studying pedagogic orientations of nature training in order to improve objectives of high and primary schools' education in Iran

5- Studying pedagogic orientations of spiritual growth in order to improve objectives of high and primary schools' education in Iran

6-1-6 Research Significance and Necessity

If there is a plan and design for education of today generation, opinions and advises of experts and philosophers should be applied. As a pattern, desirable perfection of human being and new

pedagogic methods and principles can be gained from opinions of great people in old ages such as Molavi. Formation of human personality depends on his education. Human being can pave the way of perfection by suitable pedagogy and if human's education is ignored, he will descend even inferior than animals (Habibi, 2009:23). In this study, after investigating Molavi's anthropological basics and related pedagogic orientations, objectives of Education system (primary and high schools) have been studied. Objectives of an educational system or school are determined based on some principles resulted from a view that school has on human and its ideal educational system.

Methodology

This research is aimed to study Molavi's anthropological pedagogic orientations in order to improve objectives of high and primary schools' education in Iran. Here anthropological basics mean studying Molavi's point of views in this field that have been investigated as variables. Another variable is objectives of educational periods. So research methodology is descriptive and it is applicable regarding objectives. Statistical population includes all works of Molavi and other experts about Molavi's thoughts and their anthropological subjects have been studied in particular. Also, Information related to educational goals in primary and high schools have been investigated. Regarding the study dimensions, the sample group has been chosen from an available statistical population and data were gathered from library including note taking from domestic and foreign sources and interviewing with professionals in this field so tools for gathering data were interview, using library information through note taking. Wisdom, logic, thought and reasoning were the standards for data analysis. Descriptive statistics have been used as well (classification of opinions and their similarities and differences).

In principle, wisdom is logical thinking of human being and lexically it means ability to reason or understand the relationship and differences among things. In addition, it is interpreted as thinking and mental power (Farmihani Farahani, 1999:293).

Types of intellects from Molavi's View

Molavi emphasized on rationality and wisdom and this rationality should be led to love. He wanted to create an open and clear space for human thinking and free humans from traps of blind imitation (Faydeni, 2007:296).

Molavi divided intellect into partial and holistic ones and epistemologically these divisions can be referred to intellectual ranks (Allah Bedashti, 1997:37).

Partial intellect

Partial intellect is a degree of human spirit that relates to transient and temporal world and is subjected to fantasy and doubt and it is not able to reach high principles of the world (Sheikh Shoaee, 2007:240). Partial intellect is superficial and colored with colors of sensuality and it consists of arrogance, pugnacity, hasting in judgement and useless interferences. This kind of intellect is not perfect to know facts and secrets of the world. Molavi also named it, debated intellect (Zamani, 2009:467). Partial intellect is the center of fantasies and it is as same as ignorance, darkness, blindness, hesitancy and uncertainty (Mosaffa, 2007:192).

Prudery and sensuality, scrutiny in shallow affairs of the life, lack of qualification to witness truth, having fantasy, lack of independence in thinking, dealing with causes and physical laws of nature, lack of love are other features of partial intellect. This intellect is useful only in its own area and territory and it deals with physical affairs (Zamani, 2009:468-473). After rule of partial intellect on human being, it becomes versatile and useful intellect no longer can make decision (Mosaffa, 2007:48-49).

Holistic intellect (logos)

Logos or holistic intellect is heavenly ambitious that takes its light from God and encompasses all objects and understands facts correctly. According to Molavi, this kind of intellect is specific to appointed servants and superhuman. He called it sublime intellect (Zamani, 2009:467). Logos has been meant world foundation, evolution of human mind, logos of prophets (Sheikh Shoaee, 2007:240). Logos has following characteristics: flying to eternal world, measuring mystical affairs (Zamani, 2009:471-3). According to Molavi, Logos is father of all human who have qualification of receiving facts and if they see the world as a heaven, it will be due to their permanent peace with the father (Momenzadeh, 1998:75). Logos brighten horizons whereas partial intellect blackens deeds' letter. Partial intellect forces human to do illegal things that bring about bad outcomes for human (Schimmel, translated by Badrehee, 2009:120).

Principle 2: responsibility

Responsibility has been originated from a familiar word: question. In fact, responsibility is an internal question which is being asked by human about its ability. Human asks himself whether or not he/she is using abilities as a qualified one (Alavi, 2007:110). Responsibility is a basic principle. It trains us that everybody with every position and degree is responsible to their works and affairs. The earth and heavens have been created to be used practically and scientifically by human being. By making him a lord on the earth, God has made human

being responsible and burden a great trust on her/him. Human perfection depends on his perfection in responsibility. The weaker everybody in responsibility, the more deteriorative their works and vice versa (Masjid Jameyi,2005:343). One of the most important goals of educational system is to train responsible and committed people because responsible sources believed in internalized values are one of important factors in development of every country (Mosavi Dahmoredi, 1999:65).

Responsibility from Molavi's point of view

According to Molavi, everybody should step in the same path and try to do duties responsible for them. One of the most striking aspects of Molavi's teachings is human responsibility (Schimmel, translated by Badrehee, 2010: 108).

Ayah 127 from Al'araf Surah (the elevated places) in which God says: testify if I am your lord, all said yes, thou are, we testify you are our lord so that you cannot pretend in eternal world that you are not aware of this occurrence.

Ayah 72, Ahzab Surah (the Allies) in which God says: we asked heavens, the earth and mountains to accept this trust, all of them rejected it but human being accepted it. Human being was very cruel and arrogant. According to Molavi, this trust means knowledge and cognition (Zarrinkoob, 2002:374) and human being is responsible for this trust and should be accountable to this great gift and blessing.

Principle 3: determinism and authority

Philosophical concept of determinism means that human being has to do something (sajjadi, 1996:233), authority means voluntary state of human in order to do or not to do something (Anvari, 2002:285).

Molavi's point of view about determinism and authority

Molavi rejected determinism and defended severely human being authority and freedom and stood up against determinism and Ahle Hadith. On the other hand, he had some opinions about limitation of human freedom and authority against schismatic submission and tended to "No perfect determinism no perfect authority" by rejection of determinism and submission (Khayatian,2007:153). According to Molavi, human being is free and dependent when he incorporates with nature of God and his authority disappears in God's authority and becomes involuntary (in absolute goodness of God) and it is only possible by connection to nature of God (Hashemi, 2003:130).

Principle 4: nature

In Arabic language, nature means innovative creation against mimicry and adoptive creations and it is a typical infinitive. So nature means a type of creation. So creation of human being requires the nature (Davoodi, 2011:89).

Molavi's point of view on nature

Molavi noted that being is unit that is God's nature. The world is its manifestation and human mind is its radiation. This radiation has separated from the origin and always tries to bind its origin and as cane cries for its separation from canebrake, human mind is moaning as well and shouted distraughtly and searches for its origin like a bird which raps itself against cage walls to free itself. (Babolhavaeji, 1966:278).

Cane means human holly spirit and it is true in ayah 29, surah Hejr(we inspired our soul on it) because holy spirit is of abstractions and elite of the world (Sabzehvari, by cooperation of Borojerdi, 1995:17). This cane that is the symbol of solitary human separated from its lover, talks about its suffering from separation. This cane talks about its separation from its nature (Mosaffa,2007:112).

Principle 5: spirit

Lexically spirit means breath and inspiring. Human spirit is an abstract essence because it is like breath and wind regarding mobility, life creation and latency (Makarem Shirazi,1997:250). In Quran, spirit has been outlined as a cosmological concept and it is a name for one of creatures, the one as same degree as angles. Spirit is the origin of life in the world (Bagheri (A),2010:16).

Truth of spirit is confidential, sealed and hidden. Holly texts have no words to say about it. In ayah 85, surah Isra (they will ask you about the spirit tell them the spirit is under my lord's control and order), God says: spirit is considered as an eternal cosmos and human knowledge is defective in this regard. In fact, spirit is a hidden and unknown truth (Zamani,2009:239).

Molavi's view about spirit

Pedagogical opinions of Molavi are based on mystical anthropology. Although human being is combination of body and spirit, human truth is not the body. The body is only a tool for the spirit so human's life, thought, willingness and different states depend on the spirit and all body organs and activities are under control of the spirit. Without spirit, the body is silent and valueless (Beheshti et al, volume 2, 2000:187). As other people who believe in unseen cosmos, Molavi believed in spiritual aspect of human and did not limit human body to elemental one. According to him, the body and its value depend on the spirit and it is the spirit that make body able to live in the transient world so the body has no value and cannot speak, hear and see without the spirit (Sharafi,2011:95).

In following section, the strategies for developing each of principles and their related

educational goals will be discussed. In this direction, in addition to referring to researches done in this field, suggestions will be stated for improving educational goals (primary and high schools).

Discussion

Particular Goal 1: studying pedagogical orientations of intellect in order to improve objectives of high and primary schools' education in Iran

Strategies for developing intellect considering its importance from Molavi's point of view

According to Molavi's view on intellect specially significance of logos. Partial intellect should not govern on logos so in educational centers, measures should be done to provide development of logos because if partial intellect dominates on human being, it will become versatile and prevents human to make decision so human being is equipped with characteristics of partial intellect and its disadvantages have been above mentioned. Therefore, following strategies are presented in order to develop intellectual training in educational centers:

A: reinforcement of creative and innovation spirit in students

B: prevention of extreme memorization

A: reinforcement of creative and innovation spirit in students

Creativity means representation of a new thought, behavior or product. If creativity means creation of a thing which is not existent, it is called innovation meaning creation of an individual thing without being previously existent and creation means making a thing by combination and manipulation of other things (Pirkhaefi,2008:17) so it is one of the most effective factor on intellectual growth.

B: prevention of extreme oriented memory

If learning is not done by insight and knowledge, its value will be temporal. People in different fields of study are being studied but there is no change in their thoughts and actions because they have memorized what they have learnt without any understanding (Shariatmadari, 2009:23). Focusing on this problem attracts one's attention to prevention of memorization and deep learning in order to promote educational goals.

Specific Goal 2: studying pedagogical orientations of responsibility in order to improve objectives of high and primary schools' education in Iran.

Strategies for developing responsibility considering its importance from Molavi's point of view

Responsibility is a category which has been studied in different sciences. In section 6 of the constitution in Islamic republic of Iran, human being has high munificence and value and he is a free and responsible being. Thereby it is obvious that freedom combined with responsibility has been stated in the most part of the constitution that determines foundation of the government (Bandarchi,2004:108). According to Molavi, everybody should step in the same path and try to do duties responsible for them. One of the most striking aspects of Molavi's teachings is human responsibility (Schimmel, translated by Badrehee, 2010: 108).

Regarding Molavi's emphasis on responsibility and coping with duties and its significance in Iranian Constitution and valuing human being due to this feature, it is necessary to consider measures in educational centers. So in order to improve educational goals in different academic periods, strategies for developing responsibility feeling have been present as follows:

A: social participation

B: self esteem

A: social participation

Human is a social being and is living in the society from his birth to death and always interacts with other people. Social life requires a set of social skills which will be learnt in process of sociability and correct learning results in formation of social responsibility (Iman and Jalaeian Bakhshandeh, 2010:20).

B: Self esteem

Salivalli (2001:376) defines self esteem as a degree of value, respect and interest which a person believes in her/him as a human in the world. According to Teri (2002:34), it is necessary to increase self esteem in order to prevent from problems which teenagers face with due to low self esteem.

Specific Goal 3: studying pedagogical orientations of authority and determinism in order to improve objectives of high and primary schools' education in Iran

Outcomes of believing in determinism and authority from Molavi's point of view

Human being is living in a world which affairs are not under control of human rather they have been fated in a certain way but particular actions of human being originate from his willingness and authority. On the other hand, human fate will be got due his actions which are originated from human authority (Bagheri(B),2010:155). As mentioned, human fate originates from his authority and it is evident all through human being life. So regarding Molavi's view and Imam Jafar-e Sadigh hadith (no perfect determinism no perfect authority), outcomes of this belief should be considered in educational centers in order that growth and promotion of educational settings are provided. In this direction, two outcomes of believing in "no perfect

determinism no perfect authority" have been stated because they have to be optimized in duties of educational centers.

A: increase of efforts

B: respecting social rules

A: increase of effort

Sadri Afshar et al (1994: 360 and 930) defined effort as a hard and demanding endeavor for reaching the goal and defined endeavor as a process of scrabbling and mental or intellectual work. These definitions suggest a demanding and effortful activity. Only the powerful force inherited in the human leads him to effort and endeavor and it is nothing but his authority. Students should learn that successful, efficient and creative people in political, cultural, religious and social areas have flourished in the light of effort and endeavor. So important creatures are products of demanding work, continuous testing and application of others' successes (Raoofi,1997:615-16).

B: Respecting social rules

Rules mean regulation and method (Safi,2006:17) and it is necessary to be considered by all people under governance of that society.

Specific Goal 4: studying pedagogical orientations of nature in order to improve objectives of high and primary schools' education in Iran

Strategies for developing nature considering its importance from Molavi's point of view

Global education should be based on mankind constant shares in order to meet requirements of different nations and races regarding pedagogic thought and practice and the only language that coordinates mankind world is natural language. Natural affairs are general truths that all people tend to. They are tendency to perfection, finding truth, erudition and goodness, innovation and creativity, tendency to religion, intellection, tendency to freedom and authority (Manzari Tavakoli, 2004). Considering emphasis of Molavi on natural affairs, tendency to natural manifestations and regarding all people tend to bind their origin, it is necessary to provide a context for presence of natural affairs inherited in human body. So two important strategies of natural training are referred to which are more important in duties of educational centers:

A: perfection growth

B: intellection growth

A: growth of perfection

Human being is interested in his perfections and himself so it can be said that naturally human loves absolute perfection (Pirmoradi, cited by Shahabadi,2007:42). Perfection of everybody and beings is a real thing and is an existing attribution. When human being passes all stages, he/she qualifies this attribution so that in every stage of perfection, human being can do something. If human being does not reach this degree, he/she cannot do such things (Sadat,2005:28).

B: intellection training

In Islamic concepts, intellection suggests correlation between theory and practice. In this correlation, not only thought should focus on practice and resolve practical problems but also practice should focus on thought and man life should be regulated in relative to his thoughts (Bagheri(B), 2010:162). If growth of intellection is considered in educational centers, in fact, one of the main manifestations of nature will be represented in one hand and intellectual growth will be helped on the other hand that is one of important basics of anthropology from Molavi's point of view.

Specific Goal 5: studying pedagogical orientations of spirit in order to improve objectives of high and primary schools' education in Iran

Strategies for developing spirit considering its importance from Molavi's point of view

Spirit is the power of life and movement for human being (Separi,2001:7) all powers of perception and intelligence have gathered in the spirit (Zomorodian, 2007:38) so it creates learning gift for human being (Zhalehfar,2005:93) and by a spirit ready for leaning, human being can do different activities. Molavi believed that without spirit, the body does not have the ability to see, hear and speak (Sharafi, 2011:95).

According to Molavi, without spirit, the body cannot see, hear and speak and such body is value free so the ability to see, hear and speak has to be under control of spirit and it is necessary for life, problem analysis and it is one of tools for learning in educational facilities. Strategies should be considered and for this category, two following approaches have been offered in order to grow spirit in different academic periods:

A: growth of values

B: physical growth

A: growth of values

Values are one of key concepts in studying human behavior, motives and acts. Values are used to recognize society and individual, following changes over time, explanation of motivational bases of behavior and attitudes. Relative importance and grading of values are different in various people. This difference is hidden in individual speeches and behavior. So scientific knowledge of valued systems of people can help experts and responsible people know social beds (Sahami, 2008:157). Standard of human perfection pays attention to all human values and gifts and makes them balanced and coordinative and consideration of moderation while mentioning values.

Anthropological basics	Strategies for growth of basics	Objectives of primary school	Objective of high school	Related researches
1- intellect	1-1 reinforcing creative spirit in students	Making students creative[1], helping students know and discover their personal gifts[2], reinforcing spirit of criticism, innovation, cognition, growth of personal gifts in direction of social and individual promotion[3]		Heyrani (abstract,2001), Hosseini (abstract:1997), Torrance (1972:114), Mumford et al (2012:30), Martin&Terblanche (2003:64)
	1-2 preventing from extreme memorial orientation	Growing children capabilities in listening, speaking, reading comprehension, thinking, reasoning, inferring[4]	Familiarizing with scientific truth and understanding scientific approaches in all materials	
2- responsibility	2-1 social participation	Developing a social personality, developing tendency to social groups and associations[5], preparing children for social life, being interested in consideration of social regulations and cooperating with others[6]	Increasing social growth of people, understanding affairs necessary for being socially qualified [7] and reinforcing social relationships, relation with family members, friends and participating in social activities[8]	Sobhan Nejad and Fardanesh (2000:95), Tahmasbi (2005:83)
	2-2 self esteem	Reinforcing feeling of moral munificence and motivating self esteem[9]		Kordloo(2008:4)
3- determinism and authority	1-3 increasing efforts and endeavors	Considering indolence as factor of individual and social failure by students [10]	Preventing indolence[11]	
	2-3 respecting social rules	training convincing students with consideration of people rights, familiarizing with school regulations and practicing them, being interested in consideration of social rules and regulations[12]	Familiarizing with the constitution and consideration of rules and regulations and trying to expand them[13]	
4- nature	1-4 growth of perfection	Reaching perfection[14], moral, spiritual eruditions, self purification, teaching theology and growing faith[15]		
	2-4 growth of intellection	Reinforcing spirit of searching, thinking [16]		
5- spirit	1-5 growth of values	Preparing students to understand values[17] and respect ethical rules and develop intellectual measure for understanding values[18]	Obtaining values and ethical basics[19]	Hamzeh Beigi (1996:109), Maleki (abstract,1996)
	2-5 physical growth	Growing healthy students[20] , trying to keep them healthy[21], developing correct attitude about them as a growing creature[22]	Preparing students to appreciate their physical power and applying it effectively[23] and being aware of duties and functions of body organs and keeping healthy by doing exercises[24]	Mahfuzpoor et al(2009:73)

[1]- Mirhajian Moghadam cited by Barlow, 2007:5
[2] - Alagheband (2009:247)
[3] - Bagheri (B) (2010:27)
[4] - Alagheband (2009:246)
[5] - Alaghehband (2009:246)
[6]- Higher council secretarial of Education, 2008:31
[7] - Shariatmadari, 2009:18-19
[8] - Higher council secretarial of Education, 2008:42
[9] - Higher council secretarial of Education, 2008:26
[10] - Higher council secretarial of Education, 2008:33
[11] - Higher council secretarial of Education, 2008:43
[12] - Higher council secretarial of Education, 2008:31-42
[13] - Higher council secretarial of Education, 2008:31-42
[14] -Moayeri,1997:25-27
[15] - Taghipour Zahir, 2008:77-78
[16] -Bagheri (B) 2010:27
[17] -Alagheband,2009:246
[18] - Shariatmadari,2009:16
[19] - Shariatmadari,2009:20
[20] - Moayeri,1997:34
[21] - Higher council secretarial of Education, 2008:32
[22] -Shariatnadari,2009:15
[23] - Shariatmadari,2009:18
[24] - Higher council secretarial of Education, 2008:42

By having different gifts, human being is perfect when it does not tend to only one gift; rather human should grow all gifts in a balanced way. So an action should be taken to grow values and make the spirit pleasant. According to Molavi, divine oneness is the way of reaching perfection.

Paying attention to talented spirits of students in schools gives teacher an opportunity to take best benefit from manifestation of their values.

B: physical growth

Any action taken by the body will be shared with the spirit and any changes in human spirit affect the body (Zomorodian, 2007:102-3).

Molavi pointed that human body do activities in order that radiation of spirit radiates on it (Shebeli Nemani, translated by Sobhani, 2003:139).

Conclusion and offering suggestions based on findings of present study in order to improve objectives of primary and high schools in Iran

1- in intellect category, Molavi paid attention to importance and necessity of intellect specially logos but according present findings, components of intellectual growth has not been paid special attention (creativity, innovation and prevention of extreme memory orientation) so it is necessary to pay attention to this category in educational system and it is suggested to formulate a course in all academic degrees titled as creativity in classroom or in a similar way such that shifts educational settings from knowledge transfer to knowledge production (creativity).

2- In intellectual category, it was noted that extreme memorization should be prevented in educational setting. So it is suggested that new techniques in teaching are used in order to challenge learning activities of students and it is one of suggested techniques in which problem solving in teaching and learning has been used.

3- In category of responsibility of students, it is necessary to pay attention to the factors growing it (social participation) in educational centers. So it is suggested that different student organizations play more role in different scientific, cultural, exercise fields by inviting students relative to their talents and school responsibility should be given to students based on their talent, ability and interest and a sound competition is provided among groups.

4- Regarding self esteem (that is subset of responsibility growth), it is advised that personal, mental and intellectual capabilities in students are identified resulting in increase of self esteem and self belief.

5- Considering that believing in relative determinism and authority increases effort and endeavor, so it is necessary that in educational settings, strategies for increase of effort and endeavor in students are provided by suitable approaches in addition to explaining its significance such that their conditioning should be prevented and it is effective on increase of educational quality.

6- with reference to hadith of Imam Jafar Sadiq about determinism and authority (no perfect determinism no perfect authority), Molavi had the same point of view and considered it as one of anthropological basics but according to present findings, lack of paying attention to outcomes of believing in determinism and authority is felt (efforts and endeavors and respecting social rules) because there is no similar research in educational centers. Due to its ambiguity for most of students, they think that their failures result from determinism and their successes result from authority and most of the time they want to evade their tasks and efforts. So it is necessary that professionals in this field explain it in educational centers.

7- It is necessary that some strategies are taken in educational settings to avoid emphasis on scores in order that students continue their efforts because emphasis on scores increases students' anxiety and prevents them from continuous efforts. In general, they cannot focus their attention on the course. This problem has been solved by descriptive assessment plan in primary schools so it is suitable that measures are taken to use it continuously in other educational periods.

8- Considering Molavi's emphasis on nature, there is no research on the growth of perfection, intellection and value that are natural manifestations so it is essential that this category is being paid attention by researchers.

9- considering significance of physical health required for preparation spirit, it is advised that students' physical health are paid attention not just as a course called physical activity rather by correct planning and under opinions of experts, measures are taken to pay more attention to this area because in addition to physical health, mental, spiritual and emotional health are manifested.

References

1. Ismaeelpour Niazi, Hasan (2010). Anthropology, Tehran: Andishe Javan association
2. Allah Bedashti, Ali, (1997). Methods and principles of wisdom growth in adolescent and young ages from Islamic perspective. Qom, Education
3. Anvari, Hasan (2002). Sokhan dictionary. Vol 1. Tehran: Sokhan
4. Iman, Muhammad Taghi and Jalaeian Bakhshandeh, Vajihe (2010). studying and determining the relationship between social

responsibility and social capital among Shiraz youths, applied sociology quarterly, No 37, Pp 19-42.
5. Babolhavaeji, Nosratollah (1966), spirit in religion and philosophy, Tehran: Darya
6. Bagheri, Khosro (A) (2010). Looking back at Islamic pedagogy, Vol 1, Edition 24. Tehran: School publication
7. Bagheri, Khosro. (B) (2010). Introduction to education philosophy in Islamic republic of Iran. Vol 1 (second edition) and Vol 2 (first edition). Tehran: cultural and scientific press company
8. Bandarchi, Mohammad Reza (2004). Citizenship rights in Iranian constitution. Part 1. Legal procedure magazine, No 46, Pp 15-19.
9. Beheshti, Mohammad (2008). Pedagogic basics from Quran View. Tehran. Publication organization of research center for Islamic thought and culture
10. Beheshti, Mohammad, Aboujafari, Mahdi, Faghihi, Ali Naghi and Arafi, Alireza (2000). Opinions of Muslim scientists on education and its basics. Vol 2. Qom: research center of Tehran University and theological school: Samt.
11. Pirkhaefi, Alireza. (2008). Creativity (basics and methods of pedagogy), second edition. Tehran: Hezar-e Ghoghnoos publication.
12. Pirmoradi, Mohammad Javad (2007). Ayatollah Shahababdi and logic of love nature on proving Vajib Alvojob, hadith of love and nature, papers about opinions of Ayatollah Mohammad Ali Shahabadi. Tehran: publication organization of research center for Islamic thought and culture, Pp 27-47.
13. Taghipour Zahir, Ali. (2008). Principles and basics of education, fourth edition. Tehran: publication of Payam-e Noor University
14. Habibi, Sharareh (2009). A new view on education philosophy. Tehran: Avay-e Noor.
15. Hosseini, Afzalosadat. (1997). Analysis of creativity nature and approaches to its growth. PhD dissertation, Tehran, Teaching training University
16. hamzeh Beigi, Tayebeh (1996). Identification and comparison of moral values between males and females. Research plan, Tehran, department of Islamic guidance and culture.
17. Heirani, Shabnam (2001) studying the relationship between teachers' classroom management and students' creativity of primary fourth grade in Tehran. M.A thesis. Tehran: Alzahra University
18. Khayatian, Ghodratollah. (2007) (determinism and authority) and destiny in views of Molavi (derived from summary papers of international congress of 800th year of Jalal Aldin Balkhi birth. Tehran: Khane Ketab institute with cooperation of research center of philosophy in Iran.
19. Davoodi, Mohammad (2011) role of teacher in religious pedagogy. Third edition, Qom: research center of university and theological school.
20. Higher council secretariat in Education (2008). Laws ratified in higher council of Education, Edition 9, Tehran: School.
21. Raoofi, Mohammad (1997) the student and self confidence in scientific research. Papers of the first seminar of higher Education in Iran. Vol 2. Tehran: Alameh Tabatabaee University, Pp606-625.
22. Zarrinkoob, Abdolhossein. (2002) secret of cane (an analytical and comparative critique on Masnavi). Edition 9, Vol 1. Tehran: scientific
23. Zamani, Karim. (2009). eshgh minagar: description of Molana's Masnavi Manavi, Edition 7. Tehran: Ney publication.
24. Zomorodian, Ahmad. (2007). Spirit truth: small knowledge of science of souls: edition 11. Tehran: Islamic culture publication
25. Zhalehfar, Taghi (2005), spiritual research and its behavioral effects, Zanjan, Nikan Ketab
26. Sadat, Mohammad Ali (2005) Islamic ethics, edition 33, Tehran:Samt
27. Sobhani, Jafar (2010) Iamamieh beliefs, edition 6, Qom: Imam Sadegh institute
28. Sobhan nejad, Mahdi and Fardanesh, Hashem. (2000). Social responsibility in current curriculum of Iranian primary school, Modares magazine, fourth period, No 1, Pp 95-114.
29. Sabzevari, Hadi-ibne Mahdi (1995): Masnavi description(with cooperation of Mostafa Borojerdi), vols 1 and 2. Tehran: Islamic guidance and cultural ministry, publication organization
30. Sajjadi, Seyyed Jafar (1996) dictionary of philosophical science and theosophy, Tehran: Amir Kabir
31. Sahami, Sousan (2008) valued priorities of students, research of social science in Garmsar, second year, No 2.
32. Sharghi Atefeh (2011) studying death and resurrection in Masnavi Manavi, M.A thesis, Kerman: Bahonar University
33. Shariatmadari, Ali (2009) principles and philosophy of education, edition 37: Amir Kabir.

34. Shariatmadari, Ali (2006) Islamic Education, edition 21, Tehran:Amir Kabir
35. Sheikh shoaee, Abbas (2007) meanings of intellect from Descartes and Molavi's view (derived from summary papers of international congress of 800th years of Molavi's birth), Tehran: institute of Khane ketab with cooperation of research institute of philosophy in Iran
36. -Schimmel Anne Mary (2010). I am wind and you are fire (translated by Freidoon Badreyi), third edition, Tehran:Toos
37. Safi, Ahmad (2006). Rules of Education in Iran, edition 14, Tehran:Samt
38. -Sadri Afshar, Gholam Hossein and Hokmi, Nasrin and Hokmi, Nastaran (1994), today Persian culture, Tehran: Nashr-e Kalemeh institute
39. Safavi, Seyyed Soleiman (2009), perfect human and ethics from Molavi's point of view, Qom: Salman Azadeh.
40. Tahmasbi, Farhad (2005) role of student organizations in social training of high, guidance and pre university students in Lorestan, quarterly of Islamic training research. No 1, Pp 83-100.
41. Askari Khaneghah, Asghar and Kamali, Mohammad Sharif (2007). General anthropology, edition 8, Tehran: Samt
42. Alagheband, Ali (2009) educational management preliminaries, edition 17, Tehran: publication of Payam-e Noor University
43. Faydeni, Akbar (2007) intellect from Molavi's point of view. (derived from summary papers of international congress of 800th years of Molavi's birth), Tehran: institute of Khane ketab with cooperation of research institute of philosophy in Iran
44. Farmihani Farahani, Mohsen (1999), detailed dictionary of pedagogic science, Tehran: Asrar-e Danesh
45. Quran, translated by Mehdi Elahi Ghomsheyi (2000), second edition, Qom, Alzahra publication
46. Mosafa, Mohammad Javad (2007), with an oldman from Balkh, Edition 11, Tehran: Parishan
47. Moayeri, Mohammad Taher (1997) Educational problems, sixth edition, Tehran: Amir Kabir
48. Makarem-e Shirazi, Naser (1997), Nemuneh interpretation, Vol 12, Islamieh library
49. Maleki, Amir, (1996) studying relation between socio economical bases and valued tendency of teenagers (male third grade students in field of physics and mathematics in Tehran in 1995-96), M.A thesis, Tehran: Teaching training University
50. Manzari Tavakoli, Alireza (2004), formulation of education philosophy based on nature, PhD dissertation, Shiraz
51. Mosavi Dahmoredi, Seyyed Ali (1999) the relation between job satisfaction & motivation to progress and mental health and responsibility of male pedagogic teacher in Ahvaz institutes, M.A thesis, Education department
52. Molavi, Jalal Aldin Mohammad (2000), Masnavi (introduction, analysis, correction, comments and indices from Mohammad Estelayi), sixth edition, Vol 7, Tehran: Sokhan
53. Mirhajian Moghadam, Mohammad (2007) studying the relation between learning styles and creativity and academic achievements in high school third grade students of Kerman in 2006-7. M.A thesis. Kerman: Bahonar University
54. Vaezi, Ahmad (2006). Human from Islamic perspective, edition 7, Tehran: Samt.

10/2/2012

Prevalence of Eating Disorders among Female Students of University (Tehran - Iran)

Azam Roshandel, Msc[1] (Corresponding author), Mahboobeh Safavi, PhD[2], Iran Ghasemi, Msc[3]

1. Instructor, MSc of Nursing, Faculty member, Department of Nursing, Zanjan Branch, Islamic Azad University, Zanjan, Iran.
2. Assistant professor ,PhD of Management of Health Services, Islamic Azad University, Tehran Medical Branch, Tehran, Iran.
3. Faculty member, Department of Pediatric Nursing, College of Basic Medical Sciences, Zanjan Branch, Islamic Azad University, Zanjan, Iran.

Abstract: The present paper has been carried out to investigate the prevalence of eating disorders among the female students of Islamic Azad University, central Tehran branch. The subjects of this descriptive research were 400 people who were selected using Stratified Random sampling and were assessed using demographic questionnaires, EAT-26 eating observation test and diagnostic questionnaire of eating disorder. According to EAT-26 results, 21.5 percent of the students scored above the cutting point 20 and were diagnosed to have eating disorders. According to diagnostic questionnaire of eating disorder, 1.8% suffered from anorexia nervosa and 7.8% suffered from bulimia nervosa. The frequency of eating disorders is more or less similar to the stats of the other communities. It seems that now a high level of vulnerability against eating disorder exists in the women. These results refer to the necessity of planning for prevention and related activities to elude the consequences of this disorder and as a result, improve the level of the mental health of the individuals.
[Azam Roshandel, Mahboobeh Safavi, Iran Ghasemi. **Prevalence of Eating Disorders among Female Students of University (Tehran - Iran)**. *Life Sci J* 2012;9(4):2822-2828] (ISSN:1097-8135). http://www.lifesciencesite.com. 414

Keywords: Eating disorder; Anorexia Nervosa; Bulimia Nervosa.

Introduction

Eating disorder is one of the worried factors to public healthy that it has increased since 1970 (Hoek & Hoeken , 2003). The prevalence of eating disorders and problems related to eating disorders such as low self-esteem, body dysphoria, low body image satisfaction, and disordered eating has increased dramatically over the past thirty years and continues to increase (wood, 2004). According to the American Psychiatric Association (APA), eating disorders (ED) are characterized by severe disturbances in eating behavior of the individual intended to control body weight and accompanied by distorted body image.

Further, ED is diagnosed by the criteria of Diagnostic and Statistical Manual of Mental Disorders-fourth edition - text revision (DSM -IV-TR) and includes two specific types:

Anorexia nervosa (AN) and bulimia nervosa (BN).Eating disorder not otherwise specified (EDNOS) and binge eating disorder (BED) categories are provided to code for disorders that do not meet full criteria for a specific ED (American Psychiatric Association., 2000).

AN is an eating disorder marked by an inability to maintain a normal healthy body weight, often dropping below 85% of ideal body weight (American Psychiatric Association., 2000; Chakraborty *et al*., 2010; Pritts & Susman, 2003). Due to the fear of gaining weight and becoming fat, even when emaciated, AN patients are often characterized by performing self-starvation and excessive weight-loss behaviors (National Eating Disorder Association, 2010).

BN is characterized by repeated episodes of binge eating followed by inappropriate compensatory behaviors such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise (Kugu *et al*., 2006).

The estimated prevalence of eating disorders (ED) is 1% with an incidence of eight cases per 100,000 population per year for AN and 12 cases per100, 000 population per year for BN (Fabbian *et al*., 2011). Respective lifetime prevalence rates for full and partial anorexia nervosa in women range from 0.9% to 4.3% and from 1.5% to 7% for full and partial bulimia nervosa (Ahren-Moonga *et al*., 2009).

In survey carried out in a adolescent Italian females, 0.2% AN, 2.3% BN prevalence rates were found (Vego Alonso *et al*., 2005). Eating disorders often begin during high school or college, when patients are in their teens and 20s, although earlier and later onset also occur (Joac &Carla, 2009). Especially, college students typically express concerns about body image, body shape, body size, and weight control. The incidence of eating-related problems among college women is well documented (Uzun *et al*., 2006). In some studies previously

conducted, the prevalence of ED among university students has been reported to vary between 3.5% and 28.5% (Celikel *et al*., 2008). In line with previous studies, sociocultural influences were also found to be significantly related to body change strategies and eating disorder (Maccabe & Ricciardelli, 2003). Societal ideals and values concerning weight and body shape vary among different cultures. Eating disorders appear to be more prevalent in industrialized societies where there is an abundance of food and where beauty and ttractiveness are linked to a thin ideal (Joac &Carla, 2009).

Study Aim or Purpose

The present paper has been carried out to investigate the prevalence of eating disorders (anorexia nervosa, bulimia nervosa) among the female students of Islamic Azad University, central Tehran branch. Therefore, findings of the present study will provide a baseline data regarding ED for other researchers.

Methods

Design

The research is a descriptive study with the objective of investigating the prevalence of eating disorders among the female students of the Islamic Azad University, central Tehran branch**.**

Data collection & sample

This study was conducted in Tehran, the capital of Iran. The population of the research includes all the female students of Islamic Azad University, central Tehran branch studying in different fields (3000 person). The sample of the research includes 400 students selected using Stratified Random sampling method in proportion to the frequency of the population of the research.

The research is a descriptive study with the objective of investigating the prevalence of eating disorders among the female students of the Islamic Azad University, central Tehran branch. Therefore, the researcher received a recommendation letter from the university chancellor and partook in the environment of the research, selecting the researched units which had the required specifications and then provided the subjects with the demographic questionnaires, Eating attitudes test and diagnostic questionnaire of eating disorder, extracted the necessary information and ultimately reviewed the results using methods and statistical analysis. Before the initial evaluation, the importance of eating attitude and the nature of the study were explained to all subjects, and they were asked to fill out a self-report questionnaire as honestly and accurately as possible, with the assurance of confidentiality. Then, informed consent was obtained from all participants and confidentiality was ensured.

Measures

Demographic characteristics

Demographic characteristics include age, marital status, body mass index (height and weight,) field of study, current lodging during education period, educational and the occupational status of the parents. The Body Mass Index [BMI=weight (kg)/ height (m) ^{2}] was obtained from self-reported data on weight and height using self-reported heights and weights. The CDC weight categories:

Underweight <18.5, normal 18.5-24.9, overweight 25.0-29.9, and obese > 30.0 were used in assessment of Participants' weight status (Center for Disease Control and Prevention, 2009).

The Eating Attitude Test

The Eating Attitude Test (EAT-26) assesses a broad range of symptoms of anorexia nervosa and bulimia nervosa. The scores are ranked on a six-point scale from always to never, with 3 points allotted to‘ always', 2 points to 'very often', 1point to 'often', and 0points to the others. Questions on the EAT range in possible scores from 0to 78, with the clinical cut-off point being 20 (higher score reflect more disordered eating attitude).

Respondents rate the frequency of each item on a 6-point scale from always to never, with 3point allotted to always, 2point to very often, 1point too often and 0point to others. The EAT is a screening tool developed to detect eating disturbances in non-clinical settings, where a score of 20 or above indicates negative eating attitudes and possible eating disorder (Garner *et al*.,1982;Mintz & Halloran , 2000).

This global scale exhibited satisfactory internal consistency for the current sample (α=0.85).

In Iran, based on the results test-retest, the correlation of the scores of EAT-26 in the studied group is 0.91 which shows a desirable reliability (Nobakht & Dezhkam, 2000).

The Eating Disorder Diagnostic Inventory (EDDI)

It's a questionnaire which is used by the researcher based on the DSM-IV-TR (*Diagnostic Statistical Manual of Mental Disorders* fourth edition-text revision) and ICD-10 (The International Classification of Diseases 10) to diagnose anorexia nervosa and bulimia nervosa and has been used in the present study after conducting reliability and validity and thus the people suffering from eating disorders could be identified. The aforementioned questionnaire has been used by Nobakht and Dezhkam in 2000 in the research on eating disorders among the youths and showed a favorable reliability (Nobakht & Dezhkam, 2000). In this research,

the test-retest reassessment method was used to measure the reliability of the questionnaire and the results show the value of 0.97 for correlation.

Data Analysis

To carry out statistical analysis, the SPPS statistical application (version 16) was used with descriptive statistics, preparing tables, the distribution of relative frequency, average, standard deviation and the inferential statistics of chi- square (X^2) and fisher exact tests were used to assess the relationship between the variables. For all analyses $\alpha \leq 0.05$ was used as statistically significant difference between groups.

Ethical considerations

The ethics committee of Islamic Azad University, Tehran Medical Branch gave permission for the study. Other ethical issues in this study involved the assurance of confidentiality and anonymity for the participants. The participants were given verbal and written information about the study. They had the right to withdraw from the study at any time during or after the interviews and All participants were informed of the purpose and design of the study and the voluntary nature of their participation and their anonymity would be preserved during and after the study.

Results

The results related to the personal information section and the demographics of studied units show that the majority of the people on whom the research was conducted (76.5%) were in the age range of 20 to 25 with the mean 22.07 (SD= 2.85).Most student's BMI (N=309; 77.3%) were within the normal range category, 54(13.5%) were underweight, 32 (8%) were overweight, and 5(1.3%) were obese.

The majority of the students surveyed (23.5%) were studying psychology and the majority of them (96.3%) were living with their families.

Table 1. Socio-demographic characteristics of students by status of disordered eating.

Sociodemographic	Disordered Eating yes n (%)	no n (%)	total n (%)	Statistical analysis X^2 p-value
Age				
<25	75 (21.4)	275(78.6)	350(100)	0.03;0.8
>25	10(22.7)	34(77.3)	44(100)	
Marital status				
single	70(21.5)	256(78.5)	326(100)	0.01;0.9
married	15(22.1)	53(77.9)	68(100)	
BMI				
Underweight	3(5.8)	49(94.2)	52(100)	
normal	72(23.6)	233(76.4)	305(100)	F*=10.8;0.009
Overweight	9(28.1)	23(71.9)	32(100)	
obese	1(20)	4(80)	5(100)	
Lodging during education period				
With family	83(21.9)	296(78.1)	379(100)	
Without family	2(13.3)	13(76.7)	15(100)	F*=0.62;0.7
Father's occupation				
Worker	34(17.5)	160(82.5)	194(100)	3.70;0.05
Non-worker	51(25.5)	149(45.5)	200(100)	
Mother's occupation				
Housewife	63(20.1)	250(89.9)	313(100)	1.88;0.1
Worker	22(27.2)	59(72.8)	81(100)	
Father's education				
Illiterate and elementary school	6(17.1)	29(82.9)	35(100)	
Secondary school and high school	7(11.5)	54(88.5)	61(100)	6.8;0.07
diploma	51(22.5)	176(77.5)	227(100)	
Junior college diploma or higher	21(29.6)	50(70.4)	71(100)	
Mother's education				
Illiterate and elementary school	5(16.7)	25(83.3)	30(100)	4.15;0.2
Secondary school and high school	8(17.8)	37(82.2)	45(100)	
diploma	33(18.9)	142(81.1)	145(100)	
Junior college diploma or higher	39(27.1)	105(72.9)	177(100)	

*Fisher exact test

Moreover, the fathers of 45.3% of the students were self-employed and the mothers of 80% were housewives. The education of the 44.8% of fathers and 85.3% of mothers of the students was diploma. It's noteworthy that 82.8% of the students were single and 17.3% were married. Based on the rated scores of the EAT-26 eating attitude questionnaire findings show that 78.4% of the students surveyed scored less

than the cutting point of 20 and 21.5% scored more than the cutting point of 20. Therefore, 21.5% of the students have disordered eating attitudes and the probability of being afflicted by eating disorders. Based on the (EDDI), the statistics showed that 1.8 percent of the samples suffered from anorexia nervosa and 7.8 percent suffered from bulimia nervosa. The relationship between the demographic characteristics (age, marital status, body mass index, lodging during the education period, parent's occupational status, parent's education and interestedness in field of study) and eating disorder is shown in the Table 1. As the findings presented in the table bottom show, the variable of eating disorder is only significantly related to the variable of BMI (p= 0.009) and father's occupation (p = 0.05).

Discussion

In our country, in the field of eating disorder, few studies have been carried out. This is the first study which investigates the eating disorder among the Iranian students. In the present study, the average body mass index is 21. 24(SD=2.77) which is almost compatible with the average body mass index in the findings of the researches done by (Kiziltan *et al*.,2005) (23.7 ± 3.9) and (Young *et al* .,2010)in Korea (19.26 ± 2.90).

As it was mentioned, in the present study, the majority of students surveyed based on the EAT-26 questionnaire (78.4%) scored below the cutting point of 20 and 21.5% scored a cutting point of more than 20 which means that 21.5% of the people had disordered eating attitudes and were inclined to be affected by eating disorders. In measuring the prevalence of eating disorders amongst high school students (male and female) in Sari- North of Iran-In the academic year of 2002-2003 in 10.5% of the students, abnormal attitude towards eating was observed (Zarghami &Chyme ,2003).

In their study on the students of the Islamic Azad University, Tonekabon branch (IRAN), Fadavi Roodsari and Ast(2011) reported that based on EAT-26 questionnaire, 20.3% of the students had disordered eating attitude and there's the possibility that they may be afflicted by eating disorder; however, the stats of the attitude of disordered eating in various countries is reported as follows.

UAE (24%) (Justin *et al*., 2010); (23.4%) (Eapen *et al*., 2006); Chinese (3.2%) (Liao *et al*., 2010); SouthKorea (7%) (Yang *et al*., 2010); Greek (16.7%) (Bilali *et al*., 2010); Germany (26/1%) (Rosendahl & Bormann, 2009); American (12.64%) (Sira & Pawlak, 2010); Turkey (6.8%) (Tozun *et al*., 2010); Brazil (17.4%) (Nunes *et al*., 2005).

On the other hand, our finding was concordant with the results of western society's studies that have shown the prevalence of disordered eating attitudes to be 7%to20% among female college students (Uzan *et al*., 2006). Based on the results of our study, the statistics of disordered eating attitudes is similar to European and Western countries and even larger than them. The results of the diagnostic questionnaire of eating disorder in our study showed that 1.8% of the students suffer from anorexia nervosa and 7.8% suffer from bulimia nervosa.

The prevalence of diagnosed eating disorders in various samples of college women has been reported to be 1.3% to5% although the speculation is that the prevalence is much higher (Fabbian *et al*.,2011).Kiziltan *et al* (2005) also believe that the prevalence of bulimia nervosa has been estimated to be as high as 20% in college populations and symptoms of binge eating have been detected in up to 90% of college women. In a study carried out in six European countries of France, Belgium, Italy, the Netherlands, Germany and Spain,(2010) the prevalence of anorexia nervosa and bulimia nervosa has been reported to stand at (7.4% and 2.3%),(6.3% and 2%), (5% and 2.2%), (3.3% and 0.9%), (2.1% and 0.8) and (4% and 1.5%) respectively[30]. In Hong Kong, Zhuoli and Wenfang have reported the prevalence of anorexia nervosa and bulimia nervosa to be 0.07% and 0.7% respectively (Zhuoli &Wenfang, 2010).

From the other hand, Liao in a 2010 study in China diagnosed 0.9% of the people suffering from eating disorder (Liao *et al*., 2010). In France, 4.15% of the female subjects had high EAT-26 scores. In Italy, 3.35% of the adults (male and female) had eating disorder (Preti *et al*., 2009). In a research done on the youths in Jordan, 0.6% of the samples suffered from bulimia nervosa (Yousef Mousa *et al*., 2010).

In an Australian study 9% percent of male student's report that they suffer from disordered eating and 2% meet the criteria to be diagnosed with clinical Bulimia Nervosa.

Also between 11 and 20% of female American university students score high enough to indicate an eating disorder on the Eating Attitudes Test (Yager & O'dea, 2008).

The stats of the prevalence of eating disorder vary in different countries. Various factors can be the cause of such differences. These factors are more related to the etiology of these diseases. Among the most important factors are cultural factors such as the numerousness of cultures, the influence and penetration of the Western culture (especially through the media outlets), individual factors, social class and status, the status of the society's growth and development, pervasive models in the society such as fashion and traditions, contact with the foreign cultures and the age group of the samples studied. The most recent reports, however, suggest that the

incidence of eating disorders is becoming increasingly common among women from non-western population (uzan *et al*., 2006). Given the statistics and issues just raised, the high rate of eating disorders in Iran may be a consequence of the influence of western culture which demands more extensive research in this field. The Influence of western culture from media on the other hand, may add stress to the general difficulties of adolescence and perhaps contribute to the development of eating disorders. Such a conflict between western values and Islamic traditions has also been suggested as a factor contributing to the high prevalence of BN in Asian girls (Nobakht & Dezhkam, 2000). Since based on the findings of the present research, the rate of eating disorders in the Iranian students is compatible with many studies carried out in the Western communities and is even higher than many countries, it seems that now a high level of vulnerability against eating disorders exists among the women, especially the students. By investigating the relationship between the aforesaid variables and eating disorders, a statistically significant relationship was found between the body mass index and fisher test (F= 10.8, p= 0.009). As it was depicted in the Table 2, the majority of people with overweight (28.1%) suffered from eating disorder in the division of body mass index. In the young girls, being overweight has been found to consistently predict body dissatisfaction and disordered eating behavior (Golden, 2003). Zarghami and Chimeh (2003) in their study found a statistically significant relationship between BMI and eating disorder (p= 0.001). The results of their studies showed that abnormal attitude toward eating can be found more in the obese and extremely obese people as compared to normal people.

Furthermore, Muris *et al*. (2005) reported that there's a statistically significant relationship between BMI, eating disorders and extensive efforts made to reduce weight (p< 0.001).

As it was mentioned earlier, in the present research, a statistically significant relationship was seen between the occupational status of the father with eating disorder and the results of chi square test (X^2=3.7, df =1, P=0.05) which is in accordance with the findings of Nobakht study (2000).No statistically significant relationship existed between the variables studied (age, marital status, the lodging situation during the education period, mother's occupational status, parent's education and interestedness in the field of study) and the variable of eating disorder. In their study, wildes (2005) also failed to find a statistically significant relationship between the control group and the group suffering from bulimia nervosa in terms of age (p= 0.2). Moreover, in their study,(tozun *et al*., 2010)found no statistically significant relationship between the variables of age, lodging situation and mother's occupational status with the variable of eating disorder.

In the present research, no significant relationship was observed between eating disorders and the variables indicating economic–social conditions (mother's occupation, parent's education and the lodging situation). As the other studies have shown, this is influenced by the cultural effects which include all economic– social levels, particularly the impact of the mass media (movies, TV, satellite channels, internet etc.) which has engaged almost all levels.Sociocultural change includes westernization or modernization and urbanization(Blowers *et al*.,2003).

The media serve as a strong source of information about cultural norms and ideals, adolescent boys and girls often look to the media for information about their role and value in society in an attempt to become what would be considered most socially desirable (Muris et al.,2005).Internalization of the thin ideal has consistently been found to predict levels of body dissatisfaction and eating disturbance (Golden , 2003).

The sociocultural factor-families, peer and the media have recently appeared as the three primary risk factors influencing body image and disordered eating behaviours (Wildes et al., 2005).

In line with previous studies, sociocultural influences were also found to be significantly related to body change strategies and eating problems (Makino et al., 2004; Maccabe & Ricciardelli, 2003). Social pressure to be thin is higher for females then males; thus, college females are more likely to perceive them to be overweight and will more often attempt to lose weight (Sira & Pawlak, 2010).

Accordingly, given the process of globalization and the development of Information Technology, the geographical boundaries are setting about to fade out and the non-Western nations and especially the youths in these societies are more exposed to the Western culture. Unquestionably, the models of media such as beauty and sex and health technologies have an impact on dissatisfaction with the body and unhealthy nutrition and weight control and ill-mannered behaviors in vulnerable men and women (Warren *et al*., 2010). The issue which has been taken note of in various studies is the impact of cultures' development (especially the Western culture) and the phenomenon of globalization on the increasing of problems related to the attitude and behaviors and eating disorders in such a way that eating disorders have been considered phenomena influenced by the cultures. Striegel-Moore and Smolark (2001) believe that eating disorders are more of culture reactive phenomena rather than culture-

bound phenomena and therefore a special attention should be paid to the growth of problems related to eating and body image in the developing societies.

It seems that with the growth of intercultural relations and penetration of Western patterns in Iran, the prevalence of the phenomenon of unnatural eating has also increased progressively. This unnatural attitude will turn into a disorder and bring about serious consequences for the person if it's not treated and cured appropriately; therefore, paying attention to the issue of preventing the occurrence of such disorders and putting aside its underlying factors is immensely important.

Conclusion

Therefore, necessary measures should be taken and educating the people in the form of programs of raising the public awareness, using mass media and educational instruments such as movies, pamphlets and posters to increase the knowledge of this important group of people to preclude the pandemic of eating disorders and problems related to disordered eating attitudes should be taken into consideration by the experts and nutrition managers.

Acknowledgements

The authors thank all the participants in this study for their time, the, Islamic Azad University central Tehran branch, Islamic Azad University Tehran Medical Branch.

References

1. Ahren-Moonga j, Silverwood R, Klinteberg B, and Koupil.Association of Higher Parental and Grandparental Education and Higher School Grades With Risk of Hospitalization for Eating Disorders in Females. *American Journal of Epidemiology*. 2009; **170**:566-575.
2. American Psychiatric Association.*Diagnostic and statistical manual of mental disorders*.IV-Text Revision ed.Washington:2000.
3. Ast R,Fadavi Roodsari A.Prevalence of Eating Disorder among female students of Tonekabon University (Tonekabon-Iran).*International Journal of Scientific & Engineering Research*. 2011;**2**:1-4.
4. Babaee S. Relationship between core beliefs and ability to eat with symptoms of eating disorder in students of shahid beheshti University, General psychology Senior thesis, 2006(in Farsi).
5. Bilali A,Galanis P,Velonakis E.Factors Associated with Abnormal Eating Attitudes among Greek Adolescents.*Journal of Nutrition Education and Behavior*.2010;**42**:292-298.
6. Blowers LC ,Loxton NJ,Grady-Flesser. M, Occhipinti S, Dawe S.The relationship between socio cultural pressure to be thin and body dissatisfaction in preadolescent girls.*Eating Behavior*. 2003;**4**:229-244.
7. Celikel FC, Cumurcu BE, Koc M, Etikan I, Yucel B. Psychological correlates of eating attitudes in Turkish female college students. *Compr Psychiatry* 2008; **49**:188-194.
8. Center for Disease Control and Prevention [Internet]. *Healthy weight assessment for adults*. [cited 2009 January 27]. \http://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html.
9. Chakraborty, K, & Basu, D.Management of anorexia and bulimia nervosa: An evidence-based review. *Indian Journal Psychiatry*. 2010; **52**:174-86.
10. Fabbian, F,Marco P,Giovanni S, Manzato E, Longhini C.Francesco Portaluppi. Estimation of Renal Function in Patients with Eating Disorders. *Int J Eat Disord* .2011; **44**:233–237.
11. Garner DM, Olmsted MP, Bohr Y, Garfinkel PE. The eating attitude test: Psychometric features and clinical correlates. *Psychol Med*. 1982; **12**:871-878.
12. Golden NH. Eating disorders in adolescence and their sequelae. *Best Pract Res Clin Obstet Gynaecol* .2003; **17**: 57-73.
13. Hoek HK, Hoeken D. Review of the prevalence and incidence of Eating disorders. *Int J Eat Disord*. 2003; **34**:383–396.
14. Ho TF, Tai BC, Lee EL, Cheng S, Liow PH. Prevalence and profile of females at risk of eating disorders in Singapore. *Singapore Med J* .2006; **47**:499-503.
15. Joac.urbancic,Carla j.*womens mental health a clinical guide for primary care providers*. philadelphia: wolthers kluwer, lippencott.williams&wilkins,2009.
16. Justin T,Salim K,Amami Ahmed.Eating attitude and body image concerns among female university students in the United Arab Emirates. *Appetite*.2010;**54**:595-598.
17. Klein DA,Walsh BT.Eating disorders: clinical features and pathophysiology.*Physiol Behav* 2004;**81**:359-74.
18. Kiziltan G,Karabudak E,Unver S,Sezgin E,Unal A. Nutritional status of university students with binge eating disorder.*Ankara Universitesi Tip Fakultesi Mecmusi*. 2005;**58**:167-171.
19. Klein DA,Walsh BT.Eating disorders: clinical features and pathophysiology. *Physiol Behav* 2004;**81**:359-74.
20. Kugu N, Akyuz G,Dogan O,Ersan E,Izgic F.The prevalence of eating disorers among university students and the relationship with some individual characteristics. Australian and Newzeland. *Journal of Psychiatry*. 2006; **40**:129-135.
21. Liao Y, Knoesen NP, Castle DJ, Tang J, Deng Y, Bookun R, Chen X, Hao W, Meng G, Liu T. Symptoms of disordered eating, body shape, and mood concerns in male and female Chinese medical students. *Compr Psychiatry*. 2010; **51**:516-523.
22. Maccabe MP, Ricciardelli LA.Sociocultural influences on body image and body changes among adolescent boys and girl. *The journal of social psychology* .2003; **143**:5-26.
23. Makino M, Tsuboi K, Dennerstein L.Prevalence of Eating Disorders: A Comparison of Western and Non-Western Countries. *Med Gen Med*. 2004; **6**:49-59.
24. Muris P,Meesters C,Van de blom W,Mayer B. Biological. psychological and sociocultural correlateds of body change strategies and problem in adolescent boys and girls. *Eating Behaviors*. 2005; **6**:11-22.

25. Mintz LB, O'Halloran MS. The Eating Attitudes Test: Validation with DSM-IV eating disorder criteria. *J Pers Assess*. 2000;**74**:489–503.
26. National Eating Disorder Association. 2010. Retrieved from www.national eating disorder .org
27. Nobakht M, Dezhkam M. An epidemiological study of eating disorders in Iran. *Int J Eat Disord* .2000; **28**:265-271.
28. Nunes MA,Camey S, Olinto M.T.A, Mari JJ.The validity and 4-year test-retest reliability of the Brazilian version of the Eating Attitudes Test-26. *Braz J Med Biol Res*.2005;**38**:1655-1662.
29. Preti A A, Girolamo G , Gemma VC,h, Jordi Alonso c,h, Ron de Graaf d,Ronny Bruffaerts e, Koen Demyttenaere e, Alejandra Pinto-Meza f, Josep Maria Haro f,Piero Morosini g.The epidemiology of eating disorders in six European countries: Results of the ESEMeD-WMH project The ESEMeD-WMH Investigators 2009.*Journal of Psychiatric Research*. journal homepage: www. elsevier. Com /locate/ jpsychires.
30. Pritts, S. D., & Susman, J.Diagnosis of eating disorders in primary care. *American Family Physician*. 2003;**67**:297-304.
31. Rosendahl JB, Bormann K.Dieting and disordered eating in German high school athletes and non-athletes. *Scandinavian Journal of Medicine & Science in Sports* .2009;**19**:731-739.
32. Sira N, Pawlak R.Prevalence of overweight and obesity, and dieting attitudes among Caucasian and African American college students in Eastern North carolina: A cross-sectional survey**.** *Nutr Res Pract* 2010;**4**:36-42**.**
33. Striegel-Moor R,Smolark L.Eating disorders:New directions for research and practice. Washington, DC: American Psychological Association,2001.
34. Sutherland C, Sue Hinchliff S, Hinchliff M, Rogers R. *Womens Health; A Hand Book for Nurses*. Edinburgh London new York Philadelphia St Louis Sydney Toronto,2001.
35. Thomas CL,James AC,Bachmann MO.Eating attitudes in English secondary school students: influences of ethnicity, gender, mood, and social class. *Int J Eat Disord* .2002; **31**: 92-6.
36. Tozun M, Unsal A, Ayranci U, Arslan G. Prevalence of disordered eating and its impact on quality of life among a group of college students in a province of west Turkey.*Salud publica de Mexico*. 2010;**52**:190-198.
37. Uzun O, Güleç N, Ozşahin A, Doruk A, Ozdemir B, Calişkan U.Screening disordered eating attitude, and eating disorder in a sample of Turkish female college students. *Comperhensive Psychiatery* 2006; **47**:123-126.
38. Valsamma Eapen AT, Abdel Azim Mabrouk B, Salem Bin-Othman B.Disordered eating attitudes and symptomatology among adolescent girls in the United Arab Emirates.Eating *Behaviors* 2006;**7**: 53–60.
39. Vega Alonso AT,Rasillo Rodriguez MA. Prevalence and risk profile among secondary school students**.** *Social Psychiatry Psychiatr Epidemiol*. 2005;**40**:980-987.
40. Wildes j,Simons A, Marcus M.Bulimic symptoms, cognitions, and body dissatisfaction in women with major depressive disorder.*Int j Eat disorder* 2005; **38**:9-17.
41. Warren CS, Schoen A ,Schafer KJ .Media Internalization and Social Comparison as Predictors of Eating Pathology Among LatinoAdolescents: The Moderating Effect of Gender and Generational Status . *Sex Roles* .2010; **63**:712–724.
42. Wang Z, Byrne N.M, Kenardy J, Hills A. P.Influences of ethnicity and socioeconomic status on the body dissatisfaction and eating behaviour of austarlian children and adolecente. *Eating Behaviors*.2005; **6**:23-33.
43. Wood, k. Effects of a media intervention program on the body image and eating attitude among children. *Journal of undergraduate research*.2004;**6**:1-6.
44. Yager Z, O'dea JA.Prevention programs for body image and eating disorders on University campuses: a review of large, controlled interventions. *Health Promotion International*. 2008;**23**:173-189.
45. Yang SJ, Kim JM, Jin-Sang Yoon.Disturbed Eating Attitudes and Behaviors in South Korean Boys and Girls:A School-Based Cross-Sectional Study. *Yonsei Med J*.2010;**51**: 302-309.
46. Yousef Mousa T, Abdullah Al-Domi H, Mashal RH,AbdelKhaleq Jibril M .Eating disturbances among adolescent schoolgirls in Jordan. *Appetite*. 2010; **45**:196-201.
47. Zarghami M,Chyme N. Prevalence of non-natural approach to eating and the factors correlated with the high school students,2002, Journal of Mazandaran UniInternational Journal of Scientific & Engineering university of medical sciences. *Autumn*. 2003 ; **13**:70-78 (in Farsi).
48. Zhuoli T, Wenfang Z .Eating attitudes and weight concern among Chinese middle-age women: A comparison between different age and BMI groups. *Eur J Psychiat*.2010; **24**:146-157.

9/20/2012

Effect of Presence of Trained Significance Others on Labor Outcomes and Mother's Satisfaction

Aida abd El-Razek,

Department of Maternal and Newborn Health Nursing, Faculty of Nursing, Menoufyia University
dr_aalrazek@yahoo.com

Abstract: Objective: To evaluate the Effect of Presence of trained significance others on labor outcomes and mother's satisfaction. **Intervention study design** the study was conducted at MCH of El-Basher Hospital and labor unit of El-Basher Hospital /Amman Jordon. **Subjects:** The total subjects of this study were 150 parturient women were divided into equal groups, intervention group 75 mothers who received supportive measures during labor by trained significance others choice and control group 75 mothers who not received Comfort measures during labor by trained significance others choice. A simple random sample was used. The data was collected through a period of 10 months started from July 2009 to April 2010 for 3 days per week starting at 9 am to 2 pm. **Inclusion criteria were:** primiparous pregnant women with a single, term live cephalic fetus; in active labor – cervical dilation ≥3 cm and ≤6 cm; intact membranes or amniorrhexis of ≤2 hours; uterine height < 40 cm; no evidence of cephalic-pelvic disproportion or fetal distress. **Exclusion criteria were:** unavailability of a Presence of trained significance others choice; fetal malformation; maternal disease and/or indication for elective Caesarean section. **Criteria for significant other**: educated, healthy, female. **Results** of the study revealed that mother's satisfaction, a highly significant relation was observed between intervention and control groups. There was significance difference between intervention and control groups concerning applying Comfort measures and knowledge regarding supportive measures, labor progress and effect in reducing the severity of labor pain and increase satisfaction and concerning mother's satisfaction, a highly significant relation was observed between intervention and control groups. **Based on the results of the present study, the following can be recommended:** Encourage and sensitize healthcare providers to adopt this practice in health institutions where such as supportive companion is not permitted or professional healthcare providers are designated to this role.
[Aida abd El-Razek. **Effect of Presence of Trained Significance Others on Labor Outcomes and Mother's Satisfaction.** *Life Sci J* 2012;9(4):2829-2837] (ISSN:1097-8135). http://www.lifesciencesite.com. 415

.**Keywords:** trained significance others in the delivery room, labor, mother's satisfaction

1. Introduction

The rates of maternal and neonatal mortality and morbidity decreased as a consequence of the adoption of modern obstetric practices, especially during labor and delivery. However, obstetrical interventions continued to increase, particularly the rate of Caesarean sections. Active management is based on the assumption that the preventive management of events that may potentially result in adverse effects in the mother or the fetus reduces the morbidity rates of both [1].

Comfort care defined as the care given to prevent, control, or relieve side effects and improve the women comfort and quality of life. While continuous labor comfort refers to non-medical care of laboring women throughout labor and birth by trained person [2]. Support provided during labor and delivery by professional healthcare workers, non-medical female attendants and trained women (doulas) assigned to this task has been evaluated in controlled studies [3]. Data suggest that the effects of support are associated with a reduction in the dissatisfaction or negative perception of women towards giving birth, in the use of analgesia/anesthesia, and in the frequency of instrumental vaginal delivery (forceps and vacuum extraction) and Caesarean section [3].

Based on scientific evidence, the World Health Organization recommends that the parturient should be accompanied by people she trusts and with whom she feels at ease possibly her partner, a friend, a doula, a nurse or midwife [4]. However, the effects of the comfort measures provided by the presence of the woman's chosen companion on her satisfaction, on the events of labor and delivery and on perinatal results have not yet been fully evaluated in controlled studies [5,6]. The usefulness of support and the type of support provided by family members, a partner or by friends of the woman have only been evaluated in observational studies [9].

A close female relative support a laboring women by providing emotional and physical comfort and staying by her continuously throughout labor and birth. Nurses work shifts so may not be present for an entire labor. In addition they have clinical responsibilities, and providing care to more than on laboring woman simultaneously [10]. Due to the paucity of evidence-based data available on the effects of the presence of a companion of the woman's choice during the birth process, especially in

developing countries, this study was developed to evaluate the influence of this support provider on the satisfaction of the parturient with labor and delivery and on perinatal and breastfeeding outcomes in the twelve hours following delivery.

Several authors recommended pharmacological measures during labor but these measures may harm fetal heart rate and maternal condition as well as it is an expensive measure [8]. So advanced evidence based on medical and nursing practice recommended to use the natural measures to relief labor pain which is non-pharmacological measure, not harmful to mother and her fetus and not expensive specially in developing countries like Egypt.

Significant of the study:

Presence of trained significance other to comfort and support mothers during labor was recommended by many authors [11]. Presence of significance other will enhance satisfaction leading to comfort and relieving of labor pain making labor enjoy full experience, with better fetal maternal outcome. Nurses can utilize evidence based researches to promote practices and train significance other to comfort and support laboring women to relief pain and providing adequate comfort measures for mothers throughout labor experience

Supportive care during labor plays an important role in moving back to the private arena of childbirth and the positive role of women during labor [12]. In addition to Presence of trained significance others in the delivery room has been shown to be one of the most beneficial practices in maternity care. It involves emotional support, comfort measures. Information, reassurance, encouragement, therapeutic touch, gentle assistance during moving and changing positions in labor and telling what's happening and giving feedback about the labor progress. These measures may enhance physiologic labor processes as well as women's feelings of control and competence, thus reduce the need for obstetric intervention and help in fulfilling the wishes of safety for mother and babies [7]. For these above reasons, the study of the effect of presence of trained significance others on labor outcomes and mother's satisfaction.

Aim of the Study

To evaluate the Effect of Presence of trained significance others on labor outcomes and mother's satisfaction.

Hypothesis:

The Presence of trained significance others will increase mother's satisfaction and improve labor outcome.

2. Subjects and Methods

Design:

An intervention study design was used to evaluate the Effect of Presence of trained significance others on labor outcomes and mother's satisfaction.

Setting:

The study was conducted on parturient women and their significant other during the last month of pregnancy then at labor unit of El-Basher Hospital and MCH of El-Basher Hospital Amman Jordon.

Subjects:

The total number of mothers who admitted to the labor unit of El-Basher Hospital and MCH of El-Basher Hospital Amman Jordon in the year 2008 was 1350 mothers. This number involved normal and high risk cases. So according to the study criteria the desirable sample size was calculated to the 150 mothers using type 1 error=0.05 and power of 0.80 and assuming the standard deviation of the (NRS=2).

The total subjects of this study were 150 parturient women were divided into equal groups, intervention group 75 mothers who received comfort measures during labor by trained significance others choice and control group 75 mothers who not received comfort measures during labor by trained significance others.

Type of sample:

A simple random sample was used.

Inclusion criteria were: primiparous pregnant women with a single, term live cephalic fetus; in active labor – cervical dilation ≥3 cm and ≤6 cm; intact membranes or amniorrhexis of ≤2 hours; uterine height < 40 cm; no evidence of cephalic-pelvic disproportion or fetal distress. Exclusion criteria were: unavailability of a Presence of trained significance others choice; fetal malformation; maternal disease and/or indication for elective Caesarean section. Criteria for significant other: educated, healthy, female

Sample Technique:

The data was collected through a period of 10 months started from July 2009 to April 2010 for 3 days per week starting at 9 am to 2 pm. The researcher introduced herself to the pregnant mothers and significant other obtained their consent to be recruited in the study after explaining the aim of the study. Each mother of the intervention group was interviewed individually by the researcher and provided by theoretical information about comfort measures during labor. The average time for filling each sheet was about 25 minutes depending on the response of the mother while the training significant other including 1 session to provide the theoretical information regarding labor supportive measures it assumed 30 minute. While 2nd session involved

training of significant other about comfort measures (back massage, breathing exercise, relaxation, teaching technique of bearing down, changing position, fluid intake, and immediate of breast feeding demonstrated on mothers herself. It was consumed 1 hour then the researcher assess significant other correct practice and if needed re-demonstration of measures was repeated to be sure that the significant other perfectly practices the comfort measures.

A card was given to the significant other including researcher phone number to be easily contacted with the researcher when parturient women admitted to labor unit in hospital.

Tools:

Two tools were used for data collection:

I. The first tool:

An interviewing questionnaire was developed based on the review of relevant literature, to evaluate the effect of presence of trained significance others on labor outcomes and mother's satisfaction.

Part 1:

Addressed information related to general characteristics data such as age, occupation, level of education.

Part 2:

Assessed mother's obstetrical histories.

Part 3:

Assessed mother's knowledge regarding containing information on: the activities involved in providing support to the woman (stay beside her, provide support, be affectionate, keep her calm, massage her, stimulate and encourage her), expected behavior when confronted with signs of tiredness, anxiety, concern, crying, screaming and/or the woman's feelings of inability to cope; compliance with regulations (use of standardized clothing, no eating, no smoking, no touching the equipment or material, contact the nursing staff if need to leave); and the possibility of requesting information from staff. The need to preserve the privacy of the other women was also emphasized. There were no specific instructions for the health professionals.

II. The second tool:

The tool was developed by the researcher for data collection after extensive review of the relevant literature. The outcomes included satisfaction, assessed by asking the woman about how she felt during labor and delivery (evolution of labor, having a presence of trained significance others or not, instructions received from doctors and nursing staff, healthcare provided and type of delivery). These questions were answered by choosing one of a sequence of five symbols with facial expressions corresponding to "very dissatisfied", "dissatisfied", "satisfied", "well satisfied" and "very satisfied". Satisfaction assessment was carried out between 12–24 hours post delivery at rooming-in care unit. For the purpose of analysis, satisfaction was considered to have been achieved whenever the answers of "well satisfied" or "very satisfied" were given [10,7,8]. We collected data on the following outcomes: duration of first stage of labor; amniotomy in relation to the time of hospital admission and cervical dilation; color of amniotic fluid; use of oxytocin in relation to cervical dilation; time of analgesia in relation to cervical dilation and time of admission to hospital; presence of functional dystocia and changes in fetal wellbeing; length of the second stage; time between hospital admission and delivery; time from analgesia until delivery; type of delivery (vaginal/Caesarean). Neonatal outcomes were: Apgar score at 1 and 5 minutes, birth weight, admission to the neonatal intensive care unit (NICU), and immediate mother-infant contact following delivery. Variables regarding breastfeeding were: the ability of the infant to take the breast and suckling in the delivery room and in the 12 hours following delivery, cracked nipples and the number of breast-feeds in the first 12 hours.

Ethical Considerations:

The study was carried out with co-operation of different levels of authority. An official letter was sent from the Dean of the Faculty of Nursing in Philadelphia University to the directors of El-Basher Hospitals explaining the aim of the study and the time of data collection seeking his permission for data collection. An official permission through written letters clarifying the purpose and sitting of the study was obtained from the directors of El-Basher Hospital. As an approval for data collection.

A written informed consent was obtained from the participants after explaining the purposes of the study, which include: no harm was occurring to participant, do not contradict with the cultural, traditional and religious issues, human rights were reserved, and data was confidential and used mainly for the purpose of the research. (It should be potted at the end of this topic)

Pilots study:

The pilot study was carried out 10 women of sample size to test the reliability and applicability of the tools, to identify any ambiguity of the questions and to evaluate the feasibility and clarity of the tools, and then the tools were modified according to the results of the pilot study.

Filed work:

- Development of tools for data collection after reviewing the related literature. The tool was revised for content validity by 5 experts in the field.
- The women's was selected by simple random according to the mentioned criteria.

- The researcher was meeting each woman and her trained significance others individually during the last month of pregnancy, to explain the aim of the study. The comfort measures included back massage, breathing exercise, relaxation, teaching technique of bearing down, changing position, fluid intake, and immediate of breast feeding.
- Beside discussion and lecture to improve trained significance others knowledge, brochure was used for teaching each significance others the comfort measures. Each trained significance others would receive brochure with information , to facilitate the learning and application
- While trained significance others practice training was conducted firstly by the researcher through role play approach utilization of comfort measures during labor on women then after that the trained significance others perform measures on the same women and if there was a mistake the researcher comfort re-demonstrate supportive measures again to be sure that the trained significance others understand the application of comfort measures.
- In labor unit the researcher stay beside the trained significance others while providing comfort measures to mother to be sure that she was conducted it perfectly, their performance was assessed by using observation checklist.
- Evaluation of labor progress and satisfaction for parturient women in both groups.

Limitation of the study:

- Three women and trained significance others were refused to attend the pre intervention session.
- Negative attitude of nurse's staff regarding presence of trained significance others during labor

3. Results

Table 1: show that, mean age of women in intervention and control groups was 20.40 ± 3.37 and 26.32 ± 4.29 years, respectively. Also, there were no significant differences among the two groups in the study regarding age, educational level and occupation.

Table 2: show that, mean age of trained women (significant other) in intervention and control groups was 24.40 ± 4.37 and 25.32 ± 4.29 years, respectively. Also, there were no significant differences among the two groups in the study regarding age, educational level and occupation.

Table 3: Illustrate that, most of significant other in pre antenatal classes had incorrect knowledge about definition of normal labor and importance of labor support (80% and 77.3%). While in post antenatal classes most of them had correct answer regarding both definition of labor comfort and importance of labor support (92% and 93.3%). Also significant difference were observed between pre and post antenatal classes (p<0.001)

Table 4 illustrates that, the intervention group most of significant other had correct knowledge about definition of labor support and importance of labor support (92% and 93.3%) than control group (73.3% and 80%). Also significant difference were observed between pre and post antenatal classes (p<0.001)

Table (5): Show that, there were significant differences among two studies group regarding to application of comfort measures among intervention and control groups (x^2 23.570, 3.955, 4.167, 6.543, 12.74, 4.67 and 3.967 respectively) *statistically significant p <0.05 **Statistically highly significant p <0.001

Table 6 shows that, most of mothers who were crying and screaming were lower (20%, 6.7% and 33.3, 46.7) in intervention group than control group respectively during degree of cervical dilatation. Meanwhile the rates of women calm were significant higher in intervention group than control group.

Table (7): show that, there were significant differences among two studies group regarding pain intensity in relation to cervical dilatation CX 3-4 cm (11.570, 0.054* respectively), CX 5-7 cm (13.348 , 0.013* respectively) and CX 8-10 cm (12.671, 0.015* respectively)

Table (8): Means distribution among mothers according to their duration of labor/ hours among intervention and control groups. Show that the duration of labor during all stages of labor were significant difference among studied groups (p <0.05, p <0.001 respectively) for total hours

Table (9): show that, the mean of (APGAR score) at 5th minute and at 10th minute in intervention group were significant higher (6.9±1.1 and 8.8±1.3) than in control group (4.8±0.8 and 7.03±1.5).

Table (10): Regarding satisfaction with the birth experience, having a Significant trained other during labor and deliver were strongly associated with higher satisfaction in the intervention group. Also Show that, most of mothers in both groups were unsatisfied with nurses (55, 45 respectively). The women of this group were also more satisfied with the care they received during labor, with the medical guidance given during labor, with care received during delivery, and with vaginal delivery, than women in the control group.

Table (1): Number and percent distribution of women according to their general characteristics among the intervention and control groups

Items	Intervention Group n75		Control group n75		x^2	*P* value
	No	%	No	%		
Age/ year						
> 20	21	28%	15	20	3.83	>0.05
21 – 30	40	53.3	43	57.3		
31 – 40	10	13.3	12	16		
< 40	4	5.3	5	6.7		
Educational level						
Preparatory	34	45.3	28	37.3	2.90	>0.05
Secondary	26	34.7	33	44		
University	15	20	14	18.7		
Occupation						
House wife	50	66.7	55	73.3	1.35	>0.05
Working	25	33.3	20	26.7		

Table (2): Number and percent distribution of significant others according to their general characteristics among the intervention and control groups

Items	Intervention Group n75		Control group n75		x^2	*P* value
	No	%	No	%		
Degree of relation of the significant others						
Mother	40	53.3	35	46.7	3.85	>0.05
Sister	25	33.3	27	36		
Friend	10	13.3	13	17.3		
Age/ year						
21 – 30	10	13.3	17	22.7	3.55	>0.05
31 – 40	48	64	50	66.7		
< 40	17	22.7	8	10.6		
Educational level						
Preparatory	45	60	38	50.7	3.92	>0.05
Secondary	20	26.7	25	33.3		
University	10	13.3	12	16		
Occupation						
House wife	65	86.7	67	89.3	1.92	>0.05
Working	10	13.3	8	10.7		

Table (3): Number and percent distribution of significance others in intervention group according to their knowledge regarding comfort measures pre and post intervention classes

Items	**Pre intervention n 75**		**Post intervention n 75**		x^2	***P* value**
	No	**%**	**No**	**%**		
Definition of labor support						
Correct	15	20	69	92	17.45	0.001**
In correct	60	80	6	8 %		
Importance of labor support						
Correct	17	22.7	70	93.3	18.57	0.001**
In correct	58	77.3	5	6.7		

**Statistically highly significant P<0.001

Table (4): Number and percent distribution according to their knowledge regarding comfort measures among the intervention and control groups

Items	Intervention Group n75		Control group n75		x^2	*P* value
	No	%	No	%		
Definition of labor support						
Correct	69	92	20	26.7	23.35	0.001**
In correct	6	8	55	73.3		
Importance of labor support						
Correct	70	93.3	15	20	87.78	0.001**
In correct	5	6.7	60	80		

Table (5): Number and percent distribution of study sample regarding to application of comfort measures among intervention and control groups

Comfort measures	Intervention group n 75				Control group n 75				x^2	*P* value
	correct no75	%	In correct	%	Correct no75	%	In correct	%		
Breathing exercise	69	92	6	8	10	13.3	65	86.7	23.570	0.000**
Bearing down	74	98.7	1	1.3	38	50.7	37	49.3	3.955	0.052*
Back massage	66	88	9	12	20	26.7	55	73.3	4.167	0.054*
Change position	70	93.3	5	6.7	30	40	45	60	6.543	0.012*
Fluid intake	65	86.7	10	13.3	10	13.3	65	86.7	12.74	0.001*
Relaxation	59	78.7	16	21.3	50	66.7	25	33.3	4.67	0.054*
Early attachment	70	93.3	5	6.7	45	60	30	40	3.967	0.057*

*statistically significant *P* <0.05 **Statistically highly significant *P* <0.001

Table (6): Number and percent distribution of mothers according to vocalization during their degree of cervical dilatation among intervention and control groups

Items	Intervention group n 75		Control group n 75		x^2	*P* value
	No	%	No	%		
CX 3-4 cm						
Crying	15	20	25	33.3	4.891	0.015*
Screaming	5	6.7	35	46.7	4.345	0.049*
Calm or silent	55	73.3	15	20	4.089	0.053*
CX 5-7 cm						
Crying	10	13.3	25	33.3	3.456	0.056
Screaming	15	20	40	53.3	3.761	0.048*
Calm or silent	50	66.7	10	13.3	4.045	0.044*
CX 8-10 cm						
Crying	12	16	40	53.3	4.248	0.045*
Screaming	20	26.7	30	40	4.296	0.045*
Calm or silent	43	57.3	5	6.7	4.950	0.038*

*statistically significant *p*<0.05

Table (7): Number and percent distribution of mothers according to their intensity of labor pain among intervention and control groups in relation to cervical dilatation

Degree of pain	Intervention group n 75		Control group n 75		x^2	*P* value
	No	%	No	%		
CX 3-4 cm						
Mild pain	66	88	25	33.3	11.570	0.054*
Moderate pain	5	6.7	35	46.7		
Sever pain	4	5.3	15	20		
CX 5-7 cm						
Mild pain	30	40	10	13.3	13.348	0.013*
Moderate pain	40	53.3	40	53.3		
Sever pain	5	6.7	25	33.3		
CX 8-10 cm						
Mild pain	10	13.3	5	6.7	12.671	0.015*
Moderate pain	55	73.3	20	26.7		
Sever pain	10	13.3	50	66.7		

*statistically significant *p*<0.05

Table (8): Means distribution among mothers according to their duration of labor/ hours among intervention and control groups

Stages duration /hours	**Intervention group n 75**	**Control group n 75**	***t***	***P* value**
First stage	10.48±3.02	13.5± 2.6	5.14	0.05*
Second stage	0.99± 0.50	1.745± 0.42	7.4	0.001**
Third stage	0.12 ± 3.89	0.140± 8.538	5.6	0.05*
Total /hours	10.96 ± 2.13	20.34 ± 2.60	18.8	0.001**

*statistically significant *p*<0.05 **Statistically highly significant *P*<0.001

Table (9): Number and percent distribution of neonatal outcome (APGAR score) among intervention and control groups

Items	Intervention group n 75		Control group n 75		*t*	*P* value
	No	%	No	%		
(APGAR score) at 1 min						
≥6	3	4	30	40		
6-8	45	60	35	46.7		
≥8	27	36	10	13.3		<0.05
Mean ±SD	6.9±1.1		4.8±0.8		5.6	
(APGAR score) at 5th min						
≥6	O	0	25	33.3		
6-8	25	33.3	35	46.7		<0.05
≥8	50	66.7	15	20		
Mean ±SD	8.8±1.3		7.03±1.5		2.6	

*statistically significant $p<0.05$

Table (10): Number and percent distribution of mothers according to their level of satisfaction among intervention and control groups

Items	Intervention group n 75			Control group n 75			x^2	*P* value
	SA	AD	NS	SA	AD	NS		
General satisfaction	66	6	3	5	25	45	8.893	0.019*
Satisfied with self	45	10	20	5	10	60	7.340	0.057*
Satisfied with baby	69	4	2	40	20	15	14.371	0.011*
Satisfied with nurse	9	11	55	10	20	45	9.584	0.008*
Satisfied with significant other	70	4	1	50	15	10	8.66	0.013*
Satisfied with physician	45	20	10	2	8	65	10.515	0.010*

*statistically significant $p<0.05$; NB: SA= satisfy, AD= satisfy to some degree, NS = not satisfy

4. Discussion

The labor and delivery experience is one of the most significant events in women's life, and can have strong physical, emotional, and psychological effects. Traditionally, women experienced childbirth surrounded by significant others. These are usually women from their own family. This study aimed to evaluate the effect of presence of trained significance others on labor outcomes and mother's satisfaction.

These results show that the support provided by a presence of trained significance others choice during labor and delivery had a positive effect on her satisfaction with the birth experience. Although the opinion of the health professionals were not assessed systematically, it seems that this intervention was well-accepted by them. No previous training was offered to the health workers, and the trained significance others underwent no prior preparation. Therefore, the assistance the women in both groups received during labor and delivery was the standard care routinely provided in that hospital, and there were no changes in management. It is important to emphasize that this is not a study about doulas and if on one hand there is a general belief that a labor presence of trained significance others has always positive effects, there are,, on the other hand still a lot of health facilities where presence of trained significance others are not allowed, especially in developing settings. It was and still it is expected that the results of this study could help providers to acknowledge and respect women's rights during birth.

These results are explained by **Hodnett *et al*** [21] who stated that antenatal preparation and classes include information about childbirth process, option for medication based on pain relief. The present study revealed that a significant improvement in presence of trained significance others knowledge regarding comfort measures in labor pre intervention and post intervention this finding may attributed to, that antenatal classes have a positive effect in improving presence of trained significance others knowledge. This is supported by results from **Choquette**[26] who reported that, the embodied knowledge of companion as a first educator and trustworthy source of information form a basic source of knowledge.

The current study showed a shorter duration of total hours in intervention group. Mother had less of fear, good improvement in presence of trained significance others knowledge regarding comfort measures in labor. This is supported by *Eriksson et al. & Ministry of Health* [24,25]

who stated that trained companionship contributes to reduce tension and shorten labor.

In the intervention group the majority of presence of trained significance others applied different supportive measures correctly for pain relief such as technique of bearing dawn, breathing exercise, changing position, relaxation these measures

affect pain intensity and provide a sense of well being, sense of control, decreased tension, enhanced mood and provides more oxygen for mother and fetus Show that, there were significant differences among two studies group regarding to application of comfort measures among intervention and control groups this finding supported by several authors[23,27] who reported that, breathing exercise increases relaxation and relaxation increase pain tolerance, reducing anxiety, decreased catecholamine response, increased uterine blood flow and decrease muscle tension.

In addition many investigators [16,22] reported that, the women in the experimental group felt a more positive pushing experience than the women in the control group. As presence of trained significance others applied different supportive measures correctly for pain relief such as technique of bearing dawn, give a sense of control and confidence to parturient mothers that they were always pushing in the right way and right time and their bearing down efforts were helpful. This allowed them to be calmly and efficiently coordinate push strongly for as long as possible in every contraction.

The finding of the present study revealed a statistically significant difference regarding Apgar score among intervention and control groups. This result was in the line with ***Yuenyong et al*** [15] who reported that, newborn babies were benefited from the support that the mothers were receiving in labor and babies are less admitted intensive care units. The present study also, found that the presence of trained significance others applied early attachment as one of comfort measures during labor. This is supporting the new evidence from WHO [14] for the importance of early contact as a good practice which is useful and should be encouraged in cases of low risk and normal birth

The present study also, found that, most of mothers in both groups were unsatisfied with nurses due to lack of information provided and attention given. Sometimes mothers are left alone during labor, due to the nurse's workload clinical responsibilities paperwork and shortage in nursing staff and this may cause women's dissatisfaction with their healthcare and childbirth experience. Also , some researcher [13] Reported that satisfaction with childbirth has been linked to the amount of support provided to parturient mothers, the relationship between client and caregiver.

Satisfaction was more in intervention group than control group, this may due to knowledge and good preparation of presence of trained significance others applied different supportive measures correctly, so mothers expectation regarding childbirth are met. Also, may investigators [20] who stated that mothers, whose expectations about childbirth were met, are more satisfied, labor support can increase mother's positive experiences and level of satisfaction with child birth.

In the intervention group, women's greater satisfaction with the guidance received from the doctors during labor has also been identified in another study with a different population, evaluated when the woman was accompanied by a person of her choosing [18]. When doulas or professional healthcare workers are the support providers, instructions are generally supplied by these individuals [19,28]. Support also increased satisfaction with the care received during labor and delivery, and this finding is in agreement with data already reported [6]. When the women received support from nurses.

So our results stressed the importance of utilization of supportive measures. The presence of presence of trained significance others of the woman's choice had a positive influence on her satisfaction with the birth process and did not interfere with other events and interventions, with neonatal outcome or breastfeeding.

Conclusion & Recommendation

The fact that the women with support reported higher levels of satisfaction with the medical information/guidance they received indicates that perhaps there was a change in attitude. Perhaps because there was someone else in the room, medical staff were more forthcoming and user-friendly than when no support person was present. The comfort measures have a positive effect in reducing labor pain, increase women satisfaction and improve labor outcome.

In this study may provide a basis for implementing this practice to evaluate the Effect of Presence of trained significance others on labor outcomes and mother's satisfaction. Concerning mother's satisfaction, a highly significant relation was observed between intervention and control groups. There was significance difference between intervention and control groups concerning applying comfort measures and knowledge regarding supportive measures, labor progress.

Based on the results of the present study, the following can be recommended:

Encourage and sensitize healthcare providers to adopt this practice in health institutions where such as supportive companion in not permitted or professional healthcare providers are designated to this role.

Acknowledgements

The authors wish to acknowledge the support of coordination of improvement for graduated personnel), an agency of the labor unit and MCH of El-Basher Hospital Amman Jordon, Government which allowed the training and preparation of human

resources. In addition, also to the nurses, midwives, doctors and all member staff from the institutions involved in this initiative.

Corresponding author
Aida abd El-Razek,
Department of Maternal and Newborn Health Nursing, Faculty of Nursing, Menoufyia University
dr_aalrazek@yahoo.com

References

1. Arulkumaran S, Symonds IM; (1999): Psychosocial support or active management of labour or both to improve the outcomes of labour. Br J Obstet Gynaecol, 106:617-9.
2. Simkin, P., and Bolding, A., (2004): Update Women's Health, 49(6):489-504.
3. Enkin M, Keirse MJ, Neilson JP, Crowther C, Duley L, Hodnett E, Hofmeyer J; (2000): A guide to effective care in pregnancy and childbirth. 3rd edition. New York: Oxford on non pharmacologic approaches to relieve labor pain and prevent suffering. J Midwifery University Press.
4. Hodnett ED, Gates S, Hofmeyr GJ, Sakala C; (2003): Continuous support for women during childbirth (Cochrane Review). In The Cochrane Library. Oxford: Update Software; CD003766.
5. World Health Organization; (1996): Care in normal birth: a practical guide (Maternal and Newborn Health/Safe Motherhood Unit). Geneva: WHO;
6. Brüggemann OM, Parpinelli MA, Osis MJD (2005): Evidence on support during labor and delivery: a literature review. Cad Saúde Pública, 21:1316-27.
7. Hodnett ED, Lowe NK, Hannah ME, Willan AR, Stevens B, Weston JA, Ohlsson A, Gafni A, Muir HA, Myhr TL, Stremler R, (2002): Nursing Supportive Care in Labor Trial Group: Effectiveness of nurses as providers of birth labor support in North American hospitals: a randomized controlled trial. JAMA, 288:1373-81.
8. Odalea M Bruggemann, Mary A Parpinelli, Maria JD Osis, Jose G Cecatti and Antonio SC Neto; (2007): Support to woman by a companion of her choice during childbirth: a randomized controlled trialReproductive Health, 4:5 doi:10.1186/1742-4755-4-5
9. Hodnett, ED., Gates, S., and Hofmeyr, GJ., et al (2011): Continuous support for women during childbirth. The cochrance database of systematic reviews, Issue 2:CD003766
10. Akerman, N. and Dresner, M. (2009): The management of break through pain during labor,CNS Drugs; 23(8):669-679.
11. Hodnett ED (2002): Pain and women's satisfaction with the experience of childbirth: a systematic review. Am J Obstet Gynecol, 186:S160-72.
12. El-Nemer A. (2003). Helping from the heart A feminist Ethnography of Egyptian Women's Childbirth Experiences, Thesis submitted to school of health studies division of Midwifery and Women's Health in partial fulfillment of doctorate degree in nursing science Obst and Gyne. University of Bradford, uk.2003
13. Goodman, P., Mackey, MC., and Tavakoli,. AS., (2004): Factors related to childbirth satisfaction. Journal of Advanced Nursing, 46:212-219.
14. Christianes, W., and Bracke, P., (2007): Assessment of social psychological determinants of satisfaction with childbirth in a cross-national perspective. BMC pregnancy and childbirth,5,20 htt://www.biomedcentral.com/1471-2393/5/20
15. Abushaikha, LA., and Oweis, A.,(2005): Jordanian pregnant women's expectations of their first childbirth experience, International Journal of Nursing Practice, 10(6):264-271
16. World Health Organization, (2000): Care in normal birth: a practical guide (Maternal and Newborn Health/Safe Motherhood Unit). Geneva: WHO;
17. Yuenyong, S., Jirapaet, V., and Brien, S., (2008): Support from a close female relative in labor: the ideal maternity nursing intervention in Thailand, Journal Med Assoc Thai, 91(2): 253-260.
18. Ranger, L., Altman, D., and Tyden, T., et al., (2006): Comparison of the maternal experience and duration of second stage of labor comparing two upright delivery position a randomized controlled trial. British Journal of Obstetrics and Gynecology, 113-(2): 165-170.
19. Kennell J, McGrath S.(1993): Labor support by a doula plus father vs father alone for middle-income couples – the effect on perinatal outcomes. J Dev Behav Pediatr, 14:277.
20. Langer A, Campero L, Garcia C, Reynoso S. (1998): Effects of psychosocial support during labour and childbirth on breastfeeding, medical interventions, and mothers' wellbeing in a Mexican public hospital: a randomised clinical trial. Br J Obstet Gynaecol, 105:1056-63.
21. Gagnon A, Waghorn K, Covell C. (1997): A randomized trial of one-to-one nurse support of women in labor. Birth, 24:71-7.
22. Mosallam M, Rizk DEE, Thomas L, Ezinmokhai M. (2004): Women's attitudes towards psychosocial support in labor in United Arab Emirates. Arch Gynecol Obstet, 269:181-7.
23. Gordon NP, Walton D, Mcadam E, Derman J, Gallitero G, Garrett L.(1999) : Effects of providing hospital-based doulas in health maintenance organization hospitals. Obstet Gynecol, 93:422-6.
24. Lai, ML., Lin, KC., and Li, HY., (2009): Effect of delayed pushing during the second stage of labor on postpartum fatigue and birth outcomes in nulliparous women. Journal of Nursing Research, 17(1): 62-72.
25. Hunter, L., (2009): A descriptive study of being with women during labor and birth, 54(2): 111-118.
26. Eriksson, C., Westman, G., and Hamberg, K., (2006): Content of childbirth related fear in swedish women and men analysis of an open ended question. Journal of midwifery and women's health, 51(2): 112-118.
27. Ministry of Health., (2009): companionship at birth policy, htt://health.gov.bz/www/index.php/quavision/136-quality-assurance/companion-at-birth-policy-document
28. Choquette, L.,(2oo7): Prenatal education in Ontario, Better Practices. www.beststart. Org/events/detail/prenatal eduform.htm
29. Escott, D., Slade, P., and Spiby, H., (2009): Preparation for pain management during childbirth: the psychological aspects of coping strategy development in antenatal education clinical psychology review, 29(7): 617-622.

10/11/2012

Financial Deregulation

Hassan Hemmati[1], Vahid Rafiei[2] (Corresponding author)

[1.] Assistant professor and Faculty Member of Raja University, Qazvin, Iran
[2.] Master of Accounting Raja University, Qazvin, Iran/ PGD in International Accounting and Finance University of East London

Abstract: In the present conditions, financial accounting is completely territories, following recent high profile accounting failures at Enron and other firms. The debate is deregulated. This study was done to explore whether such regulation is the costs and efforts. The results of analyses contributed to the following results: Even though more laws have been passed, this has not stopped great accounting frauds from resulting in instability in capital market and they have hampered the increase of wealth of our society.
[Hassan Hemmati, Vahid Rafiei. **Financial Deregulation.** *Life Sci J* 2012;9(4):2838-2841] (ISSN:1097-8135). http://www.lifesciencesite.com. 416

Keywords: accounting failures -Enron-deregulation-capital market

Introduction

The debate over whether financial accounting should be deregulated began in the United States in the late 1990s and spread to Europe over the past ten years. The height of the debate spawned a vast literature dealing with the pros and cons of financial deregulation all over. Financial accounting is quite forcefully administered in several territories, with the enforcements typically becoming more stringent following recent high profile accounting failures at Enron and other firms, it should be examined whether such regulation is worth the costs and efforts required to administer it. Specifically, what need to be examined are the factors that are responsible for imposing the regulations in the first place. Are they imposed to control accounting fraud? Or does fraud occur because of the "standard and regulation overload" which creates an incentive to evade the standards?

The Necessity of Sec Reporting Requirements

At the present time, the SEC's requirements state that public corporations need to file form 10-K, in which they are required to disclose the subsequent information (Browne 2004):

- Description of the business
- issues that have been voted by stockholders,
- Legal courses of action,
- Share repurchases
- Management's discussion and analysis of results of operations
- Quantitative and qualitative admission on market risk
- Financial statements and additional information
- Modifications and disagreements with auditors regarding the disclosure of accounting and financial information,
- Company directors and executives
- Compensation of executives
- Share ownerships
- Breakdown of tax, accounting and consulting fees for financial statements and other information.

The question is now whether capital markets can survive without the required annual submission of financial reports which are required by the SEC? Some individuals believe that managers cannot be relied on to reveal the information that investors needed to make investment decisions. For instance, Salomons (1983) asserts that investors would be critically hurt: "Managers may have more to gain by withholding information than from disclosing it. We cannot depend on the market to discipline promptly companies that are free to choose what and how to report to investors. Even if good accounting can be relied on to drive out bad in the long run, investors may suffer too much damage in the short run to permit freedom from regulation"

This puts forward the theory that minimum revelation levels and particular measurement tools, such as U.S. GAAP and SEC requirements will still be required to decrease the information imbalance existing between a firm's accountants and shareholders. Another standpoint states that there are motives for the filing of financial reports by public corporation. In contrast, if corporations want to acquire finance through the sale of shares, they will encourage the development of trust that shareholders put in the company's present and upcoming financial performance by filing complete financial reports. In contrast, if control (management) and

ownership (shareholders) are two different things then present shareholders will need information about the financial credibility and working results of the firm if they are expected to go contributing their funds. If a corporation does not file well-timed and credible information, stakeholders will lose faith and stop giving funds to that firm. In this respect, Warren Buffett talks about the significance of informing stockholders (1996): "We will be candid in our reporting to you, emphasizing the pluses and minuses important in appraising business value. Our guideline is to tell you the business facts that we would want to know if our positions were reversed. We owe you no less. Moreover, as a company with a major communications business, it would be inexcusable for us to apply lesser standards of accuracy, balance and incisiveness when reporting on ourselves than we would expect our news people to apply when reporting on others. We also believe candor benefits us as managers: The CEO who misleads others in public may eventually mislead himself in private".

If firm executives wish to create faith and long-term value, they will not attempt to over state the share price by incorrectly reporting accounting figures. Buffett clarifies the share price approach of his company Berkshire Hathaway in the below manner (1996): "To the extent possible, we would like each Berkshire shareholder to record a gain or loss in market value during his period of ownership that is proportional to the gain or loss in per-share intrinsic value recorded by the company during that holding period. For this to come about, the relationship between the intrinsic value and the market price of a Berkshire share would need to remain constant and by our preferences at 1-to-1. As that implies, we would rather see Berkshire´s stock price at a fair level than a high level".

Corporate managers who possess long-term vision and value-based compensation packages will offer pertinent financial statements to stakeholders in order to acquire finance for the growth of their firms. The reason behind an independent audit is to obtain estimation on a firm's financial statements. Financial statements, in combination with an independent auditor's report, are submitted to clients, creditors, current and prospective investors, and other involved parties. The external auditor's report offers endorsement to the firm's financial figures. Independent audits are required because of the innate clash between a firm's management and the individuals who make use of financial reports. An external audit may create trust in a company's financial statements, making it feasible to estimate conformity with management responsibility, carry out financial calculations and make decisions on resource allocation.

The Argument for Deregulation

The basic argument in defense of accounting deregulation is that accounting information should be regarded like other products and services and therefore regulators should step away and allow the forces of demand and supply to determine the quantity that is supplied. Several arguments have been put forth to support this point of view. Of these, one main argument is that, even if there is no regulation, there are private economics-based (Adam Smith's Invisible Hand Theory) motivations for the firm to provide authentic information about its business and financial position to interested stakeholders outside the firm, and if it does not do so, the expenses of the firm's activities will increase.

The foundation of this perspective is that if there is no information about the firm's activities, other stakeholders, such as the title-holder of the firm (or the shareholders) who do not participate in the operation of the firm, will believe that the managers might be running the firm for their own profit. This means that the managers will run the firm for their own personal profit, and will not do so with the aim of increasing the profitability of the firm (there is believed to be a lack of correlation of targets between the owners and the managers). In addition to this, it will be believed that possible 'external' shareholders will want the managers to take advantage of every opportunity available, and if there are no protections, they will decrease the amount they are willing to fork out for the shares of that company. In the same manner, following this economics-based point of view of 'rationality' (self-interest), prospective creditors (such as banks and bondholders) are expected to want managers to embark on opportunistic operations with the finance the lenders are willing to lend, and for this reason, if there are no protections, these creditors will ask the firm for a higher rate at which they loan their money, i.e, a higher interest rate. The assumptions listed above assume that the managers and the shareholders will work to maximize their own self-interest.

Why Is This A Bad Idea?

Despite proofs in support of deregulation, several individuals state very firmly that less regulation is healthier for any profession, regardless of how serious the problem at hand may be. Governmental regulation is always believed to be detrimental for any profession, unproductive, and always more costly in general as compared to allowing the market place to run things out on its own. This perspective has been supported by such individuals as Ronald Reagan

as well Grover Norquist (who went so far as to state that the government should not have any say in anything).

The disasters of Enron were a direct consequence of there being too little or too ineffective regulation. There were unquestionably quite a few other elements at play, but had accountants and auditors, even financial institutions been appropriately monitored, the issues would be not be acute as it was and it would be much less difficult to handle.

Enron's fraudulent financial statements did not clearly describe its financial position to shareholders and analysts (Bratton 2002, Mack 2002). Other than this, the managers and auditors made clever use of accounting and auditing loopholes to show a distorted picture of earnings to show a favorable portrayal of its financial performance (Healy 2003). Starting from 1997 until its collapse, the main objective of Enron's accounting and financial operations were to show an inflated picture of reported income, cash flow and asset values and a deflated picture of liabilities (Bodurtha 2003). All this constituted the practice of feeding investors what they wanted to hear: They wanted to see that the company they had invested in was realizing high rates of returns, and Enron provided them with that.

It is generally felt that accountants are operating in the best interests of their own firms and agencies and the firms that they work for, rather than operating to update the public ethically and correctly. If financial accounting is regulated, this prevents any organization and accounting and auditing firm to conceal the facts about the firm and its financial standing from the general public. By regulating financial accounting, firms and their accountants are being forced to be more frank and forthright regarding their financial dealings and depicting their accurate financial position.

The most critical justification to regulate accounting standards is to shield the investors. Be it a publicly listed firm, or a firm that offers the majority of its shares to its employees, both have to be safe guarded form deceitful practices. This is very critical and the main reason why the government and regulatory authority have moved to regulate accounting standards and practices. It has been demonstrated by incidences in the past that not having robust accounting procedures in place and implemented, can only lead to fraudulent practices on the part of firms and corporations.

There are divided opinions pertaining to the theories to regulate accounting standards. In spite of this, despite the divided opinions, the opinion to regulate accounting firms presents a robust case. It is not only the conscientious action to take, but it will also protect investors from firms and potential fraud. By failing to regulate accounting standards, rules and practices there will only be room for mistrust in the accounting system.

Will Deregulation Result in the Dissemination of Accurate Information?

For shareholders to make the decisions necessary for investment, they should possess sound financial information. This is why regulations are necessary to control the information that is provided to shareholders (Blundell 2004). It is for this reason that auditors have been appointed to make sure that the information present in financial statements should be dependable and have been ready in accordance with generally accepted accounting principles (GAAP).

The foregoing discussion shows that while some individuals believe that enforcing regulations only averts the development of improved accounting standards, decreases the accountability of professional organizations and raises investors' financial risk, arbitrarily imposing regulations is also a problem. With randomly enforced rules, attention is no longer given to whether the accounting standards result in sensible numbers, but on conformity with regulations (Boardman and Laurin 2000). It would be very safe to assert that the soul of the standard is taken out and in its place mere formalities are placed. Besides this, the independent auditors' standards are put to one side, and their only duty is to comply with accounting standards.

It can be very safe to say that random accounting standards do not stop fraudulent accounting practices, but they do stop the creation of improved practices. In spite of the complicated regulatory system, investors cannot be deceived for long. At one time or another, frauds are found out and the share prices of firms that have utilized window dressing to portray a better financial position are caught out and penalized appropriately. In spite o this, when regulations are removed, corporation expenses are brought down, better tools for measuring financial performance can result, and there is a reason to present additional financial information to investors and in this way help to make rating quality better.

Conclusions and Recommendations

Many answers have been hunted for the disasters caused by financial statement frauds. Some believe the solution is to create more regulations to stop financial wrongdoing by punishing the parties concerned. The issue, however, is that repeatedly these regulations result in consequences that counteract to their original

motives and stop the development of fresh accounting standards that would offer a better portrayal of a firm's financial performance. Others believe that competition between the various accounting standards should be allowed so that firms can opt or the set of accounting standards they are going to utilize to create their financial statements and operating results. Nevertheless, financial and accounting frauds have occurred even when varying sets of accounting standards have been utilized (Basset and Storrie 2003). Other proposals include creating codes of ethics aimed at increasing the ethical responsibilities and accountabilities of directors, auditors and other parties concerned (Bayless 2009).

Nevertheless, even though more laws have been passed, for instance the Sarbanes Oxley Act of 2002, and the significance of improving ethical values and corporate responsibility has been harped on, this has not stopped great accounting frauds from resulting in instability in capital markets, and, for this reason they have hampered the increase of wealth in our society. This issue could be alleviated if scrutiny tools, such as boards of directors and independent auditors, are intensified. Boards of directors need to carry out an independent, active and key role in the administration of management activities, and to behave as the security guards of efficient corporate governance. Boards of directors should also devise a compensation system for company directors that will promote long-term value development for the firm itself, in the sense of a continuous return on invested funds, over and above capital expenditure.

Concerning independent auditors, their stakes must be allied with those of financial report users so that they distribute correct auditing judgments. One method in which these interests could be aligned is by forming a competitive financial report market. In this market, only trustworthy financial statements would be considered legitimate, since the user of financial statements would be responsible for paying auditing firm's fees. In this manner, independent auditors would try to act in accordance with the public concern and state whether financial statements have material errors or irregularities that could impact users' financial decisions. Changing motivations would result in the creating of accurate, well-timed and credible financial statements. This would result in solidity to the capital market, and the trust created in forms would lead to more financial development.

In the end, we must evaluate whether there is a requirement for the information needs asked for by regulatory organizations (Gaermynck et al 2008). Public corporations utilize capital markets to acquire finance for their projects. To acquire this finance they need to create trust in investors. So, even when there are no explicit financial reporting needs, these firms will still be persuaded to file financial statements with the motive of obtaining the resources they need to expand.

References

1. Bassett R, Storrie M 2003, "Accounting at Energy Firms after Enron: Is the 'Cure 'Worse Than the 'Disease'? *"Policy Analysis*, 469. February 12.
2. BAYLESS, M. (2009). The myth of executive compensation: do shareholders get what they pay for? *Applied Financial Economics*. 19, 795-808.
3. Blundell, J 2004. "Remember Blundell´s Law," *The Scotsman*, June 30.
4. BOARDMAN, A., & LAURIN, C. (2000). Factors affecting the stock price performance of share issued privatizations. *Applied Economics*. 32, 1451-1464.
5. Bodurtha, J 2003."Unfair Values" - Enron's Shell Game. *The McDonough School of Business*, p.2
6. Bratton, WW.2002. "Enron and the Dark Side of Shareholder Value". *Tulane Law Review*: 6. Available at: http://papers.ssrn.com/sol3/papers.cfm?abstract_id=301475. [Accessed 13 March 2010]
7. BROWNE, F. X. (2004). Corporate finance: stylized facts and tentative explanations. *Applied Economics*. 26, 485-508.
8. Buffett, W 1996. An Owner's Manual, Available at: http://www.berkshirehathaway.com/ownman.pdf [Accessed 10 March 2010]
9. GAEREMYNCK, A., VAN DER MEULEN, S., & WILLEKENS, M. (2008). Audit-Firm Portfolio Characteristics and Client Financial Reporting Quality. *European Accounting Review*. 17, 243-270.
10. Healy, PM (2003). "The Fall of Enron" *Journal of Economic Perspectives* 17 (2): 9. Available at: http://www-personal.umich.edu/~kathrynd/JEP.FallofEnron.pdf. [Accessed 12 March 2010].
11. Mack, T 2002 "The Other Enron Story". *Forbes*. Available at: http://www.forbes.com/forbes/2002/1014/062_print.html. [Accessed 11 March 2010]
12. Salomons, D, 1983 "The Political Implications of Accounting and Accounting Standard Setting," *Accounting and Business Research* 13(50): p. 107.

10/2/2012

The investigation of the solutions of improving Human Development Index in Iran during fifth development plan

Abdolsami Sepahi [1], Dr. Mohammad Rahim Rahnama [2], Mohammad Amin Hounakzahi [3], Shahram Rastin [4], Abdolalim Dorrazehi [5]

[1.] PhD Student in Geography and Urban Planning, International Branch of Ferdowsi University of Mashhad, Mashhad, Iran
[2.] Associate Professor, Department of Geography, Faculty of Letters and Humanities, International Branch of Ferdowsi University of Mashhad, Mashhad, Iran
[3.] MA degree in Geography and Urban Planning, University of Sistan and Baluchestan, Zahedan, Iran
[4.] MA degree in geography and rural planning, Payam NOOR University, Birjand, Iran
[5.] MA degree in Geography and Urban Planning, University of Sistan and Baluchestan, Zahedan, Iran
sepahi1387@yahoo.com

Abstract: Generally Human Development Index (HDI) is "the process of developing the selections in capability space for achieving a better life". Based on this definition, we can investigate the changes of HDI in a definite time period. The current study attempts to investigate and present effective solutions in improving HDI in fifth development plan. The results of this investigation showed that HDI in Iran during 1975 to 2005 increased from 0.571 in 1975 to 0.759 in 2005. This increase is due to the increase of life expectancy and literacy index increase. The results of this study showed that in the recent 40 years, the capital income compared to two mentioned indices had fewer shares in improving development level. To achieve high development level in terms of humanity during the fifth development plan, the change of economical, social structures is necessary in the society. To achieve the goals of 20-year vision and fifth development plan, some solutions with the comparison between the countries in the region and the Islam world was presented.
[Abdolsami Sepahi, Dr. Mohammad Rahim Rahnama, Mohammad Amin Hounakzahi, Shahram Rastin, Abdolalim Dorrazehi. **The investigation of the solutions of improving Human Development Index in Iran during fifth development plan**. *Life Sci J* 2012;9(4):2842-2845] (ISSN:1097-8135). http://www.lifesciencesite.com. 417

Keywords: Human development index; Iran; Fifth development plan; solution

1. Introduction

The first article of third chapter of fifth development plan of Islamic Republic of Iran defined the aim of this article improving the human development index to the countries with high human development level and consistency of education, health and employment indices and identification of the ways to increase of HDI levels is necessary and it is the purpose of this paper.

In the first universal report of human development in 1990, human development is defined as the process of developing the human selection. The comparison of this approach with three views of economical welfare, removing the main needs and the human resources development helps for better understanding of human development (the first national report of human development, 1999, 34).

Generally, economical welfare approach considers consuming the goods and services as the basis of better life and as real income determines the consumption amount of people of the services and goods, economical welfare index is the real income while human development approach knows the consumption of goods and services as one of the elements of better life and considers fulfilling mental needs and developing mental capabilities as another element of better life that is achieved via developing mental ability namely with education. Thus, it shows the academic achievement besides capital income in measuring human development (Davoodi, 1998, 97).

The approach of removing the basic needs aims providing the minimum material and non-material needs but it follows this aim via giving a set of goods and services and from one hand due to the lack of considering the development of spiritual and materialistic capacities and on the other hand due to the emphasis on minimum things, instead of emphasis on better life is different from human development approach. Although, in human resources development approach, we emphasize on creating the capacities and developing the capabilities, the aim is not having access to better life (Hosseini, 1996, 12).

Thus, the emphasis on the concept of developing human selections is a holistic approach to better life and it emphasizes on creating the capacities instead of emphasizing on the consumption of the goods and services and it guarantees the stability of human development. Thus, such approach as the concept of human development is the basis of

measurement. HDI by relying on this approach attempts to mea sure three main capacities of literacy, access to materialistic facilities for better life and long life with health. This index to measure the first capacity applies adults literacy rate based on two third of the general value and combinational rate of being registered in various academic levels based on one third of general value and to measure the second capacity, applies the real purchase power and to measure the third capacity, applies life expectancy at birth time (Hayati, 1996, 45). The current study aimed to present effective solutions in improving human development during the fifth plan in Iran. One of the strengths of this issue is the uniform comparison and the introduction of similar and standard position among other countries. Also, the facility of doing the calculations is the important issue in investigating human development index. One of the weaknesses of this issue is more emphasis on quality issues. Also, in the calculation process of this index, due to its presentation by western countries, the share of religious factors in human development process is less emphasized. Increasing human improvement of the society is including various indices in which the value of each society should be considered.

Review of literature

In 1990, for the first time in UN organization report, the condition of the countries was published based on HDI. In 1998, Farhad Nourbakhsh in Glasko University investigated the HDI and his proposed index had some modifications and ranked the selected countries and Canada has the first rank (Noorbakhsh, 1998, 28).

Hanham in 2000 investigated HDI in western Virginia State in USA including the investigation of income, education, poverty and life expectancy for various parts of western Virginia (Hanhamn, 2000, 1-70).

In Iran, management and planning organization in Iran presented its report titled " The first national report of human development of Islamic Republic of Iran) as the most complete report. According this report, HDI in recent decade was developed and its condition was inclined to the increase of human development level and was developed compared to HDI of Turkey, Egypt, Arabia and Iraq but was developed less compared to southern Korea and Malaysia (First national report of human development of Islamic Republic of Iran, 200, 50).

2. The execution stages of human development index

HDI was applied for the first time in 1990 by UN (UNDP, 1991). This organization was used for grading the countries in terms of human development model and by considering the similar importance of the indices was used for ranking. The civil plan of UN in this model applied life expectancy index, literacy percent and per capital income for grading the countries. But in regions, cities to investigate the development degree, we can apply many indices (Hekmatnia, 2006, 212). By the above model to apply various indices (even by valuating the applied factors) we can provide combined index (including structural, economical and social) for the regions and provinces for the required goals and determine the priorities (Ziari, 1999, 136). The stages of this method are as following:

After the variables were selected, in the first stage:

Its matrix table is drawn and for each of the regions in Iran in the columns, the indices are defined in the rows.

After the formation of data matrix table in the second stage:

Each of the variables are applied to use in statistical analyses by the following formula:

$$Xj = \frac{\max_j x_{ij} - row_j x_{ij}}{\max_j x_{ij} - \min_j x_{ij}}$$

It is standardized.

In the third stage:

All the standardized indices that are achieved in the second stage by the following formula:

$$xI_{ij} = \frac{1}{n}\sum_{i=1}^{n} I_{ij}$$

The average of the data of first formula was calculated and for the regions in the country, average index was calculated. It can be said that the achieved average shouldn't be more than 1 or less than zero.

Fourth stage:

In this stage that is main stage, the development index is achieved by the following formula:

$$HDI = (1 - I_{ij})$$

It is calculated that as the value is close to one, it shows more development and as it approaches zero, it shows the lack of development and deprivation (Sepahi, 2009, 67).

The position of Iran human development among the countries in the world and Islam countries

In the most recent report of UN organization during 2007, 2008 of Iran among 177 countries in the world was in the rank of 94 all over the world. Among the countries in the region of United Arabia Emirate, Kuwait, Qatar, Oman, Arabia are in advanced group. In life expectancy index is in average row in rank 24 and in literacy index with 0.82 is among 20 countries with above 50% Muslim population is in the twelfth rank. The rank of Iran in achieving the per capital income among the Islam world as seventh rank.

The rank of Iran among the indices related to human development in the world

Iran in 1975, 1980, 1985, 1990, 1995, 2000 and 2005 had figures 0.571, 0.578, 0.615, 0.653, 0.693, 0.722 and 0.759 of HDI that showed the development of this index in the recent 35 years.

Among the indices of HDI in Iran for each 100'000 physician had 87 physicians that were in Islamic countries and only 5 Islamic countries are lower than Iran. In terms of literacy index, it is located in row 13 of Islam world countries. In terms of the prevalence of AIDS it is in the fourth rank of Islamic countries with Jordan, Kuwait, Liberia, Oman, Maldives, Qatar, Saudi Arabia, Syria, Arabic united Emirate, Uzbekistan and Yemen. In terms of mal-nutrition it is in high condition among Islamic countries as third rank that is at the same rank with Al-Jazayr, Saudi Arabia, Syria, Egypt and Iran condition is better than 15 other Islamic countries. In access to healthy drinking water among Islamic countries is in the third rank and Iran condition is better than 17 other Islamic country. Pakistan, Bangladesh, Kumur, Al-Jazayer, Gambia, Guinea, etc are in critical condition.

Effective solutions in improving Iran human development levels in the region and the world

Improving human development condition is associated directly with life expectancy indices, literacy, per capita income. As Iran was located in average row to Arabic countries, the difference of per capita income in the first degree and second degree is the difference of life expectancy index among Iran and Arabic neighboring countries. To improve the condition of human development in the fifth plan based on the following findings, we can refer to the following items:

1- Modification of comprehensive economical structure for productive employment, productive, reducing the dependency on the import of foreign products and increasing the export of manufacturing products.
2- Improving the health level of the society with the development of medical facilities as balanced and regional in the country.
3- Changing the acceptance method of medical fields and considering the regional and provincial needs for future years.
4- Providing special conditions to absorb Iranian experts in various fields for activity in Iran and the conditions are associated first with economical issues and research facilities of the experts.
5- Doing the organized cultural work in increasing the national capabilities to absorb Iranian experts in abroad.
6- The development of technology-oriented fields with effective manufacturing capability for domestic and foreign market.
7- Development of fossil fuel alternative energies and launching laboratories equipped with new technologies of healthy energy.
8- Increasing the acceptance in post-graduate fields with applied nature and balancing between theoretical and technical fields in BA level.
9- Special consideration of sport and developing the facilities based on regional requirements
10- The reduction of theoretical fields students to advanced countries and increasing applied fields to the required productive population in future years.
11- The exchange of information and knowledge between universities of Islamic and world countries.
12- Special consideration to regional capabilities to create balanced development in the country.
13- Basic change of education structure of Universities based on applied needs of the society.

The development of aerial domestic and foreign transportation and presenting good infrastructures of land, marine and air transportation.

3. Conclusion

This study was done with the aim of presenting effective solutions in improving human development in Iran in fifth development plan. After expressing theoretical basics of human development and scientific methods, the evaluation of Iran condition was investigated. The results showed that among the effective indices in improving HDI, per capita income index of Iran requires the improvement

of higher ranks. Also, two indices life expectancy and literacy in 40 years had the highest effect in improving the condition of human development in Iran. To achieve 20-year vision goals, it is required to consider Iran as the best regional country in terms of economy and development with Islamic foundation. It is required that in the existing conditions in economical, scientific, political and social condition as scientifically some progresses were made and the barriers of development in Iran were with the modification of economical, education, life, defense, political structure. Also, the establishment of regional balance is of great importance economically. Presenting development infrastructures in transportation, health and medical education is necessary.

Corresponding Author:
Abdolsami Sepahi
Department of Geography and Urban Planning
International Branch of Ferdowsi University of Mashhad
Mashhad
E-mail: sepahi1387@yahoo.com

References

1- United Nation Development Pl an (UNDP), (1574-1576): Human development report. 1992-1993. Budget and planning organization. Tehran.
2- Hosseini, Mirabdollah. 1996. HDI in rural areas of provinces in Iran, Jihad journal. No. 192-193. Tehran.
3- Hekmatnia, Hassan. Mirnajaf, Mosavi. 2006. The application of the model in Geography with emphasis on urban and regional planning. Elme Novin publications. Yazd.
4- Hayati, Ali. 1996. An introduction to human development report of UN plan. 1996. The development of human development. International Bolton. No. 12.
5- Davoodi, Ahmad. 1998. Iran and human development. Plan and budget journal. No. 21. Tehran.
6- Ziari, Keramatollah. 1999. The principles and methods of regional planning. Yazd University publication.
7- Budget and plan organization. 1999. First national report of human development of Iran Islamic Republic. Plan and budget organization. Tehran.
8- Sepahi, Abdolsami. 2009. The Geography and rural development. Koleposhti publications. Tehran.
9- Hanham,Alison.(2000).A Human development index for west Virginia counties. Working paper.
10- Noor Bakhsh, Farhad.(1998).A Modified human development index, world development,vol.20.
11- UNDP (1991) Human Development report, Oxford Univercity press, New York.
12- UNDP (2007-2008) Human Development report, Oxford Univercity press, New York.

9/6/2012

Immunomodulatory and Chemo preventive activity of *Bacillus subtilis* sulphated Levan

Faten S. Bayoumi[1],azza M.El Amir [2], El Deeb S.O[2]. , Hassan Abd el Zaher[3],Haiam S.A [1]

[1] Immunogenetics Department. NRC, Egypt
[2] Zoology Department, Faculty of Science, Cairo University.
[3]National Research Centre
Corresponding Author: Drfaten100@link.net

ABStract: Aim: To investigate the possible immunomodulatory and chemopreventive effects of a bacterial polysaccharide drug (*Bacillus subtilis* sulphated Levan; BSL) for prevention of tumor development through antipromotion and antiprogression effects in vivo studies. The antipromoting effect of BSL, was assessed by estimating different aspects of such activities ;tumor necrosis factor-α (TNF-α) level, apoptotic and necrotic cell damage, DNA fragmentation, nitrous oxide (NO) and COX-2 (Cyclooxygenase-2) levels**.** Antiprogression mechanism was evaluated through recording of vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF) and histopathological examination. In addition, BSL was also compared with garlic which is known as a natural compound with chemopreventive action. **Results** No significantly elevation in the NO or TNF-α levels were recorded when compared with control on receiving BSL, while, garlic possessed lower significant inhibitory effect. Apoptosis and necrosis states were induced as a mode of cell death. It was concluded that BSL was a potent anti-inflammatory and anti-apoptotic agent. Furthermore, a significant DNA fragmentation inhibition (insignificant lesser extent and decrease in VEGF level was determined by recieving BSL and garlic. Also, histopathological examinations showed that, BSL maintained nearly normal liver architecture and inhibited hepatocellular preneoplas induced by the cancer promoting material used in the experiment (diethylnitrosoamine) (DEN). C**onclusion**, BSL activity as anti-tumor agent due to its antipromotion and antipropagation actions was proved.
[Faten S. Bayoumi, azza M.El Amir, El Deeb S.O, Hassan Abd el Zaher,Haiam S.A. **Immunomodulatory and Chemo preventive activity of *Bacillus subtilis* sulphated Levan.** *Life Sci J* 2012;9(4):2846-2856] (ISSN:1097-8135). http://www.lifesciencesite.com.418

Key words: BSL, histopathological examination, antipromotion, antiprogression

Introduction

Cancer is a serious problem in Egypt. In Egypt, HCC was reported to account for about 4.7% of chronic liver disease (CLD) patients (Rahman *et al*., 2001). The epidemiology of HCC (the most common type of liver cancer) is characterized by marked demographic and geographic variations. A number of different studies suggested that immunotherapeutical approaches will be successful for the treatment of this disease (Greten *et al*., 1999; Butterfield, 2004). Carcinogenesis can be viewed as a process that involved accelerated, and abnormal, cellular changes in which the genes controlling proliferation, differentiation, and apoptosis are transformed under selective environmental pressures (Bertram, 2000). Genetic damage, from accumulated carcinogenic exposure, becomes evident during neoplastic transformation. Specific genes have been discovered that, when altered, may play a role in epithelial carcinogenesis. These include both tumor suppressor genes and proto-oncogenes, which encode proteins that are involved in cell cycle control, signal transduction, and transcriptional regulation. These affect different stages of carcinogenesis including initiation, promotion, and progression (BerenblumI and Armuth, 1981; Heidelberger *et al*., 1983 and Soria *et al*., 2003). The initiation phase is a rapid (within hours or days), irreversible event that occurs. Promotion phase is a protracted process that may require several years or decades to be established,this consists of the expansion of mutated cells to form an actively proliferating, multicellular premalignant lesion. During the progression phase, another irreversible event occurs over a relatively short period, perhaps less than 1 year, in which new clones with increased proliferative capacity, invasiveness, and metastatic potential are produced (Surh, 1999). Due to the fact that, the initiation and progression phases are irreversible and relatively transient events, the promotion phase of carcinogenesis may provide the best target for cancer prevention (Umar *et al*., 2001).

Chemoprevention, by definition, is the use of agents to slow the progression of irreversible events or inhibit carcinogenesis, thereby lowering the risk of developing invasive or clinically significant disease (Hong and Sporn, 1997; Kelloff *et al*., 2001). Consequently, an effective chemopreventive agent should intervene early in the process of carcinogenesis to eliminate premalignant cells before they become malignant (Smith *et al*., 1995;

Wattenberg, 1995; Hong and Sporn, 1997; Kelloff *et al*., 1999a).

B. subtilis produces and secretes large amounts of various proteins into the culture medium (Priest 1977). For the last two decades numerous attempts have been made to use this bacterium as an efficient host for the expression of proteins (Simonen and Palva, 1993). Levans are natural polymers of the sugar fructose found in many plants and microbial products. Levan is also produced by *B. subtilis* (natto), which is used to make fermented soybeans (Meng *et al*., 2003). Commercial interest in the production of levan has intensified in recent years (Vina *et al*., 1998). Levan has some potential pharmaceutical applications owing to its anticarcinogenic and hypocholesterolemic properties (Kim *et al*., 1998). Levan has a number of effects on the immunologic system, including tumor suppression and enhancement of leukocyte antitumor activity (Pileggi *and* Khin, 1962).

In this study, we aimed to evaluate the potential of in vivo anti-cancer and immunomodulatory properties of purified bacterial polysaccharides (*Bacillus subtilis* sulphated levan).

2.MATERIALS AND METHODS:

2.1. Materials

2.1.1. Levan Sedimentation from Culture Liquid

Levan was isolated from culture filtrate of *Bacillus subtilis* after the stage of fermentation using sedimentation by ethanol. Ethanol (96%) was added to the culture filtrate in a ratio of 2 :1 and mixed for 24 hr at room temperature. Sediment was then separated from the culture filtrate by decantation and used for investigations as levan.

The production of levan was indicated after acid hydrolysis by chromatography (Tanaka *et al*., 1978). The chromatography was sprayed with aniline phthalate **(**Block *et al*., 1955). Sulphation of levan was carried out with chlorosulfonic acid (Hussein, 1994).

2.1.2. Garlic

Garlic was purchased from (Tomex, ATOS pharma, Cairo, Egypt) as tablets (200 mg) and administrated, as a suspension in physiological saline, orally to the mice in a dose of 250 mg/kg.

2.1.3. Diethylnitrosoamine (DEN)

Carcinogenicity in the mice was induced by a single dose of intraperitoneal (i.p.) injection of DEN (200 mg/kg) and promoted by adding 0.05 % sodium phenobarbital to drinking water.

2.2. Methods

2.2.1. Experimental Design

This study was carried out on a total number of 200 adult male Swiss albino mice with average weight of 25-30 g obtained from the Laboratory Animal House of NRC, Dokki, Egypt. The animals were acclimatized to the laboratory conditions with a lighting schedule of 12 hr light, temperature 24±1°C, and relative humidity 55±5% and were housed in Tarson Cages (8-10 mice per cage) for 1 week before the commencement of the experiment.

Mice were divided into seven groups (16 animals in each):

***Control gp.*:** Mice that are normal healthy and untreated gp.

Saline gp.: Mice that orally received saline twice a week for 6 wk.

BSL gp.: Mice that received 80mg/kg body wt. BSL i.p. twice a week for 6 wk.

Garlic gp.: Mice that received 250mg/kg body wt. orally twice a week for 6 wk.

***DEN gp.*:** Mice that received 200mg/kg body wt. i.p. once, in addition, 0.05% sodium Phenobarbital was added to the drinking water after 2 wk of DEN injection.

BSL+DEN gp.: Mice that received 80mg/kg body wt. BSL i.p. 24 hr before and after DEN injection followed by 80mg/kg body wt.BSL i.p. twice a week for six weeks.

Garlic+DEN gp.: Mice that received 250mg/kg body wt. garlic 24 hr before and after DEN injection followed by 250mg/kg body wt. garlic orally twice a week for six weeks.

On the 6th week, blood samples were collected. The animals were sacrificed; liver tissues were excised and rinsed in cold PBS to remove excess blood. One portion was preserved in 10% buffered formalin then embedded in paraffin for immune-histochemistry and pathological investigation. The other portion was used for the preparation of 20% (w/v) liver homogenate by homogenization in ice Ripa buffer, centrifuged using cooling centrifuge at 1000 xg for 10 min at 4°C. The supernatant was stored at -80°C for later assessment of MDA(Malondialdehyde),HDAC(HistonDeacetylase) and GST (glutathione-S-transferase)activity as well as GSH level.

2.2.2. Measurement of LD_{50}

The LD_{50} of BSL was determined following Behrens and Karber (1935). Two Groups (8 in each) were used, the first group (control) received sterile saline i.p. The other group received BSL in a dose of 1g/kg body weight. Mortalities were recorded within the first 24 hr following the administration of BSL.

The LD_{50} was determined according to the following formula:

$$LD_{50} = Dm - \sum (z \times d)/n$$

Where:

Dm = highest dose which kill all animals in the group

Z = the mean number of dead animals in two successive groups

D = the constant factor between two successive groups

n = the number of animals in each of the dose levels

2.2.3. Assays for estimation of BSL anti-promoting mechanisms and anti-inflammatory activities

a.. Estimation of nitric oxide level

Nitrite accumulation was used as an indicator of NO production in blood using an assay based on the Griess reaction (Gerhäuser *et al.,* 2003).

b. COX-2 immunohistochemistry

COX-2 was detected immunohistochemically by using polyclonal rabbit anti-COX antibody and polyclonal rabbit anti goat Ig/HRP. Fluorescent images were visualized using a fluorescent microscope (Axiostar plus, Zeiss, Goettingen, Germany) equipped with digital camera (PowerShot A20, Canon, USA).

c. Determination of TNF-α

The level of TNF-α was determined by using an ELISA using a monoclonal antibody to mice TNF-α. The TNF-α level in the animal's serum was determined using the standard curve equation

d. Apoptosis /necrosis stain

The type of the cell death was investigated using acridine orange/ethidium bromide staining (Kinneer and Ma (2002)

2.2.4. **Assays for estimation of BSL anti-progression Mechanisms**

a.Determination of serum total protein

The determination of serum total protein was performed according to Doumas (1975), using kits of Bio-Analytics.

b.Quantitative DNA fragmentation analysis

This method is based on the notion that extensively fragmented double-stranded DNA. The protocol includes the lysis of cells and the release of nuclear DNA, a centrifugation step with the generation of two fractions (corresponding to intact and fragmented DNA, respectively), precipitation of DNA, hydrolysis and colorimetrical quantitation upon staining with DPA, which binds to deoxyribose (McConkey *et al.,* 1989).

Calculations

The percentage of fragmented DNA calculated using the formula:

% Fragmented DNA= (S+T)/(S+T+B) X 100

Where,

S, T and B are the OD at 600nm of fragmented DNA in the S, T (fragmented) and B fractions, respectively.

The fragmented DNA released by cells undergoing apoptosis and lysis during the experiment was recovered in the fraction S should therefore be taken in consideration in particular circumstances.

c. Determination of VEGF

The level of VEGF was determined by using ELISA technique as previously described in TNF-α experiment using monoclonal antibody to mice VEGF.

d. Determination of PDGF

Estimation of PDGF was preformed using ELISA technique as explained in experiment of TNF-α level determination by using monoclonal antibody to mice PDGF, **(**Banchroft *et al*., 1996).

2.2.4. Statistics Analysis

Results were expressed as mean ± S.E. from n = 6-8. Statistical analysis was preformed by Student's t-test using instate soft ware (Version 3.05). Statistical significance was accepted at the level of *P<0.05*.

3.RESULTS

3.1. Statistical results of assays for estimation of BSL Anti-promoting mechanisms and anti-inflammatory Activities:

In the evaluation of NO level in mice serum the results were normalized to the total protein content in the serum using total protein assay as indicated in methods. For the determination of the total protein, a standard curve was plotted (Fig. 1) to be used in the calculation of the serum total protein.

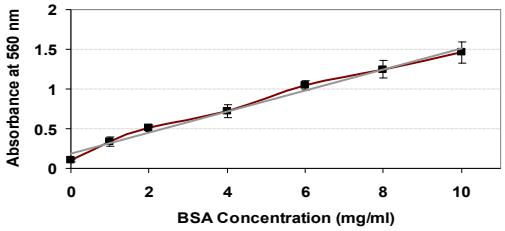


Figure 1: Standard curve for total protein (mg/ml) using BSA.

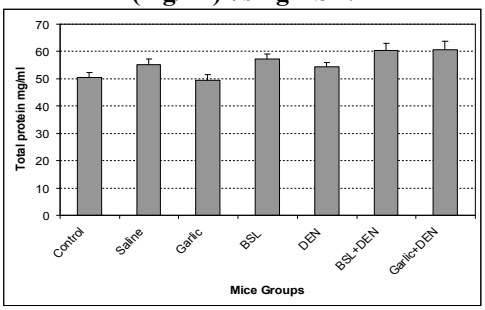


Figure 2: The determination of total protein concentration (mg/ml) in all animal groups. Results were expressed as Mean±S.E.

3.1.1. Estimation of nitric oxide level

NO is a highly diffusive hydrophobic molecule and is therefore a key signaling molecule in inflammation-driven diseases, including cancer. A standard curve of sodium nitrite was plotted in each experiment to calculate the nitrite content in the mice serum (Fig. 3).

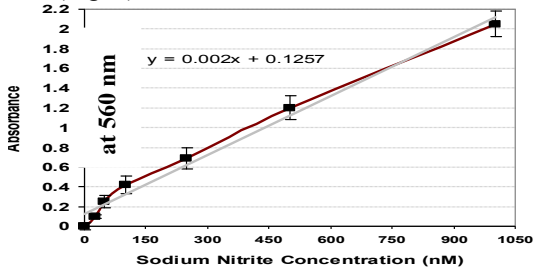


Figure 3: Standard curve for sodium nitrite using Griess assay.

The effect of BSL on NO level was performed through determination of the nitrite level in mice serum.

The results showed that NO level in control group and mice received saline, garlic, BSL, DEN, BSL+DEN and garlic+DEN were 21.5, 24.3, 23.1, 24.25, 28.8, 25.9 and 26.5nmol nitrite/mg protein, respectively. These results demonstrated NO level in control and saline groups were not significantly altered by administration of garlic or BSL (Fig. 4).

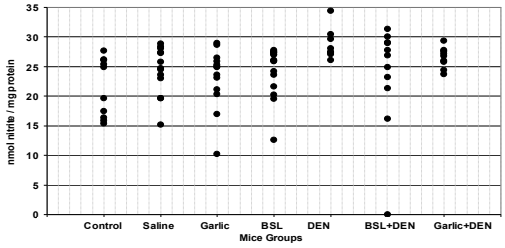


Figure 4: Determination of the nitrite level as an index of NO in mice serum (nmol nitrite/mg protein).

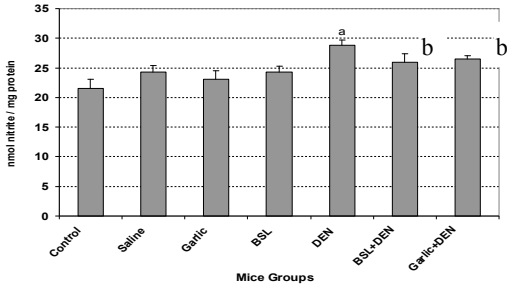


Figure 5: Determination of the nitrite level as an index of NO in mice serum. Results were expressed as Mean±S.E.

a: Significantly different from control gp at (P<0.05).

b :Significantly different from DEN gp at (P<0.05).

Administration of DEN led to significant (*P<0.05*)1.3 times elevation in the NO when compared with control. Such elevation was not significantly affected by receiving BSL or garlic (Fig. 5).

3.1.2.Immunochemical evaluation of the promotion marker COX-2

Inhibition of COX-2 is recognized as one of the most feasible strategies for cancer chemoprevention and treatment, so evaluation of COX-2 expression in the animal liver immunohistochemically was performed. Immunohistochemical staining for COX-2 expression in the mice livers showed that, there was no COX-2 detection in control, saline, BSL and garlic treated groups where, aggressive COX-2 detection observed in DEN group. This very high COX-2 expression was not affected by BSL or garlic treatments in the mice that received DEN then treated with BSL or garlic (Fig. 6).

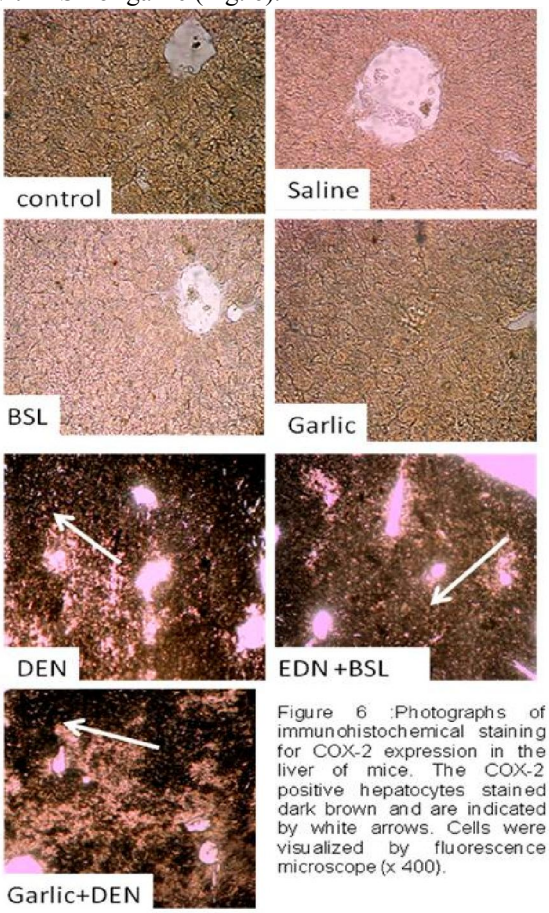


Figure 6 :Photographs of immunohistochemical staining for COX-2 expression in the liver of mice. The COX-2 positive hepatocytes stained dark brown and are indicated by white arrows. Cells were visualized by fluorescence microscope (x 400).

1.3. Effect of BSL on TNF-α

The effect of BSL on TNF-α reflect its pro-inflammatory activity which play a dangerous role in cancer promotion. ELISA reader measured the level of TNF-α in all groups' sera as 580.5, 611, 1031.5,

698.8, 1611.3, 430.7 and 1002.1ng/ml in control, saline, garlic, BSL, DEN, BSL+DEN and garlic+DEN groups, respectively.

TNF-α level was significantly (*P<0.05*) elevated in garlic group to 1.7 times, whereas treatment with BSL did not significantly alter this value (Fig. 7). Administration of DEN significantly elevated TNF-α level to 2.8 times compared with control. This elevation was significantly (*P<0.05*) decreased by administration of BSL. Meanwhile, garlic induced a lower significant inhibitory effect on TNF-α level (Fig. 7).

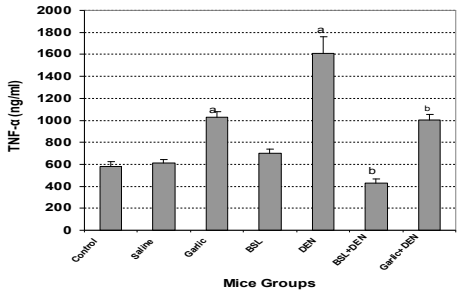


Figure 7 Effect of BSL on mice serum TNF-α level (ng/ml) Results were expressed as Mean±S.E.

a: Significantly different from control gp at (P<0.05).

b: Significantly different from DEN gp at (P<0.05).

1. 4. Apoptosis and necrosis staining

To investigate whether the liver cells of BSL treated mice underwent apoptosis or not, we studied the type of cell death using acridine orange/ethidium bromide staining to distinguish between apoptotic, necrotic, and viable cells. This experiment resulted in absence of apoptotic and necrotic cells in control, saline and garlic groups where, apoptotic cells appeared in slightly small number in BSL and DEN groups. The highly aggressive appearance of the apoptotic cells occurred in BSL+DEN group which showed complete absence of the necrotic cells. In the opposite side garlic+DEN treated group showed high presence of necrotic cells and no apoptotic cells appeared. The results indicate that hepatocytes of BSL treated mice had mainly undergone apoptosis with condensed chromatin and not necrosis and this demonstrates the apoptotic property of BSL and that garlic increases necrosis rather than apoptosis (Fig. 8).

2.2. Assays for estimation of BSL anti-progression mechanisms

Investigation of the possible anti-progression activity of the BSL was performed using a series of tests to estimate DNA fragmentation, VEGF, PDGF and histopathological examinations.

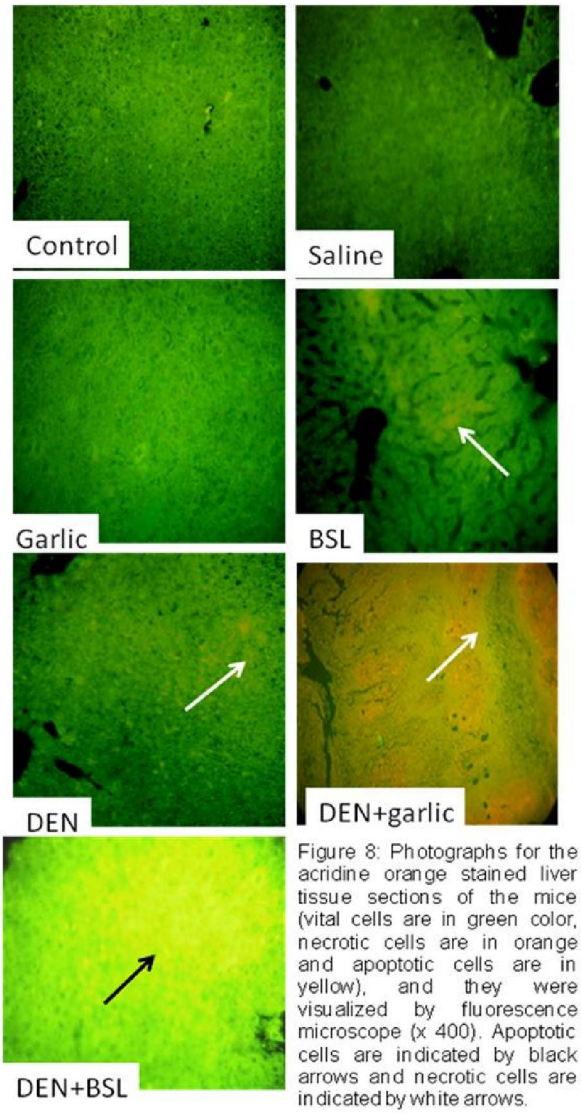


Figure 8: Photographs for the acridine orange stained liver tissue sections of the mice (vital cells are in green color, necrotic cells are in orange and apoptotic cells are in yellow), and they were visualized by fluorescence microscope (x 400). Apoptotic cells are indicated by black arrows and necrotic cells are indicated by white arrows.

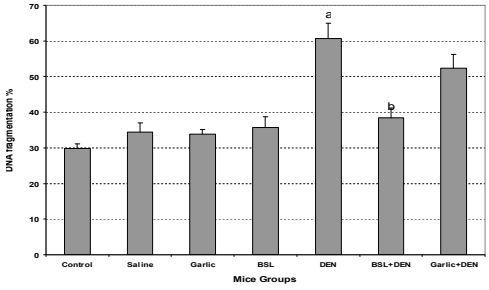


Figure 9 Effect of BSL in DNA fragmentation percentage in mice liver tissue homogenate. Results were expressed as Mean±S.E.

A: Significantly different from control gp at (P<0.05).

b: Significantly different from DEN gp at (P<0.05).

2.2.1. Effect of BSL on DNA fragmentation

Reactive oxygen species (ROS) generated in inflamed tissues can cause injury to cells and damage to DNA, which could also contribute to tumor development. DNA fragmentation is an index of DNA damage. DNA fragmentation experiment resulted in 29.78, 34.47, 33.9, 35.8, 60.7, 38.4 and 52.3 DNA fragmentation percentage in control, saline, garlic, BSL, DEN, BSL+DEN and garlic+DEN groups, respectively. All control, saline, garlic and BSL treated groups showed DNA fragmentation percentage of (29-35 %). While, administration of DEN leads to a 2 times elevation in the DNA fragmentation percentage compared with control group. Such elevation was significantly (*P<0.05*) decreased by receiving BSL and to lesser extent insignificantly by receiving garlic (Fig. 9).

2.2. 2. Estimation of VEGF level

VEGF is a growth factor essential to angiogenesis initiation and regulation. Upregulation of VEGF expression has been demonstrated to be strongly associated with tumor growth, angiogenesis, and increased resistance of liver cancer. VEGF level was estimated in different groups of mice (control, saline, garlic, BSL, DEN, BSL+DEN and garlic+DEN groups) recording 689.8,805.1, 640.8, 798.5, 1271.6, 694.1 and 616.1 ng/ml, respectively. Accordingly, it was obvious that control and saline groups VEGF level was not significantly altered by administration of garlic or BSL (Fig. 10).

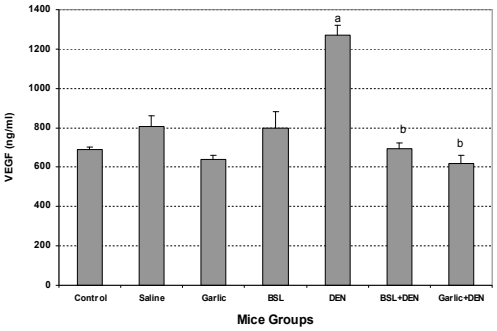


Figure 10 Effect of BSL on mice serum VEGF level (ng/ml) as measured by ELISA kit. Results were expressed as Mean±S.E.

a Significantly different from control gp at (P<0.05).
b Significantly different from DEN gp at (P<0.05)

Administration of DEN significantly (*P<0.05*) increased VEGF level to 1.8 fold of the control. Such increasing was significantly normalized by receiving BSL and garlic as shown in figure (10).

2.2.3. Estimation of PDGF level

PDGF is an angiogenic growth factor that increased during neoangiogenesis observed in tumor. Control, saline, garlic, BSL, DEN, BSL+DEN and garlic+DEN groups showed 2887.7, 3208.7, 2510.8, 2987.5, 2257.9, 2848.3 and 2190.1ng/ml PDGF level, respectively. This demonstrated that PDGF level were not significantly altered by administration of BSL or garlic.DEN administration did not significantly affecting PDGF level, also treatment with garlic or BSL before and after DEN did not significantly altered PDGF level (Fig. 11).

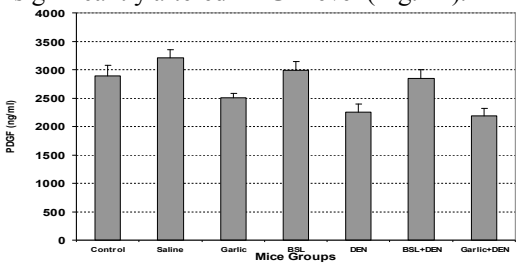


Figure 11 Effect of BSL on mice serum PDGF level (ng/ml) as measured by ELISA kit. Results were expressed as Mean±S.E.

a Significantly different from control gp at (P<0.05).
b Significantly different from DEN gp at (P<0.05).

2.2.4.Histopatological Examination

There was no histopathological alteration observed in control and saline groups and the normal histological structure of the central vein and surrounding hepatocytes in the hepatic cords recorded in Table (1) and (Fig. 12). BSL group showed sever dilatation in the central vein as recorded in (Fig. 12) where, administration of garlic causes dilatation and congestion in the central veins. The portal areas showed sever dilatation of the portal vein associated with inflammatory cells infiltration surrounding the bile duct in the DEN group (Fig. 12). In BSL+DEN group there was mild dilation in the central veins with diffuse Kupffer cells proliferation in between the hepatocytes (Fig. 12). Kupffer cells were proliferated in diffuse manner between the hepatocytes associated with dilation and congestion in the portal vein in garlic+DEN group (Fig. 12).

In BSL group portal veins showed sever dilation. Where, in DEN group double nuclei were observed in multiple numbers of hepatocytes associated with karyomegaly degeneration in other hepatocytes also, there was constriction in the central zone of some nuclei in the hepatocytes as a stage for division and diffuse proliferation and hyperplasia were observed in Kupffer cells in between the degenerated and cytomegalic hepatocytes. The portal area showed dilatation in the portal vein with inflammatory cells infiltration surrounding the bile duct in BSL+DEN group. The hepatocytes showed double nuclei in the most of them with cytomegaly and karyomegaly, as well as, degeneration in garlic+DEN group (Fig. 13).

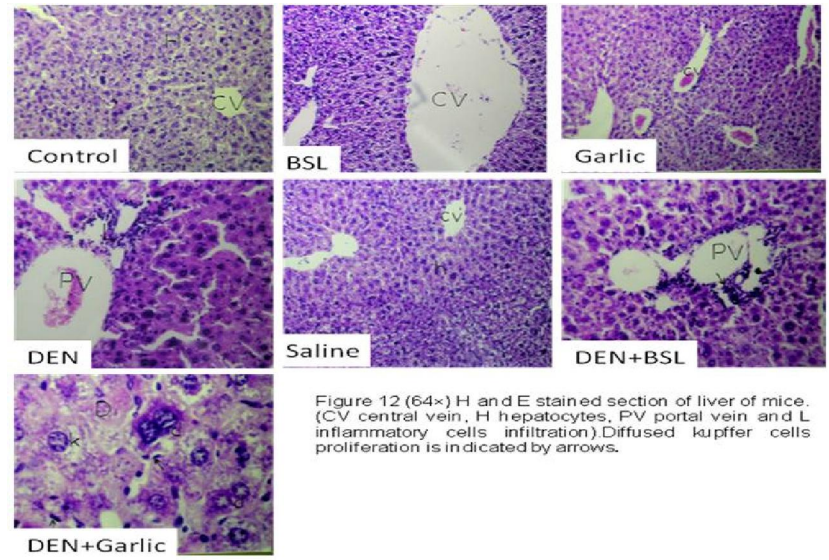


Figure 12 (64×) H and E stained section of liver of mice. (CV central vein, H hepatocytes, PV portal vein and L inflammatory cells infiltration).Diffused kupffer cells proliferation is indicated by arrows.

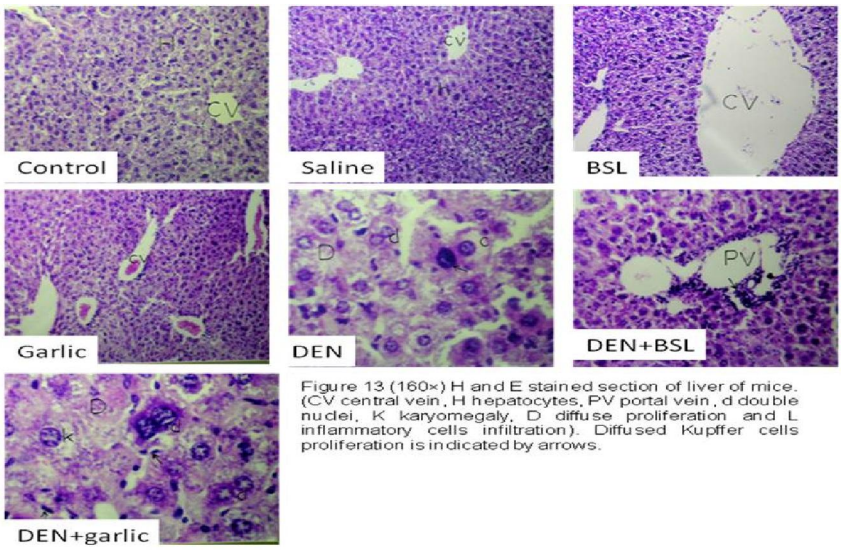


Figure 13 (160×) H and E stained section of liver of mice. (CV central vein, H hepatocytes, PV portal vein, d double nuclei, K karyomegaly, D diffuse proliferation and L inflammatory cells infiltration). Diffused Kupffer cells proliferation is indicated by arrows.

Table 1 Histopathological Alterations in the Different Groups of Mice's Liver sections.

Mice / Histopathological Alterations	Control group	Saline group	BSL group	Garlic group	DEN group	BSL + DEN group	Garlic +DEN group
Degenerative change (fatty degeneration)	-	-	-	-	+	-	+
Inflammatory cells infiltration in the portal area (portal infiltration)	-	-	-	-	++	+	-
Kupffer cells proliferation (kupffer cell hyperplasia)	-	-	-	-	+++	+	+++
Karyomegaly (nuclear enlargement)	-	-	-	-	+++	-	++
Cytomegaly	-	-	-	-	+++	-	++
Double nuclei (bi or multinucleation)	-	-	-	-	+++	-	++
Pyknosis Nuclear Chromatin & Hyperchromachia (hyperchromosia)	-	-	-	-	+++	-	-
Nuclear constriction for mitosis (mitosis)	-	-	-	-	+++	-	-
Dilated portal vein	-	-	++	-	++	+	+
Dilated central vein	-	-	++	+	++	+	-

+++ = Severe reaction, ++ = moderate reaction, + = weak, - = absent of the reaction

4.DISCUSSION

In recent years, the morbidity and mortality of cancer still reaches a high plateau and is a major public health problem worldwide. Chemoprevention, i.e. the use of either synthetic or naturally occurring agents to inhibit pre-cancerous events, has become recognized as a plausible, cost-effective and necessary approach to reduce cancer morbidity and mortality (Hong and Sporn, 1997; Wattenberg, 1997; Sporn and Suh, 2002). So, searching for new compounds for the treatment and prevention of cancer was the aim of numerous studies and the aim of our study .

Proliferation plays an important role in several steps of the carcinogenic process (Barret, 1993). It is involved in the fixation of a miscoding lesion in the newly made DNA (Ames and Gold, 1990). To investigate BSL *in vivo* activity as an antiproliferator and antiprogresser, DEN has been used as an effective experimental model in the field of carcinogenesis (Laughton *et al*., 1989).

The potency of COX-2 inhibitors *in vivo* could be attributed to the inhibition of the enzyme in the tumor, as well as, in stromal cells, resulting in antiproliferative, pro-apoptotic actions within the tumor, and anti-angiogenic , pro-immune surveillance activities in endothelial and myeloid cells. The combination of COX-2 inhibitor with standard cancer chemotherapeutic and/or radiation may provide additional therapeutic paradigms in the treatment of various human cancers (Mazhar *et al*., 2005).

The present results indicated that BSL was able to induce apoptosis rather than necrosis as mode of cell death in BSL treated mice when compared with untreated groups when liver tissue of mice stained with acridine orange. Modulation of the oxidative stress, inhibition of HDAC activity, NO inhibition and prevention of DNA damage which are the properties of BSL may lead to p53 regulation and/or caspases induction and this cause apoptosis induction in mice liver tissue since HDACs play an essential role in the regulation of apoptosis (Sambucetti *et al*., 1999). Also, NO plays a critical role in apoptosis via nitrosylation of caspase-9 (Torok *et al*., 2002). Mutations in genes that regulate apoptosis pathways are common in most cancers (Sun *et al*., 2004). Animal studies have also demonstrated that, certain chemopreventive agents could induce apoptosis in tumor cells *in vivo* without affecting normal cells (Sun *et al*., 2004). In accordance with our results, Gamal-Eldeen *et al*. (2009) reported that, different fractions of water-soluble polysaccharide extract derived from *S. latifolium* showed a disturbance in cell cycle including arrest in both S-phases in lymphoblastic leukemia (1301 cells). This disturbance was associated with an induced-cell death due to apoptosis, but not necrosis. On the other hand, our results revealed that, garlic increases necrosis rather than apoptosis in mice liver and this is may be due to increased TNF-α and NO. Since allicin the major component of garlic, induced tumoricidal activity and increased the production of TNF-α and NO in murine peritoneal macrophages in a dose-dependent manner (Kang, *et al*., 2001). Allicin inhibits the apoptosis of macrophages in a depleted nutritional state through the MEK/extracellular signal-regulated kinase pathway (Cho *et al*., 2006).

Liver infiltration by phagocytes, during liver injury, provided a source of ROS which cause damage to DNA, proteins and lipids when their generation exceeds the ability of the antioxidant systems to remove them (Simile *et al*., 2005; Calvisi *et al*., 2008). In the current study, BSL showed down regulation of DNA fragmentation in BSL treated mice before and after DEN injection when compared with DEN-induced mice, suggesting that, BSL prevents DNA damage. The decrement in the rate of oxidative DNA damage by BSL which could involve induction of the DNA repair system serves as a basis for chemopreventive mechanisms.

Angiogenesis, the development of new blood vessels from endothelial cells, is a crucial process in tumor pathogenesis as it sustains malignant cells with nutrients and oxygen (Fayette *et al*., 2005). During angiogenesis, endothelial cells are stimulated by various growth factors, such as VEGF and FGF, and are attracted to the site where the new blood supply is needed by inflammatory cytokines and chemoattractants (Albini *et al*., 2005; Presta *et al*., 2005).

There is a tight interplay between innate immune and endothelial cells, inflammatory leukocytes (neutrophils, macrophages, and others) release a number of factors that influence endothelial cell behavior [VEGF, hepatocyte growth factor (HGF), MMP2, and IL-8]. Inflammatory leukocytes might provide the angiogenic stimulus in the initial phases of tumorigenesis, as well as growth stimulus permitting accumulation of further mutations that eventually render the tumor inflammation-independent and malignant (Heryanto *et al*., 2004). Therefore targeting tumor angiogenesis is an attractive strategy to treat cancer. The production of VEGF is considered essential for angiogenesis and the migration of cancer cells and high VEGF expression level is associated with a wide array of malignancies.

VEGF mRNA expression is upregulated by a wide array of oncogenes (including H-ras and K-ras, src, p53, and C-jun) and growth factors (including epidermal growth factor [EGF], transforming growth

factor [TGFα,TGF β], insulin-like growth factor-1, and PDGF) In the current study, administration of BSL before and after DEN resulted in a significant decrease in VEGF level in mice serum compared with DEN-induced mice. This decreasing effect might be due to BSL inhibitory effect on NO and TNF-α since Shin *et al*. (2000) and Josko and Mazurek (2004) reported that, TNF-α was exerted its regulatory effect on both iNOs and VEGF and as line of evidence suggests NO activates the transcription factor hypoxia-inducible factor-1 alpha (HIF-1α) (Sandau *et al*., 2001a; Sandau *et al*., 2001b; Sharp, 2001) which in turn targets VEGF and can promote angiogenesis (Ravi *et al*., 2000). In the same line with our findings Bae *et al*. (2005) found that, polysaccharides isolated from *Phellinus gilvus* inhibited VEGF gene expression in the B16F10 melanoma cell line that constitutively express VEGF.

In the current study we found that, administration of garlic before and after DEN resulted in significant decrease in VEGF level compared with DEN-induced mice. The antioxidant activity of garlic might be responsible for this effect. Mousa *et al.* (2005), demonstrated inhibition of fibroblast growth factor-2 and VEGF-induced tube formation in human endothelial cells and inhibition of *ex vivo* neovascularization in chick chorioallantoic membrane assay by alliin. The anti-angiogenic effects of alliin were mediated, at least in part, by increase in cellular NO and p53 protein expression.

Over expression of growth factor and growth factor receptors such as EGF, PDGF, and others can result in enhanced proliferation by cancer cells (Masuda *et al*., 2001). Many growth factors (i.e., EGF and PDGF) bind their receptors and generate large increases in ROS (Martin, 2006). So, we estimated PDGF level in mice serum and found that BSL and garlic showed no effect on PDGF level in the serum of treated mice.

Our findings were further supported by the histopathological examination of liver sections, which illustrated that liver tissue of DEN-treated mice showed damage, manifested as degenerative change, inflammatory cells infiltration in the portal area, Kupffer cells proliferation (Kupffer cell hyperplasia), karyomegaly (nuclear enlargement), cytomegaly, double nuclei, pyknosis nuclear chromatin and hyperchromachia, nuclear constriction for mitosis, dilated portal vein, dilated central vein. On the contrary, liver tissue of mice treated with BSL before and after DEN injection showed more or less normal hepatic lobular architecture and this effect was seen to a lesser extent in the animals treated with garlic before and after DEN injection compared to DEN induced mice.

Accordingly, these histopathological findings as an end-point biomarker primarily confirm the chemopreventive potential of BSL in inhibiting hepatocellular preneoplas induced by DEN.

Altogether, the results of the present study indicates that BSL could be represented as promising cancer chemopreventive agent against hepatocarcinogenesis, since it has tumor anti-promoting activity via its immunomodulatory activity as, it has anti-inflammatory and proliferative effect on the macrophage cells and apoptosis induction. Also, BSL had anti-progression properties through inhibition of proliferation of hepatocarcinoma cells and inhibition of angiogenesis.

5.REFERENCES

1-Albini A, Tosetti F, Benelli R and Noonan DM (2005): Tumor inflammatory angiogenesis and its chemoprevention. *Cancer Res., 65: 1 (0637-10641.*

2-Ames BN and Gold LS (1990): Too many rodent carcinogens, mitogenesis increases mutagenesis. *Science, 249: 970–97*

3-Barret JC (1993): Mechanisms of multistep carcinogenesis and carcinogen risk assessment. *Environ. Health Perspect, 100: 9–20*

4-Bertram JS (2000): The molecular biology of cancer. *Mol. Aspects Med., 21: 167–223.*

5-Banchroft JD, Stevens A and Turner DR (1996): Theory and practice of Histological Techniques Fourth Ed. Churchil Livingstone, NewYork, London, San Francisco, Tokyo

6-Bae J, Jang H, Yim H, Jin H (2005): Polysaccharides isolated from *Phellinus gilvus* inhibit melanoma growth in mice. *Cancer Lett., 218: 43–52.*

7-Berenblum I and Armuth V (1981): Two independent aspects of tumor promotion. *Biochim. Biophys. Acta., 651: 51–63.*

8-Behrens B and Karber C (1935): Wie sind reichenversuche fur biologische auswertugen. Am zwechmassigsten anzwordnen? *Arch. Exp. Pathol. Pharmakol., 177: 379-38*

9-Block RJ, Vurrum EL and Zweig U (1955): A manual of paper chromatography and paper electrophoresis" Academic Press, New York, *P. 127.*

10-**Butterfield LH (2004):** Immunotherapeutic strategies for hepatocellular carcinoma. *Gastroenterology, 127: 232-241*

11-Calvisi DF, Pinna F, Ladu S, Pellegrino R, Muroni MR, Simile MM, De Miglio MR, Frau M, Tomasi ML, Seddaiu MA, Daino L, Virdis P, Feo F and Pascale RM (2008): Aberrant iNOS signaling is under genetic control in rodent liver cancer and potentially prognostic for human disease. *Carcinogenesis, 29: 1639–1647.*

12-Cho SJ, Rhee DK and Pyo S (2006): Allicin, a major component of garlic, inhibits apoptosis of

macrophage in a depleted nutritional state. *Nutrition, 22: 1177–1184.*

13-Doumas BT (1975): Colorimetric method for the determination of serum total protein. *Clin. Chem., 21: 1159-1161.*

14-Fayette J, Soria JC and Armand JP (2005): Use of angiogenesis inhibitors in tumour treatment. *Eur. J Cancer, 41: 1109–1116.*

15-Gamal-Eldeen AM, Ahmed EF and Abo-Zeid MA (2009): *In vitro* cancer chemopreventive properties of polysaccharide extract from the brown alga, Sargassum latifolium. *Food Chem. Toxicol., 47: 1378–1384.*

16-Gerhäuser C, Klimo K, Heiss E, Neumann I, Gamal-Eldeen A, Knauft J, Liu JU, Sitthimonchai S and Frank N (2003): Mechanism-based *in vitro* screening of potential cancer chemopreventive agents. *Mutat. Res., 523–524, 163–172*

17-Greten T and Jaffee E (1999): Cancer vaccines. *J Clin.Oncol.,17:1047-10*

18-Heryanto B, Girling JE and Rogers PA (2004): Intravascular neutrophils partially mediate the endometrial endothelial cell proliferative response to estrogen in ovariectomised mice. *Reproduction, 127: 613–620*

19-Heidelberger C, Freeman AE, Pienta R, Sivak A, Bertram JS, Casto BC, Dunkel VC, Francis MW, Kakunaga T, Little JB, 18-Schechtman LM (1983): Cell transformation by chemical agents a review and analysis of the literature . Areport of the U.S. Environmental Protection Agency Gene-Tox Program. *Mutat. Res., 114: 283–385*

20-Hong WK and Sporn MB (1997): Recent advances in chemoprevention of cancer. *Science, 278: 1073–1077*

21-Josko J and Mazurek M (2004): Transcription factors having impact on vascular endothelial growth factor (VEGF) gene expression in angiogenesis. *Med. Sci. Monit., 10: 89–98*

22-Kang MS, Moon EY, Cho CG and Pyo S (2001): Immunomodulating effect of garlic component, allicin, on murine peritoneal macrophages. *Nutrition Research, 21: 617–626*

23-Kelloff GJ, Lieberman R, Steele VE, Boone CW, Lubet RA, Kopelovich L Malone WA, Crowell JA, Higley HR and Sigman CC (2001): Agents, biomarkers, and cohorts for chemopreventive agent development in prostate cancer. *Urology, 57: 46–51*

24-Kelloff GJ, Sigman CC and Greenwald P (1999a): Cancer chemoprevention: progress and promise. *Eur. J Cancer, 35: 2031-2038*

25-Kim MG, Seo JW, Song KS, Kim CH, Chung BH and Ki-Rhee S (1998): Levan and fructosyl derivatives formation by a recombinant levansucrase from Rahnella aquatilis. *Biotech. Lett., 20: 333–336*

26- Kinneer K and Ma Q (2002): Chemoprotection by phenolic antioxidants: inhibition of tumor necrosis factor induction in macrophages. *J. Biol. Chem., 277: 2477–2484.*

27-Laughton MJ, Haliiwell B, Evans PJ and Hoult JRS (1989): Antioxidant and pro-oxidant actions of the plant phenolics quercetin, morin, glossypol and myricetin effects on lipid peroxidation, hydroxyl radical generation and bleomycin dependant damage to DNA, *Biochem. Pharmacol., 38: 2859–2865.*

28-Martin KR (2006): Targeting Apoptosis with Dietary Bioactive Agents. *Exp. Biol. Med., 231: 117–129.*

29-Masuda M, Suzui M and Weinstein I (2001): Effects of epigallocatechin-3-gallate on growth, epidermal growth factor receptor signaling pathways, gene expression, and chemosensitivity in human head, neck squamous cell carcinoma cell lines. *Clin. Cancer Res., 7: 4220–4229*

30-Mazhar D, Gillmore R and Waxman J (2005): COX and cancer. Q J Med., 98: 711–718.

31-McConkey DJ, Nicotera P, Hartzell P, Bellomo G, Wyllie AH and Orrenius S (1989): Glucocorticoids activate a suicide process in thymocytes through an elevation of cytosolic Ca+2 concentration. *Arch. Biochem. Biophys., 269: 365*

32-Meng G and Futterer K (2003): Structural framework of fructosyl transfer in Bacillus subtilis levan sucrase. *Nat. Struct. Biol., 10: 935–941*

33-Mousa AS and Mousa SA (2005): Anti-angiogenesis efficacy of the garlic ingredient alliin and antioxidants: role of nitric oxide and p53. *Nutr. Cancer, 53: 104–110*

34-Pileggi R and Khin BW (1962): Enzymatic colorimetric method. J Biol. Chem. 40: 585–589

34-Priest FG (1977): Extracellular enzyme synthesis in the genus Bacillus. *Bacteriol. Rev., 41: 711-753*

35-Presta M, Dell'Era P, Mitola S, Moroni E, Ronca R and Rusnati M (2005): Fibroblast growth factor/fibroblast growth factor receptor system in angiogenesis. *Cytokine Growth Factor Rev., 16: 159–178*

36-Rahman El-Zayadi A, Abaza H, Shawky S, Mohamed MK, Selim OE and Badran HM (2001): Prevalence and epidemiological features of hepatocellular carcinoma in Egypt-a single center experience. *Hepatol. Res., 19: 170-179*

37- Ravi R, Mookerjee B, Bhujwalla ZM, Sutter CH, Artemov D, Zeng Q, Dillehay LE, Madan A, Semenza GL and Bedi A (2000): Regulation of tumor angiogenesis by p53-induced degradation of hypoxia-inducible factor 1 alpha. *Genes Dev., 14: 34–44*

38-Sambucetti LC, Fischer DD, Zabludoff S, Kwon PO, Chamberlin H, Trogani N, Xu H and Cohen D (1999): Histone deacetylase inhibition selectively alters the activity and expression ofcell cycle proteins leading to specific chromatin acetylation and antiproliferative effects. *J Biol. Chem., 274: 34940-34947.*

39-Sandau KB, Zhou J, Kietzmann T and Brune B (2001a): Regulation of the hypoxia-inducible factor 1alpha by the inflammatory mediators nitric oxide and tumor necrosis factor-alpha in contrast to desferroxamine and phenylarsine oxide. *J. Biol. Chem., 276: 39805–39811.*

.**40-Sandau KB, Fandrey J and Brune B (2001b):** Accumulation of HIF-1alpha under the influence of nitric oxide. *Blood, 97: 1009-1015.*

41-Simonen M and Palva I (1993): Protein secretion in Bacillus species. *Microbiol. Rev., 57: 109-137*

42-Sharp PA (2001): RNA interference—2001. *Genes Dev. 15: 485–490*

43-Shin KY, Moon HS, Park HY, Lee TY, Woo YN, Kim HJ, Lee SJ and Kong G (2000): Effects of tumor necrosis factor-alpha and interferon-gamma on expression of matrix metalloproteinase-2 and -9, inhuman bladder cancer cells. *Cancer Lett., 159: 127–34*

.**44-Soria JC, Kim ES, Fayette J, Lantuejoul S, Deutsch E and Hong WK (2003):** Chemoprevention of lung cancer. *Lancet Oncol., 4: 659–669*

45-Sporn MB and Suh N (2002): Chemoprevention: an essential approach to controlling cancer. *Nat. Rev. Cancer, 2: 537–543*

46-Smith TJ, Hong J-Y, Wang Z-Y and Yang CS (1995): How can carcinogenesis be inhibited? *Ann. NY Acad. Sci., 768: 82–90*

47-Simile MM, Pagnan G, Pastorino F, Brignole C, De Miglio MR, **Muroni MR, Asara G, Frau M, Seddaiu MA, Calvisi DF, Feo F**, **48-Ponzoni M and Pascale RM (**2005**):** Chemopreventive N-(4-hydroxyphenyl) retinamide targets deregulated NF-fkappagB and Mat1A genes in the early stages of rat liver carcinogenesis. *Carcinogenesis, 26: 412-417.*

48-Surh Y-**J (1999):** Molecular mechanisms of chemopreventive effects of selected dietary and medicinal phenolic substances. *Mutat. Res., 428: 305-327.*

49-Sun S, Hail N and Lotan R (2004): Apoptosis as a novel target for cancer chemoprevention. *J Nat. Cancer Inst., 96: 662–672*

50-Torok NJ, Higuchi H, Bronk S and Gores GJ (2002): Nitric oxide inhibits apoptosis down stream of cytochrome c release by nitrosylating caspase 9. *Cancer Res., 62: 1648–53*

51-Umar A, Viner JL and Hawk ET (2001): The future of colon cancer prevention. *Ann. NY Acad. Sci., 952: 88–108*

52-Vina I, Bekers M, Karsakenvich A, Linde R, Gonta S and Toma M (1998): Some roperties of fructose biopolymer levan produced by Zymomonas mobilis. Biomass for Energy and Industry. Proceedings of the International Conference, *pp 460–463.*

53-Wattenberg W (1997): An overview of chemoprevention: current status and future prospects. *Proc. Soc. Exp. Biol. Med., 216: 133–141*

54-Wattenberg LW (1995): What are the critical attributes for cancer chemopreventive agents? *Ann. NY Acad. Sci., 768: 73–81.*

**Akmowledgment:* Department of Natural and Microbial Products Chemistry, NRC, Egyp

11/10/2012

Radionuclides Differentiation during the Secondary Processes of Pb-Zn Mineralization, Gabal El Rousas, Eastern Desert, Egypt

Sh.M.Talaat[1] and A.I.M.Ismail[2]

[1] Faculty of Women, for Art, Science and Education, Ain Shams University, Cairo,Egypt.
[2] Geological Science Department, National Research Center, Dokki, Cairo, Egypt.
Shadia_talaat@yahoo.com

Abstract: The primary mineralization of Pb-Zn in Gabal El Rousas on the Egyptian Red Sea hills was subjected to secondary processes led to the redistribution of those mineralization and became much abundant than the hypogene minerals. This study is restricted on the differentiation in the associated radionuclides during these secondary processes. Seven samples from the mineralized ore and six samples from the hosting Miocene sedimentary rocks were collected and studied radiometrically using the Hyper Pure Germanium (HPGe) detector. The results showed that the ^{238}U and ^{226}Ra are concentrated in the hosting rocks, while ^{40}K on the other hand is concentrated in the mineralized zones. ^{232}Th did not change much due to its immobility, while in the mineralized group, ^{214}Pb and ^{214}Bi are nearly half the activity concentration of their parent ^{226}Ra which is due to the escape of some ^{222}Rn during the secondary processes that affected the primary mineralization. With respect to the environmental impact, the absorbed dose rate, annual effective dose rate, radium equivalent, radioactivity level index and external radiation hazard index for the mineralized samples are three times lower than the hosting sedimentary rocks.
[Sh.M. Talaat and A.I. M. Ismail. **Radionuclides Differentiation during the Secondary Processes of Pb-Zn Mineralization, Gabal El Rousas, Eastern Desert, Egypt.** *Life Sci J* 2012;9(4):2857-2864] (ISSN:1097-8135). http://www.lifesciencesite.com.419

Keywords: Gabal El Rousas / Gamma ray spectroscopy/ Natural radioactivity / Radiation hazard indices

1. Introduction

As a result of the activity concentration of primordial radionuclides ^{238}U, ^{226}Ra, ^{232}Th series, and ^{40}K that exist in air, water, human's body, food, building supplies and earth's coating, many creatures have exposed to such natural radiation(1). There is a wide broaden existence of natural radioactivity in the earth surroundings and in different geological structures, rocks, water, air and soils (2). Such concentrations are not identical all over the world; they broadly fluctuate with diverse locations. The present study aims to discuss the distribution and differentiation of the main radionuclides; ^{238}U, ^{226}Ra, ^{214}Pb, ^{214}Bi, ^{232}Th and ^{40}K in the mineralized and hosting rocks at Gabal El Rousas area, Eastern Desert, Egypt. The environmental background level of natural radiation, dose rate, annual effective dose, radium equivalent activity, radioactivity level index and external hazard were investigated. The X-Ray Diffraction (XRD) tests for two representative samples are carried out.

Regional Setting

Gabal El Rousas (lead Mountain) area is located at longitude 34^0 46' E and latitude 25^0 11' N. It is located about 120 km south of Al Quseir (Fig.1a), 16 km north of Marsa Alem and about 7 km west Red Sea coast. Gabal El Rousas proper is an isolated low hillock (Fig.1b) dissected by shallow blind gullies. The maximum elevation is 111 m, and its relief is about 17 m. It is flat topped and is mostly capped by terrace gravels and sands that cover the Miocene limestone bed rocks (3).

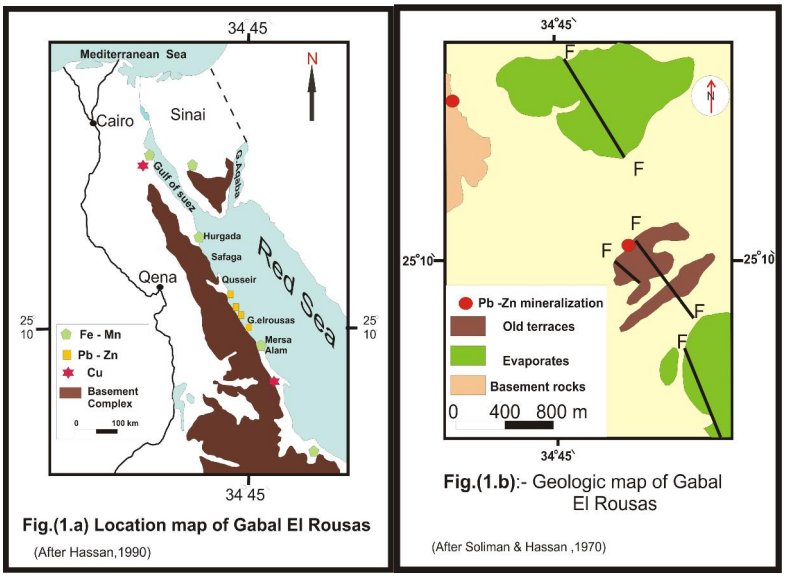
The bed rocks of Gabal El Rousas are the limestone and vaporates which covered by gravel terraces and overlies the basement rocks. Gabal El Rousas is characterized by major and minor faults with small displacements (Fig. 1b). The Pb-Zn mineralizations are intense in the major fault zones with epigenetic minerals and their oxidation products (4). The secondary minerals are abundant which indicate intense alteration processes.

Analytical Technique

Samples collection and preparation

Thirteen representative samples from two sites (1 and 2) were collected from the mineralized bed rocks. The samples from site 1 (seven samples) represent the mineralized group. The samples from site 2 (six samples) are the non-mineralized group. All these samples were dried, trodden, homogenized, weighted and transferred to polyethylene marinelli beakers having volumes of 100 ml and 250 ml. In order to allow for ^{226}Ra and its short-lived progenies to reach radioactive equilibrium and to make sure that radon gas is confined within the volume and also the daughters remain in the samples, these samples were sealed for a approximate period of four weeks before counting using gamma ray spectroscopy(5). Each sample was measured during an accumulating time between 20 hours and 24 hours. After that an empty

cylindrical plastic container (polyethylene marinelli beaker) was placed in the detection system, for a counting period of 48 hours, in order to collect the background count rates.



Figures: (1a and 1b): Location and geological maps of the studied area

2 Experimental technique.

Two techniques are used in this study: the first is the Hyper Pure Germanium (HPGe) detector for gamma (ɣ) analysis of all samples. The second is the X-Ray Diffraction (XRD) analysis for two samples; one from each group to identify the mineral constitutes. Mineralogical analysis involved (XRD) using a diffractometer BRUKUR D_8 ADVANCE using CuKα radiation with secondary monochromatov ($\gamma = 1.5405\ A^0$). The X-ray tube was operated at 40 Kv and 40 mA. The diffraction angle; two theta (2 θ) was scanned at a rate of $2^o\ min^{-1}$.

The high purity germanium (HPGe) detector was used for the measurements of gamma ray spectroscopy. The HPGe detector, model (GEM-50210-P), a P-type crystal, from EG & G ORTEC was used for gamma-ray measurements. This detector has a resolution (FWHM) of 1.9 keV for the 1332 keV gamma-ray line of ^{60} Co and a relative efficiency of about 50%. The efficiency calibration for the HPGe detector was carried out by using a ^{152} Eu point source to obtain a broad energy range (from 121.78 to 1408 keV). The relative efficiency curve was normalized for the100 ml capacity marinelli beakers and for a 250 ml capacity polyethylene container by three different concentrations of chemically pure potassium chloride solution in distilled water. The absolute efficiency curves were obtained for each size. Activity concentrations were averaged from photopeaks at several energies. The ^{234m}Pa activities determined from the 1001 Kev photo peak was assumed to represent actual ^{238}U [6]. The activity concentration for ^{226}Ra was derived from the gamma-ray transition of ^{226}Ra (186.1 kev), for ^{214}Pb (351.9, 295.1 kev) and (609.3, 1120.3, 1764.5 kev) for ^{214}Bi. While the activity concentration of ^{232}Th series was derived from the gamma-ray transition of ^{228}Ac (338.4, 911 kev) and ^{208}Tl (583.1, 2614.4 kev). ^{40}K was determined from the 1460 kev photo peak [7]. Also XRD analysis measurements were performed which was made at the National Research Center, Dokki, Cairo, Egypt.

Radioactivity Counting

The computation of the activity concentration C ($Bqkg^{-1}$) for each of the radionuclides in the understudied samples was calculated by using the net area count after the background corrections for each photo peak- knowing that the counting time for each sample was approximately 24 hours- using the following expression [8]:

$$C(Bqkg^{-1}) = \frac{C_n}{\varepsilon\ P_\gamma\ M_s} \qquad (1)$$

where C_n is the count rate under each photo peak due to each radionuclide, Ɛ represents the detector efficiency for the specific ɣ-ray, while P_γ is the absolute transition probability of the specific ɣ -ray and lastly M_s is the mass of the sample (kg).

The following relation was used to obtain the lowest limits of detection (LLD) [9]:

$$LLD = \frac{4.66\ S_b}{\varepsilon \times I_\gamma} \qquad (2)$$

where S_b is the estimated standard error of the net background count rate in the spectrum of the radionuclide, Ɛ represents the counting efficiency and I_γ is the abundance of gamma emissions per radioactive decay. The LLD value for ^{238}U was obtained to be 1.307 Bqkg^{-1} while that of ^{232}Th and ^{40}K were 1.344 and 9.347 Bqkg^{-1} respectively.

Hazard Indices

The activity concentrations of ^{238}U, ^{232}Th and ^{40}K measured in each of the studied samples indicate the quantity of radioactivity present but do not provide a measure of radiation risk in the form of an absorbed dose rate. The absorbed dose rate, D (nGyh^{-1}) in air at 1 m above ground level due to the presence of ^{238}U, ^{232}Th and ^{40}K in the studied samples was calculated using the following equation [1]:

$$D\left(nGyh^{-1}\right) = 0.462\ A_{Ra} + 0.604\ A_{Th} + 0.0417\ A_K \quad (3)$$

where A_{Ra}, A_{Th} and A_K are the average specific activities of ^{226}Ra, ^{232}Th and ^{40}K in Bqkg^{-1} respectively.

The annual effective dose (E_{ff}): The annual effective dose equivalent was calculated from the absorbed dose by applying the dose conversion factor of 0.7 SvGy^{-1} and the outdoor occupancy factor of 0.2 [1]. The effective dose rate in units of mSv per year was calculated using the following formula:

Outdoor annual effective dose

$$= D \times 8760\ h \times 0.2 \times 0.7\left(SvGy^{-1}\right) \times 10^{-6}\ mSvy^{-1} \quad (4)$$

Radium Equivalent Activity (Raeq): The term radium equivalent represents the weighted sum of the individual activities of ^{226}Ra, ^{232}Th and ^{40}K based on the assumption that 10 Bqkg^{-1} of ^{226}Ra, 7 Bqkg^{-1} of ^{232}Th or 130 Bqkg^{-1} of ^{40}K produce the same gamma-ray dose rates which is calculated using the following relation [10].

$$Ra_{eq} = A_{Ra} + 1.43\ A_{Th} + 0.07\ A_K \leq 370 \quad (5)$$

where A_{Ra}, A_{Th} and A_k are the specific activities of ^{226}Ra, ^{232}Th and ^{40}K in Bqkg^{-1}, respectively.

Radioactivity level index (I_γ): The radioactivity level index is used to estimate the level of radiation risk especially gamma ray, associated with natural radionuclide in specific materials. Its definition as follows [11]:

$$I_\gamma = A_{Ra}/150 + A_{Th}/100 + A_K/1500 \leq 1 \quad (6)$$

where A_{Ra}, A_{Th} and A_K are the specific activities of ^{226}Ra, ^{232}Th and ^{40}K in Bqkg^{-1}, respectively.

The external hazard index (H_{ex}): The external hazard index (Hex) is the quantity of radium equivalent activity after modification, which is defined as follows [10]:

$$H_{ex} = A_{Ra}/370 + A_{Th}/259 + A_K/4810 \quad (7)$$

Where A_{Ra}, A_{Th} and A_k are the specific activities of ^{226}Ra, ^{232}Th and ^{40}K in Bqkg^{-1}, respectively. The value of H_{ex} must be lower than unity in order to keep the radiation hazard insignificant.

3. Results and Discussions

Radionuclides Distribution

^{238}U activity was determined indirectly from the gamma rays emitted by its daughter products [12]. The activity of ^{238}U cannot be directly determined, since the isotope emits only a weak (0.064%) gamma-ray at 49.55 keV. However, any of the gamma-emitting daughter nuclides in equilibrium with ^{238}U such as ^{234}Th or ^{234m}Pa could be used for this purpose [13, 14]. The daughter radionuclides (^{234}Th and ^{234m}Pa) were selected as an indicator of ^{238}U activity. Progeny of ^{238}U are relatively short-lived, and thus it is reasonable to calculate gamma radiations of this sequence as ^{238}U. Therefore, secular equilibrium was assumed between ^{238}U and ^{234}Th and ^{234m}Pa, and thus ^{234m}Pa activities determined from the 1001 keV photo peak, was assumed to represent actual ^{238}U activities [6]. The specific activity of ^{40}K was measured directly by its own gamma-ray at 1460.8 keV, while activities of ^{232}Th series was calculated based on the mean value of its respective decay products which are in secular equilibrium. The specific activity of ^{226}Ra was measured using the 186.1 keV from its own gamma-ray (after the subtraction of the 185.7 keV of ^{235}U).

The results represented by the specific activity (Bq kg^{-1}) of different radionuclides in the studied samples for both sites are presented in table 1.Table 1 (site1) shows the activity concentrations for ^{226}Ra ranging from 28.80 ± 3.58 Bq kg^{-1} to 43.10 ± 8.18 Bq kg^{-1} with an average of 34.49 ± 5.47 Bq kg^{-1}, while it is from 5.84 ± 0.66 Bq kg^{-1} to 8.73 ± 1.26 Bq kg^{-1} with an average of 7.31 ± 0.88 Bq kg^{-1} for ^{232}Th and from 321.59 ± 3.50 Bq kg^{-1} to 399.96 ± 5.38 Bq kg^{-1} with an average of 347.73 ± 4.15 Bq kg^{-1} for ^{40}K. These three averages are in agreement with the world wide values documented at 35, 30, and 400 Bqkg^{-1} for ^{226}Ra, ^{232}Th, and ^{40}K respectively [1]. It can be also noticed that in Table 1 (site 1), the activity concentrations of ^{226}Ra are nearly two times the values for its daughters: ^{214}Bi and ^{214}Pb.

Table 1 (site 2) shows the activity concentration of ^{238}U ranging from 160.94 ± 24.33 $Bqkg^{-1}$ to 237.75 ± 24.23 $Bqkg^{-1}$ with an average of 201.84 ± 25.77 $Bqkg^{-1}$, this average is in disagreement with the worldwide value which is documented at 35 Bq kg^{-1} [(1)], while it is ranging from 172.49 ± 9.87 $Bqkg^{-1}$ to 209.78 ± 9.68 $Bqkg^{-1}$ with an average of 193.05 ± 7.55 $Bqkg^{-1}$ for ^{226}Ra. As for ^{232}Th, it is ranging from 8.93 ± 0.70 $Bqkg^{-1}$ to 10.25 ± 0.89 $Bqkg^{-1}$ with an average of 9.58 ± 0.99 $Bqkg^{-1}$ and that of ^{40}K ranges from 99.00 ± 5.42 $Bqkg^{-1}$ to 113.65±4.54 $Bqkg^{-1}$ with an average of 108.72 ± 3.96 $Bqkg^{-1}$, both averages for ^{232}Th and ^{40}K are in agreement with the worldwide value documented at 30 and 400 $Bqkg^{-1}$ respectively [(1)]. It can be seen that the highest activity concentration of ^{238}U, ^{226}Ra and ^{232}Th are 237.75±24.23 $Bqkg^{-1}$, 209.78±9.68 $Bqkg^{-1}$ and 10.25 ± 0.89 $Bqkg^{-1}$, respectively which were registered in site 2 while ^{40}K is registered in site 1 with a value of 399.96 ± 5.38 $Bqkg^{-1}$.

The mean activity concentration for ^{232}Th was close in values as recorded in the mineralized and no-mineralized groups, which is attributed to its immobility to be altered.

The most contribution in the mineralized group (site 1) is ^{40}K with percentage of (89%), followed by ^{226}Ra (9%) and ^{232}Th (2%) as shown in fig. (2a). While Fig. (2b) shows that the ^{238}U is the most contribution in the non-mineralized group (site 2) with percentage of (39%), followed by ^{226}Ra (38%), ^{40}K (21%) and ^{232}Th (2%).

The ratio $^{226}Ra/^{238}U$ is nearly around unity in the non-mineralized hosting rocks, which means that the uranium migration-in and migration-out is nearly the same. The $^{238}U/^{232}Th$ ratio is ranged between 17.49 and 23.51 which mean that there is a migration of uranium to the hosting rocks. The disequilibrium between ^{226}Ra and ^{238}U is very clear in the mineralized samples as the ^{238}U is under limit of detection, while ^{226}Ra ranges between 28.8 $BqKg^{-1}$ and 43.1 $BqKg^{-1}$, which means migration-out of uranium.

Mineralogy and its reflection on radionuclides distribution

XRD was made for two samples, one mineralized sample (S-1-1) from site 1 and the other is non mineralized sample (S-2-3) from site 2. The results are shown in (figs 3 and 4). The sample (S-1-1) (fig.3) which represents the mineralized group contains Hemimorphite $\{Zn_4Si_2O_7(OH)_2(H_2O)\}$ (55.7%), Hydrozincite $\{Zn_5(OH)_6(CO_3)\}$ (30.2%) and Calcite, $\{CaCO_3\}$ (14.1%). These minerals are formed during the alteration processes (oxidation) for the primary hypogene minerals [(4).] While the mineral constituents of the sample (S-2-3) which represent the non-mineralized group (fig. 4) are mainly Minamlite $\{Na_{36}K_1Ca_{27}\}$ $\{Al_3(SO_4)_2(OH)_6\}$ (56.3%), Hematite $\{Fe_2O_3\}$ (12.9%), Kaolinite $\{Al_2Si_2O_5(OH)_4\}$ (23.6%) and Anatase $\{TiO_2\}$ (7.2%).

Soliman and Hassan [(3)] in their study on Gabal El Rousas reached the conclusion that high concentration of lead (Pb) meets low concentration of Zinc (Zn) and vice-versa. As it is known that the existence of radium is associated with the existence of lead and based on the above conclusion, and since in our study there is high concentration of Zinc in site1, therefore, it can be interpreted as low concentration of radium which is the case with mineralized samples understudy.

In site 2, one of the main constituent minerals is the hematite which is a ferric oxide (Fe_2O_3). Uranium is usually associated with ferric iron as adsorbed ions and so the hosting sediments have high uranium content than the mineralized, as it contains hematite (12.9%).

Hazard indices

The activity concentration values of ^{226}Ra, ^{232}Th and ^{40}K of the studied areas can be used to calculate the total gamma absorbed dose rate in air at 1 m above the ground. As shown in table (2), the average absorbed dose rate value calculated by using equation (3) for site 1 varies from 30.25 to 41.86 $nGyh^{-1}$ with an average value of 34.85 $nGyh^{-1}$ that is in agreement with the world wide value (59 $nGyh^{-1}$) [(1)]. Consequently, the annual effective dose range is recorded by using equation (4) to be from 0.04 to 0.05 $mSvy^{-1}$ with an average value of 0.04 $mSvy^{-1}$ which is also in agreement with the world wide value (0.5 $mSvy^{-1}$) [(1)].

The average absorbed dose rate value for hosting rocks in site 2 varies from 89.21 to 107.85 $nGyh^{-1}$ with an average value of 99.51 $nGyh^{-1}$ using equation (3) that is in disagreement with the world wide value (59 $nGyh^{-1}$) [(1)], accordingly, using equation(4), the annual effective dose ranges from 0.11 to 0.13 $mSvy^{-1}$ with an average value of 0.12 $mSvy^{-1}$ which is in agreement with the world wide value (0.5 $mSvy^{-1}$) [(1)]. For both mineralized samples (site 1) and non-mineralized samples (site 2), the average values for the annual effective dose are 0.04 and 0.12 $mSvy^{-1}$ respectively which are less than the average recommended value (0.5 $mSvy^{-1}$) considering that this is in good agreement with the average world wide limits[(1)].

Table (1): Activity (Bq kg^{-1}) and ratios between Radionuclides for the studied samples.

Sample	234mPa	226Ra subseries Bq/Kg			232Th series Bq/Kg		Average	40K	226Ra/238U	238U/232Th
	Bq/Kg	226Ra	214Bi	214Pb	228Ac	208Tl		Bq/Kg		
S-1-1	ULD*	32.06±3.26	16.40±0.81	15.03±0.46	5.51±0.58	6.18±0.75	5.84±0.66	325.83±3.42		
S-1-2	ULD	31.22±2.76	17.37±0.79	18.67±0.28	5.52±0.60	8.04±0.37	6.78±0.48	327.10±3.35		
S-1-3	ULD	28.80±3.58	18.69±0.90	15.64±0.41	6.10±0.62	6.53±0.85	6.31±0.74	321.59±3.50		
S-1-4	ULD	41.59±8.43	20.15±1.55	19.10±0.66	6.57±1.10	9.89±1.11	8.23±1.10	399.96±5.38		
S-1-5	ULD	43.10±8.18	19.52±1.34	18.16±0.51	6.27±0.96	8.73±0.87	7.50±0.92	355.47±4.72		
S-1-6	ULD	33.07±9.19	17.96±1.54	20.67±0.61	7.24±1.54	10.22±0.99	8.73±1.26	346.31±5.17		
S-1-7	ULD	31.55±2.89	17.46±0.69	19.56±0.06	6.40±0.55	9.22±0.38	7.81±0.46	357.87±3.52		
Site (1)	ULD	34.48±5.47	18.22±1.09	18.12±0.43	6.23±0.85	8.40±0.76	7.31±0.80	347.73±4.15		
S-2-1	198.60±19.98	201.96±5.54	159.76±1.92	156.60±1.08	8.05±0.88	9.81±0.52	8.93±0.70	111.63±2.99	1.02	22.25
S-2-2	236.87±18.78	172.73±3.90	164.02±1.56	158.23±0.86	7.54±0.76	12.61±0.41	10.07±0.59	109.60±2.47	0.73	23.51
S-2-3	160.94±24.33	172.49±9.87	168.25±2.50	181.93±1.64	7.66±1.43	10.75±0.79	9.20±1.11	113.65±4.54	1.07	17.49
S-2-4	209.17±30.06	200.97±9.87	163.86±2.64	177.48±1.66	8.02±1.33	11.34±1.26	9.68±1.29	105.61±4.94	0.96	21.6
S-2-5	167.68±37.25	209.78±9.68	149.53±2.47	162.68±1.73	7.79±1.59	10.86±1.07	9.33±1.33	99.00±5.42	1.25	17.98
S-2-6	237.75±24.23	200.37±6.44	165.25±2.01	174.55±1.24	9.23±1.16	11.27±0.63	10.25±0.89	112.85±3.39	0.84	23.2
Site (2)	201.84±25.77	193.05±7.55	161.78±2.18	168.58±1.37	8.05±1.19	11.11±0.78	9.58±0.99	108.72±3.96	0.98	21.00

ULD* represnts the Under Limit of Detection

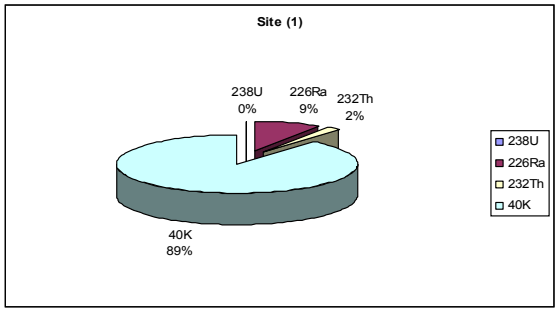


Fig.: (2a) Contribution of the different radionuclides in the mineralized group

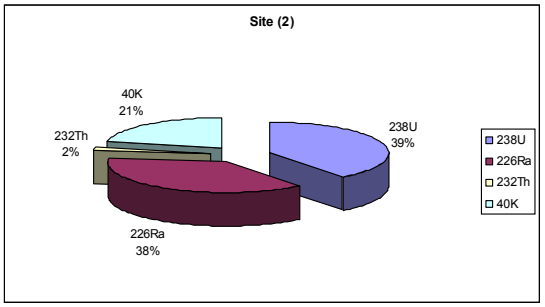


Fig.: (2b) Contribution of the different radionuclides in the non-mineralized group

Figs: (2a and 2b) Contribution of the different radionuclides for the studied area

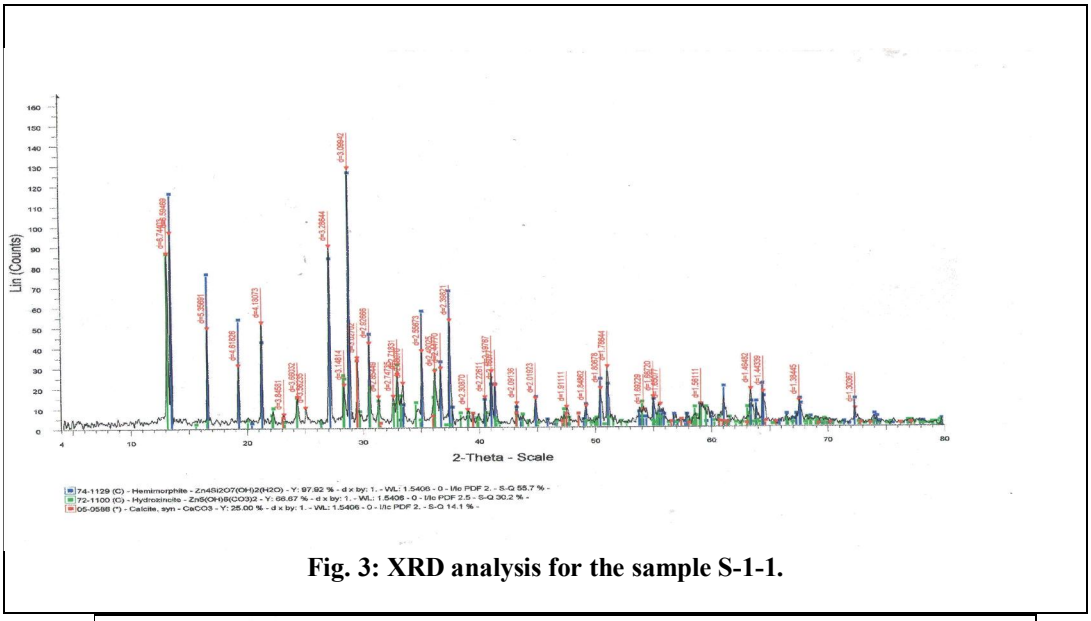


Fig. 3: XRD analysis for the sample S-1-1.

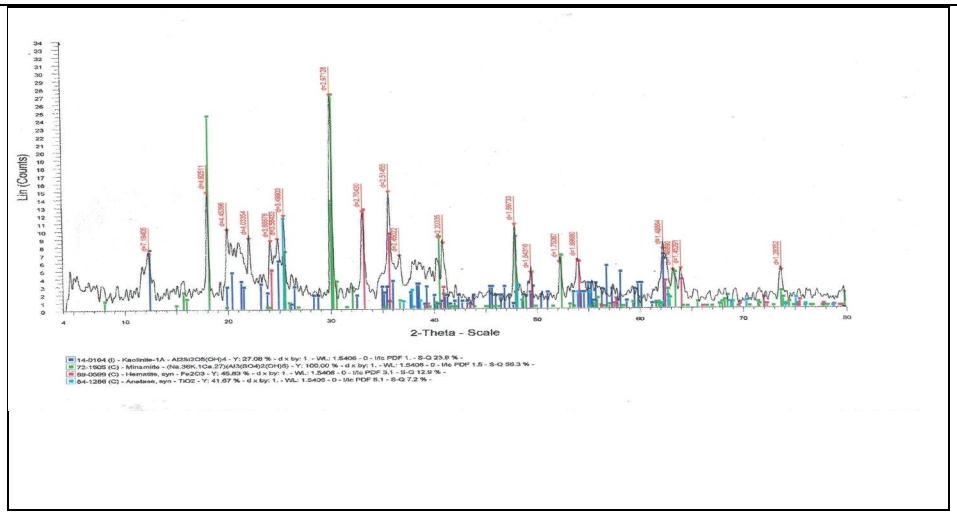


Fig.4: XRD analysis for the sample S-2-3

Radium equivalent activity (Raeq) is a widely used hazard index and it is calculated as given by equation (5). Table (2) summarized the average Raeq results for all studied samples. For the mineralized group (site 1), these values varied from 59.67 $Bqkg^{-1}$ to 83.57 $Bqkg^{-1}$ with an average value of 69.29 $Bqkg^{-1}$. As for the non-mineralized group (site 2), the average Raeq varied from 192.18 $Bqkg^{-1}$ to 232.39 $Bqkg^{-1}$ with an average of 214.36 $Bqkg^{-1}$. The estimated average values in the present work are lower than the recommended maximum value of 370 $Bqkg^{-1}$ [11]. By comparison with measured average values from some other countries, it is observed that the average value of this work is lower than the measured values of 366.9 $Bqkg^{-1}$ at southeast part of Eskisehir, Turkey [15], 266 $Bqkg^{-1}$ in Xiazhuang Granite Area (China) [2] and 493.8 $Bqkg^{-1}$ at eastern desert of Egypt[16]. On the other hand the average value in the present work is higher than the measured value of 122.79 $Bqkg^{-1}$ in sandstone at southwestern Sinai, Egypt [17].

The radioactivity level index Iγ calculated by equation (6) in site1 is less than unity which is in agreement with the recommended value, while in site 2 it is greater than the recommended value [11].There are some limited cases where the absorbed dose and the radioactivity level index Iγ do exceed the normal level of the province of Gabal El Rousas due to the presence of uranium in site 2.

The external hazard was calculated by equation (7) and it must not exceed the limit of unity for the radiation hazard to be negligible which is the case for our results for both sites as they are less than unity hence; they are in agreement with the world wide limit [10]. It can be seen through Table 2 that the values of the average absorbed dose rate, annual effective dose, radium equivalent activity, radioactivity level index and that of the external hazard, in the non-mineralized group, were nearly three times those recorded in the mineralized group.

Table (2): The range and the average of absorbed dose rate (D), annual effective dose (E_{ff}), radium equivalent activity (Raeq), radioactivity level index (Iɣ) and external radiation hazard index (H_{ex}) for the studied samples

Hazard indices	Mineralized group (N*= 7)		Non-mineralized group (N*= 6)	
	Range	Average	Range	Average
D ($nGyh^{-1}$)	30.25 – 41.86	34.85	89.21 -107.85	99.51
E_{ff} ($mSvy^{-1}$)	0.04 - 0.05	0.04	0.11 - 0.13	0.12
Raeq ($Bqkg^{-1}$)	59.67 – 83.57	69.29	192.18 -232.39	214.36
Iɣ	0.46 - 0.64	0.53	1.31 - 1.58	1.46
H_{ex}	0.17 - 0.23	0.19	0.52 - 0.63	0.58

N* represents the number of samples

Conclusion

In conclusion, this study covered the analysis of 13 samples for mineralized and non-mineralized groups and reached the following:

(1) The specific activity of ^{40}K is the largest contributor activity for the mineralized group, while both the ^{238}U and ^{226}Ra are the largest contributors for the non-mineralized group.

(2) The average activity concentrations of ^{238}U in non-mineralized groups are higher than the world wide limit due to its association with the ferric iron mineral (hematite).

(3) The average activity concentrations of ^{232}Th and ^{40}K for both the mineralized and the non-mineralized groups are in agreement with the world wide limits.

(4) The estimated average for the absorbed dose rates, annual effective dose, radium equivalent activity, radioactivity level index and the external hazard index in hosting sedimentary rocks are three times higher than those in the mineralized samples.

(5) The average absorbed dose rates and radioactivity level index of hosting sedimentary rocks are higher than the worldwide limit due to the effect of hydrothermal solution on the Miocene sedimentary rocks and its redistribution due to secondary alteration processes.

(6) The (XRD) data for the mineralized sample (S-1-1) states the presence of major contents of Hemimorphite (55.7 %), Hydrozincite (30.2 %) and Calcite (14.1%), all played their roles in the distribution of radium.

(7) The (XRD) data for the non-mineralized sample (S-2-3) states the presence of major contents of minamlite (56.3%) followed by Kaolinite (23.6%), Hematite (12.9%), and Anatse (7.2%), which played their role in the distribution of uranium.

Corresponding author
Sh.M. Talaat
Faculty of Women, for Art, Science and Education, Ain Shams University, Cairo,Egypt.
Shadia_talaat@yahoo.com

References

1. UNSCEAR; United Nations Scientific Committee on the Effects of Atomic Radiation, Sources and Effects of Ionizing Radiation. Report to the General Assembly with Scientific Annexes. United Nations, New York (2000).
2. Yang YX, Wu XM, Jiang ZY, Wang WX, Lu JG, Lin J, Wang LM, Hsia YF; Radioactivity concentration in soils of the Xiazhuang granite area , China. Appl Radiat Isot., 63: 255 (2005).
3. Soliman M.S. and Hassan M.M.; Geology and geochemistry of the Pb and Zn mineralizationin Gabal El Rousas., Ranga and Abu Anz areas, Eastern Desert, Egypt. 5th Arab science Congress, Damascus (1970).
4. Hassan M.M.; Studies on Lead-Zinc sulphide mineralization in the Red Sea coastal zone, Egypt. Proceeding, 8th IAGOD Symp., Ottawa, Canada (1990).
5. Abbady A.G.E., Uosif M.A.M., El-Taher A.; Natural radioactivity and dose assessement for phosphate rocks from Wadi EL-Mashash and El-Mahamid Mines, Egypt. J. Environ. Radiat. 84: 65 (2005).
6. Yucel H., Cetiner M.A., Demirel H.; Use of the 1001 keV peak of 234mPa daughter of 238U in measurement of uranium concentration by HPGe gamma-ray spectrometry. Nucl Instrum Method Phys Res A 413:74 (1998).
7. Merdanoglu B., Altinsoy, N.; Radioactivity concentration and dose assessment for soil samples from Kestanbole granite area, Turkey. Radiat. Prot. Dosimetry 121 (4): 399 (2006).
8. Jibiri N.N., Farai P.I., Alausa K.S; Estimation of annual effective dose due to natural radioactive elements in ingestion of food stuffs in tin mining area of Jos-Plateau, Nigeria. J. Environ. Radiat. 94: 31 (2007).
9. Jibiri N.N., Bankole S.O.; Soil radioactivity and radiation absorbed dose rates at roadsides in high-traffic density areas in Ibadan Metropolis, southwestern Nigeria. Radiat. Prot. Dosimetry 118, 453 (2006).
10. Huy N.Q., Luyen T.V.; Study on external exposure doses from terrestrial radioactivity in southern Vietnam. Radiat. Prot. Dosimetry 118, 331(2006).
11. Organization for Economic Cooperation and Development, Exposure to radiation from the natural radioactivity in building materials. Report by a Group of Experts of the OECD Nuclear Energy Agency. OECD, Paris, France (1979).
12. Sutherland R.A., de Jong E.; Statistical analysis of gamma emitting radionuclide concentrations for three fields in Southern Saskatchewan, Canada. Health Phys 58, 417 (1990).
13. Papachristodoulou CA., Assimakopoulos P.A., Patronis N.E., Ioannides K.G.; Use of HPGe gamma-ray spectrometry to assess the isotopic composition of uranium in soils. J. Environ Radioact 64(2–3):195 (2003).
14. Zhang W., Yi J., Mekarski P., Ungar K., Hauck B., Kramer G.H.; A gamma–gamma coincidence spectrometric method for rapid characterization of uranium isotopic fingerprints. J Radioanal Nucl Chem. 288, Issue 1,43-47 (2011).
15. Orgun Y., Altinsoy N., Gultekin A.H., Karahan G., Celebi N.; Natural radio activity levels in grantic plutons and groundwater in Southeast part of Eskisehir,Turkey. App. Radiat. Isot. 63:267 (2005).
16. Arafa W., Specific activity and hazards of granite samples collected from the Eastern Desert of Egypt. J. Environ Radioact. 75:315-327 (2004)
17. ElAassy I.E., ElGaly M.M,, Nada A.A., El Feky M.G., Abd El Maksoud T.M., Talaat Sh. M and Ibrahim E.M.; Effect of alteration processes on the distribution of radionucliedes in uraniferous sedimentary rocks and their environmental impact, southwestern Sinai, Egypt. J Radioanal Nucl Chem; 289 n.1, 173- 184 (2011).

11/10/2012

Improved anti-inflammatory effect of Silymarin in rats induced liver carcinogenesis

Ali Alkaladi[1] and Aser Mohamed Abdelazim[2,3]

[1] Department of Biological Sciences, Faculty of Science, King Abdulaziz University, Saudi Arabia.
[2]Department of medical Science, Faculty of Art and Science, King Khalid University, Saudi Arabia.
[3]Department of Biochemistry, Faculty of Vet. Medicine, Zagazig University, Zagazig, Egypt.
alkaladi@kau.edu.sa

Abstract: In the present work the protective role of silymarin in rats-induced liver carcinogenesis was studied. Twenty eight male albino rats were randomly assigned to five groups: Group A ; served as control, (Group B) ; HCC-induced group, Group C ; HCC-induced group and treated with silymarin for 2 weeks and (Group D); HCC-induced group and treated with silymarin 2 weeks before induction the carcinogenesis and 2 weeks after induction of carcinogenesis. HCC –induced rats were treated with an oral dose of 20 mg/kg of DENA. Rats treated with silymarin received a daily single dose of (40 mg/kg body weight) suspended in saline by gavages. Blood samples were collected for determination of ALT,AST, bilirubin, AFP, IL-2 and IL-6 in serum, liver samples were collected for studying the gene expression of IL-2, IL-6 and GAPDH and histopathological examination. Our results demonstrated that ALT, AST, bilirubin levels were significantly lower in silymarin treated groups if compared with non treated HCC-induced rats. Circulating AFP, IL-2&6 were significantly low in silymarin treated groups if compared with HCC-induced rats. The expression level of IL-6 showed the highest expression level in non treated HCC-induced rats with high expression level of IL-2 in control groups. In conclusion silymarin improve the anti-inflammatory status in HCC-induced rats.

[Ali Alkaladi and Aser Mohamed Abdelazim . **Improved anti-inflammatory effect of Silymarin in rats induced liver carcinogenesis.** *Life Sci J* 2012;9(4):2865-2869] (ISSN:1097-8135). http://www.lifesciencesite.com. 420

Key words: Hepatocellular carcinma, silymarin, IL-2, IL-6, AFP, DENA, liver, Blood, falvanoids

1. Introduction

Primary liver cancer (or hepatocellular carcinoma, HCC) is the sixth most common cancer worldwide in terms of numbers of cases of 626,000, and the third most common cause of death from cancer (598,000 deaths annually) **[1].** Since over 80% of deaths are in developing countries, liver cancer has been a major public health problem in these parts of the world. The rate of hepatocellular carcinoma (HCC) has been increasing in Egypt with a doubling in the incidence rate in the past few years. This has been attributed to several biological (e.g. hepatitis B and C virus infection) and environmental factors (e.g. aflatoxin, AF). Other factors such as cigarette smoking, occupational exposure to chemicals such as pesticides, and endemic infections in the community, such as schistosomiasis, may have additional roles in the etiology or progression of the disease [**2**]**.** The major etiologies and risk factors for the development of HCC are well defined, and 1–6% of cirrhotic patients will develop HCC per year depending on etiology, activity and duration of underlying liver disease HCC has a high prevalence in Africa and Asia mainly due to endemic hepatitis B virus (HBV) infection and additional aflatoxin B1 intake [**3**]**.** Furthermore, the prevention of the progression of existing chronic liver disease by the treatment of inherited metabolic and autoimmune liver disorders, and particularly by antiviral therapy of HBV- and HCV-infected patients which may prevent progression to end-stage liver disease and cirrhosis **[4].** In general, more experience with gene expressing profiles, proteomic approaches and recent progress in metabonomics will produce a large number of potential biomarkers. These approaches will allow the identification of patients at high risk for the development of HCC [5]**.** One of the most frequently used tumour markers for HCC surveillance is alpha-fetoprotein (AFP), generally used associated with ultrasounds. The plasma level of this marker is proportional to the size and evolutionary stage of the tumour [**6**]**.** Silymarin, a flavonolignan isolated from *Silybum marianum*, has also been used for centuries as a natural remedy for liver diseases and now reported to have cancer preventive and therapeutic effects. Results of studies in experimental animal models suggest that silymarin has a broad spectrum of hepatoprotective effects. A number of studies suggest that factors related to the inflammations e.g. of the ovarian surface epithelium (OSE) such as ovulation, In particular, inflammatory mediators and several cytokines produced by activated innate immune cells such as tumour necrosis factor (TNF)-a, and IL-6 have been shown to promote tissue growth and progression **[7].**

2. Materials and Methods:

Protocol and experimental design

Twenty eight male albino rats with average weight and age at beginning of the experiment equals 120±10 grams and 4-5 months respectively, were housed in groups of sevens in stainless steel cages in room with temperature 23 °C±2°C and relative humidity of 55% ± 5%, with a light-dark phase of 12 hours with free access to basal diets and water. All animals from all experimental groups were left to free access to water and designed basal diet all over the experimental period. After acclimatization for 7 days, all rats were randomly assigned to five groups: Group A (n = 7); served as control they did not receive any type of treatments during the experiment, (Group B) (n = 7); HCC-induced group; they did not receive any treatment, Group C (n= 7); HCC-induced group and treated with silymarin for 2 weeks and (Group D) (n = 7); HCC-induced group and treated with silymarin 2 weeks before induction the carcinogenesis and 2 weeks after induction of carcinogenesis.

Induction of carcinogenesis and silymarin treatment

HCC –induced rats were treated with an oral dose of 20 mg/kg of DENA (Sigma-Aldrich Co., St. Louis, Missouri, USA) for 9 weeks (5 days/week) followed by another oral dose of 10 mg/kg of NDEA for 6 weeks (5 days/week) according to the protocol cited by Seufi *et al.* **[8].** Then rats were received three times a week for 17 weeks 0.04 cc of a 40 percent solution of CCl_4 (Sigma, St. Louis, MO, USA) in olive oil by oral gavages. Rats treated with silymarin (Sigma, St. Louis, MO, USA); received a daily single dose of (40 mg/kg body weight) suspended in saline by gavages. Rats were subsequently sacrificed at the indicated times after a one-week washout to eliminate acute effects of CCl4, According to the protocol cited by Fujii *et al.*[**9].**

Blood and tissue sampling

Blood samples were collected from rats, kept for a time, centrifuged at 3000 r.p.m. for 15 minutes, the resulting serum were collected and used for biochemical determinations. The liver was sectioned and fixed in phosphate-buffered 10% formaldehyde for histological analysis. The remaining portions of the liver were collected in RNase-free tubes and snap-frozen in liquid nitrogen for gene expression. Samples for histopathological examinations were immediately fixed in 10% formalin until examination.

Biochemical determinations

ALT, AST Total Bilirubin concentrations (Vitro scient kinetic) were determined in all rats serum. While the quantitative measurement of serum AFP, IL-2 and IL-6 concentration was performed using enzyme immunoassay method (Diagnostic System was determined by Reverse transcriptase polymerase chain reaction (RT-PCR), First strand cDNA was synthesized using two steps Superscript II kit (Invitrogen, Carlsbad, CA). RT-PCR was performed using IL-2 and IL-6 specific oligoneuclotide primers pair, and glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as housekeeping gene. The primer pairs for amplification were designed as the following, IL-2 according to Zhaia *et al.* [**10**] were forward5'-TGCCTGAAAATGAACTCGG-3' and reverse 5'-CTGGCTCATCATCGAATTGG-3', IL-6 primers according to Klein *et al* **[11]** were; forward 5'GATGCTACCAAACTGGATATAATC-3', reverse 5'-GGTCCTTAGCCACTCCTTCTGTG-3' and for and for GAPDH, forward, 5`-CCCGTAGACAAAATGGTGAAGGTC-3`and reverse, 5`-GCCAAAGTTGTCATGGATGACC-3`with product sizes 164, 249, and 215 respectively. The amplification was performed using thermal cycler (Takara MP, Japan) PCR for was performed with the following cycling conditions; 28-30 cycles at 94°C denaturation for 90 s, 50 and 60 °C annealing temperature respectively for 60 s, and 72 °C elongation temperature and chilled in ice for 5 minutes. Then the amplified PCR products were electrophorised on 1.5% Agarose gel in 1X Tris acetate EDTA running buffer (1 x TAE) with condition of 100 Voltage/ 40 min as described by Uchida *et al.* **[12].**

Statistical analysis

The data was processed using the statistical package for social science (SPSS Inc., Chicago, IL, version 13, USA). All results are expressed as mean ± SD. Comparison among groups was made by Student's t-test (unpaired), One-way analysis of variance (ANOVA). Duncan's test was used for testing the inter-grouping homogeneity. Statistical significance was set $P \leq 0.05$.

3. Results and Discution:

As shown in table (1); the results were expressed in mean ±SE indicated the effect of silymarin on HCC-induced rats as the following

Liver function tests

There is significant decline in hepatic AST and ALT and Bilirubin in silymarin treated HCC-induced groups if compared with non treated HCC-induced groups at ($P \leq 0.05$). **Alpha- feto protein concentration**

AFP as a marker for hepatic carcinoma; show highest level in HCC-induced groups. The level significantly declined in silymarin treated groups if compared with their control.

Cytokines levels

IL-2 and IL-6 were used to evaluate the effect of silymarin on HCC-induced rats; there is a

significant decrease in the level of IL-2 and IL-6 in HCC-induced rats serum after their treatment with silymarin if compared with their control.

Table 1: Illustrates Effect of Silymarin on hepatic enzymes, bilirubin, AFP, IL-2 and IL-6 in Hepatocellular carcinoma induced rats.

Mean ±SE	ALT (µU/ml)	AST (µU/ml)	Bilirubin (mg/dl)	AFP (ng/ml)	IL-2 (Pg/ml)	IL-6 (Pg/ml)
Control	22.2±0.5^{a}	52.24±3.4^{a}	1.4±0.2^{a}	5.9±0.36^{d}	126.4±2.9^{b}	38.04±0.87^{d}
HCC	54.2±3.8^{c}	155.4±1.4^{c}	6.02±0.3^{c}	22.6±0.16^{a}	162.8±12.2^{a}	67.2±0.83^{a}
HCC+ Silymarin after carcinogenesis	32.3±3.6^{b}	58.13±4.2^{ab}	2.5±0.9^{ab}	12.9±0.46^{b}	147.7±1.9^{ab}	56.3±0.56^{b}
HCC+ Silymarin before and after carcinogenesis	22.5±0.8^{a}	52.97±5.4^{a}	2.30±0.2^{b}	9.7±0.27^{c}	140.4±4.3^{ab}	51.9±0.76^{c}

Means within the same column carrying different superscripts are significant at (P ≤0.05).

IL-2 and IL-6 mRNA expression level in rats liver tissues

Figure (1); IL-2 show the highest expression level in control group if compared with other experimental groups while IL-6 show highest expression in HCC-induced groups, the expression level of both IL-2 and IL-6 was equal in both silymarin treated HCC-induced rats.

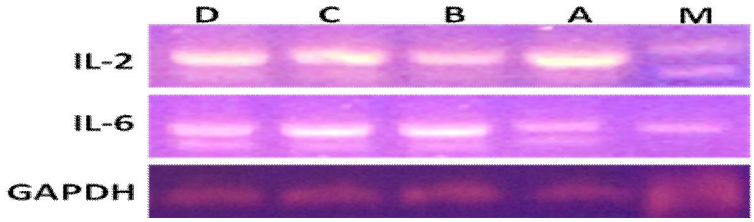


Fig. 1: the mRNA expression level of IL-2 and IL-6 compared to GAPDH in HCC-induced rats liver tissues treated/non treated with silymarin. M; molecular marker, A; control group, B; non treted HCC-induced group, C; Silymarin treated group after induction of carcinogenesis and D; Silymarin treated group after and before induction of carcinogenesis.

Histopathological examination

As shown in figure (2); Normal central vein and liver cords were appeared in control group, while in non treated HCC-induced group there was a focal area of HCC with the rest of liver tissue showing moderate dysplasia, micro vesicular steatosis was appeared in silymarin treated group after induction of carcinogenesis. Silymarin treated group after and before induction of carcinogenesis showing lobular inflammation with aggregates of chronic non-specific inflammatory cells.

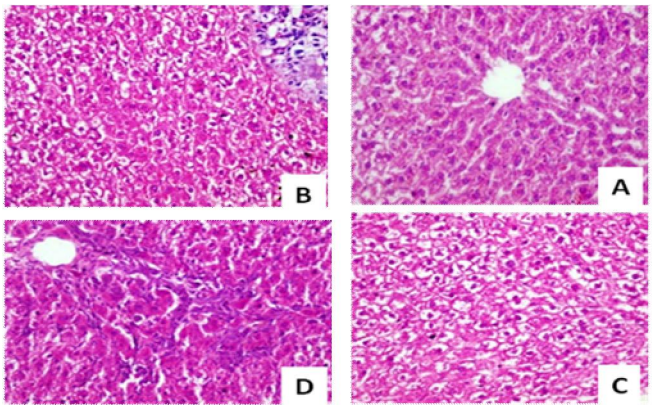


Fig. 2: Photomicrograph of rat liver (H&E, original magnification × 400), A; control group, B; non treated HCC-induced group, C; Silymarin treated group after induction of carcinogenesis and D; Silymarin treated group after and before induction of carcinogenesis.

In the present study we tended to evaluate the effect of silymarin as one of flavonolignan which has a potent effect as cancer treatment with other medical importance **[13]** on the HCC-induced rats. In our study the hepatocelluar carcinoma was confirmed by the high serum level of hepatic enzymes, bilirubin and alpha-fetoprotein *(Table 1)* and histopathological examination *(Figure 2)* in DENA treated groups. Cytokines were determined to evaluate the effect of silymarin on the inflammatory/immune mediators in HCC-induced rats. In general the role of inflammation in cancer has been the focus of extensive research **[14].** Determining whether an association between cytokines likes IL-2 or IL-6, and cancer exists, are important because such knowledge could inform preventative strategies or help in the development of methods for early diagnosis of cancer **[15].** Most studies on the role of inflammation have focused on IL-6 signalling which seems to play the main role **[16].** IL-6 is one of the major immunoregulatory cytokines present in the body cells. Both cancer cells and associated macrophages produce IL-6, and high serum levels of IL-6 are known to be associated with specific immune and metabolic alterations that finally lead to cancer cachexia, one of the main causes of death in cancer patients. IL-6 has been demonstrated to be involved in the autocrine growth of many cancer cells most likely by increasing their capacity to secrete matrix metalloproteinase (MMP)-9 **[17].** On the other hand IL-6 plays an important role in the development of ascites as well as the spread of many cancers like ovarian cancer through its induction of tumor angiogenesis, thus leading to rapid progression and short survival **[18].** IL-2 as one of main factors of the cell-mediated immune response with IL-6, which acts as a second signal for the production of IL-2 and induces the expression of the IL-2 receptor (RIL-2) on cytotoxic T lymphocytes. IL-2 is the key cytokine in the regulation of the antineoplastic immunity. The activity of IL-2 is the synergistic effect of IL-2 and other cytokines deriving from the activated immune system may play an active role in the anti-tumor cytotoxic attack by counteracting neoplastic cell growth. However, some cytokines IL-6 **[19].** Recent studies have demonstrated that a high serum level of IL-6 may be considered an indicator of the inflammatory and oxidative status of patients with carncer **[20]** these data come in the same line of our observation; the expression level and serum concentration of IL-6 in our experinamtal HCC-induced rats were significantly higher than in other experimental groups other in the same line demonstrated that Cancer patients' IL-6 concentrations were higher than healthy controls' in most studies, but the results of investigations comparing IL-6 in cancer patients and individuals with benign diseases were less consistent **[15].** The paracrine effects of IL-6 have also been demonstrated. High levels of IL-6 induce an immune suppressive status in the tumor microenvironment by inhibiting IL-2 synthesis, T cell activation and proliferation, and by promoting lymphocyte apoptosis **[21]** this explains the low mRNA expression level of IL-2 in HCC-induced experimental group in our study. On the other hand silymarin protects animals against multiple types of experimental liver injury such as acetaminophen, carbon tetrachloride, ethanol, iron overload, bile duct obstruction and amanita mushroom poisoning **[13].** Some positive results have been reported in humans; indeed, silymarin has been claimed for clinical applications in the treatment of viral hepatitis, fatty liver, cirrhosis, and radiation toxicity due to its antioxidative, anti-lipid-peroxidative, antifibrotic, immunomodulating, anti-inflammatory, and even liver regenerating effects **[22].** Our results approved that silymarin improve the anti-inflammatory status in HCC-induced rats this appeared through the low level of IL-2 and IL-6 observed in experimental rats treated with silymarin, our results demonstrated also the protective role of silymarin before induction of carcinogenesis. In the same line of our data; many studies have demonstrated that silymarin can suppress the proliferation of a variety of tumor cells such as prostate, breast, ovary, colon, lung, and bladder, through cell cycle arrest at the G1/S-phase **[23].**

4. Conclusion

Silymarin has the ability to improve the anti-inflammatory status in HCC-induced rats through decrease circulating IL-2 and IL-6. Also it has the ability to reduce their gene expression level in livers it can be used as a potent protective and therapeutic agent in liver induced carcinogenic patients.

Corresponding author:
Dr. Ali Alkaladi
Department of Biological Sciences, Faculty of Science, King Abdulaziz University, North Campus, PO Box 11508, Jeddah, 21463, Saudi Arabia.
Email: alkaladi@kau.edu.sa

References

1. Parkin, D., F. Bray, Ferlay, *et al.,* 2005. Global cancer statistics, 2002. CA Cancer J Clin. 55:74–108.
2. Wagida, A., M. Hussein,A. Hassan, *et al.,* 2008. Changing pattern of hepatocellular carcinoma (HCC) and its risk factors in Egypt: Possibilities

for prevention. Mutation Research 659:176–184.
3. El-Serag, H. and K. Rudolph, 2007. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology. 132(7): 2557–2576.
4. Llovet, J., Y. Chen, E. Wurmbach E *et al.,* 2006. A molecular signature to discriminate dysplastic nodules from early hepatocellular carcinoma in HCV cirrhosis. Gastroenterology. 131(6):1758–67.
5. Marcus, A. and R. Peter, 2010. Future perspectives in hepatocellular carcinoma. Digestive and Liver Disease 42S:302–309.
6. Marrero, J., Z Feng, Y. Wang, *et al.,* 2009. Alpha-fetoprotein, Des-gamma Carboxyprothrombin, and Lectin-Bound Alpha-fetoprotein in Early Hepatocellular Carcinoma AFP, DCP, and AFP-L3 in Hepatocellular carcinoma. Gastroenterology.
7. Clendenen, T., E. Lundin, A. Zeleniuch-Jacquotte, *et al.,* 20011. Circulating inflammation markers and risk of epithelial ovarian cancer. Cancer Epidemiol Biomarkers Prev20:799–810.
8. Seufi, A., S. Safinz, K. Tarek, *et al.,* 2009. Preventive effect of the flavonoid, quercetin, on hepatic cancer in rats via oxidant/antioxidant activity: molecular and histological evidences. Journal of Experimental & Clinical Cancer Research. 28:80-86.
9. Fujii, T., Y. Suguru, Y. Gregory, *et al.,* 2010. Rat model of carbon tetrachloride induced liver fibrosis: Histopathological changes and expression of CD133 and epidermal growth factor. Gastroenterology, 10:79.
10. Zhaia, Q., F Nancy and C. Fang-Jie, 1997. Gene expression of IL-10 in relationship to TNF-a, IL-1b and IL-2 in the rat brain following middle cerebral artery occlusion. Journal of Neurological Sciences. 152:119–124.
11. Klein, G., M. Matheny, M. King, *et al.,* 2002. Induction of uncoupling protein 1 by central interleukin-6 gene delivery is dependent on sympathetic innervation of brown adipose tissue and underlies one mechanism of body weight reduction in rats. Neuroscience. 115, 3:879-889.
12. Uchida, K., T. Kaneko, H. Miyazazki, *et al.,* 2000. Excellent salinity tolerance of Mozambique tilapia (Oreochromis mossambicus): Elevated chloride cell activity in the branchial and opercular epithelia of the fish adapted to concentrated seawater. Zoo Sci. 17: 149-160.
13. Hoofnagle,J.,2005. Milk thistle and chronic liver disease. Hepatology, 42: 4.
14. Baillargeon, J., E. Platz, D. Rose, et al., 2006. Obesity, adipokines, and prostate cancer in a prospective population-based study. Cancer Epidemiol Biomarkers Prev. 15(7):1331–1335.
15. Katriina, H., E. Shah and A. Debbie,2008. Systematic review of the association between circulating interleukin-6 (IL-6) and cancer. European journal of cancer 4 4:9 3 7–9 4 5.
16. Lane, D., I. Matte, C. Rancourt, *et al.,* 2011. Prognostic significance of IL-6 and IL-8 ascites levels in ovarian cancer patients. BMC Cancer. 11:210.
17. Rabinovich, A., L. Medina, B. Piura, *et al.,* 2011. Regulation of ovarian carcinoma SKOV-3 cell proliferation and secretion of MMPs by autocrine IL-6. Anticancer Res. 27:267–72.
18. Lo, C., M. Chen, M. Hsiao, *et al.,* 2011. IL-6 transsignaling in formation and progression of malignant ascites in ovarian cancer. Cancer Res. 71:424–34.
19. Mantovani, G., A. Macciò, C. Madeddu, *et al.,* 2003. Antioxidant agents are effective in inducing lymphocyte progression through cell cycle in advanced cancer patients: assessment of the most important laboratory indexes of cachexia and oxidative stress. J Mol Med (Berl) 81:664–73.
20. Macciò, A. and C. Madeddu, 2012. Inflammation and ovarian cancer. Cytokine. Xxx: xxx–xxx article in press.
21. Mantovani, G., A. Macciò, E. Massa, *et al.,* 1999. Relationships between Fas expression, activation molecule CD25, and functional activity of tumor-associated lymphomonocytes from neoplastic effusions. Oncol Rep. 6:235–239.
22. Singh, R., M. Gu and R. Agarwal, 2008. Silibinin inhibits colorectal cancer growth by inhibiting tumor cell proliferation and angiogenesis. Cancer Res. 68: 2043–2050.
23. Hogan, F., N. Krishnegowda, M. Mikhailova, *et al.,* 2007. Flavonoid, silibinin, inhibits proliferation and promotes cell cycle arrest of human colon cancer. J. Surg. Res. 143: 58–65.

11/10/2012

Insulin Versus Oral Hypoglycemic Drug Combination In Controlling Hyperglycemia In HCV Patients During Interferon Therapy

Mohamed Masjhahit [1], Mohamed El Basel [2]and Waleed El Nabawy[3]

[1]Internal Medicine Departments, Faculty of Medicine Fayoum University
[2] Internal Medicine Departments, Faculty of Medicine Cairo University
[3] Internal Medicine Departments, Faculty of Medicine Beni Suef University
mashahit@hotmail.com

Abstract: Hepatitis–C virus is common in many areas of the world particularly in Egypt and interferon therapy helps around 40 % of the patients to eradicate the virus and good glycemic control is needed to get better results of interferon therapy This work aimed to study the efficacy of insulin therapy compared to oral hypoglycemic drugs in HCV patients receiving interferon therapy. Ninety six patients were included in the study divided into three groups (A) TREATED WITH INSULIN (B) treated with oral hypoglycemic drugs and (C) treated with two oral hypoglycemic drugs plus a bed time basal insulin. HbA1c,AST, ALT and the weight of the patients were measured at the start before intervention and 3 months after intervention.Results this study showed that insulin therapy – group-A - is more effective than oral hypoglycemic drug combination group-B and also more effective than group-C - treated with oral drugs and basal insulin – in reducing HbA1c ($p = 0.001$) and in improving weight and reducing AST AND ALT ($P < 0.05$). Also oral drugs plus a basal insulin at bed time - group – C was more effective than oral drug combination alone (group-B)in reducing HbA1c and the difference was statistically significant $p < 0.05$ and improving weight $p < 0.05$ and improving AST AND ALT but the results are statistically non significant (p=0.09 and 0.07). Conclusion insulin therapy is more effective than oral hypoglycemic drug combination in controlling blood glucose, improving liver enzymes and prevention of weight loss with some weight gain.

[Mohamed Mashahit, Mohamed El Basel and Waleed El Nabawy. **Insulin Versus Oral Hypoglycemic Drug Combination In Controlling Hyperglycemia In HCV Patients During Interferon Therapy.** *Life Sci J* 2012;9(4):2870-2874] (ISSN:1097-8135). http://www.lifesciencesite.com. 421

Key words: T2DM, HbA1c, HCV, interferon, insulin, resistant, oral hypoglycemic drugs

1. Introduction:

Hepatitis –C virus (HCV) is causing a major problem in Egypt as it is widely spread and affects near 15 - 20 % of the general population (1)

A clear link is present between type -2 diabetes mellitus (T2 DM) and HCV infection, about 25 - 40% of HCV patients have T2 DM and 0ne tenth of T2DM has HCV(2)

Control of diabetes in HCV patients is more difficult due to the state of sever insulin resistance, the presence of and Islet cell anti bodies and the presence of many inflammatory cytokines (3- 6)

Interferon (INF) is widely used for treatment of selected patients with HCV and up to 40 % of patients became HCV negative after 48 weeks of INF therapy (7)

Diabetic control is one of the parameters that affect the response of INF therapy in HCV patients (8- 11)

Many oral dugs and many types of insulin are used to control T2 dm HCV patients during INF therapy and most of the patients on oral drugs need combination therapy to achieve good glycemic control (12)

The work aimed at comparing the efficacy and safety of oral hypoglycemic drug (s) and insulin in HCV patients treated with interferon.

2. Patients and Methods

Ninety six patients with uncontrolled (T2 DM) and HCV receiving a single weekly INF SC injection - there age ranged from 35 to 45 years old, 51 males and 43 females whom HbA1c ranged from 7.9 to 10.4 mg % before intervention treated with different oral drugs (mono-therapy or combination therapy. Carful medical history and clinical examination were done for all patients and patients with thyroid disorders or highly elevated liver enzymes were excluded HbA1C, AST & ALT and body weight were measured before intervention and three months later at the end of the study.

Patients are divided into three groups

Group –A Included 36 patients for whom premixed insulin was given before breakfast and dinner in suitable doses with adjusting the doses every 3 weeks according to the fasting and post meal glucose readings with a third pre lunch dose of regular insulin if needed

Group - B Included 36 patients for whom oral hypoglycemic dugs were given (metformin- SU- DDP-4 inhibitors- and TZDs) in different combination using the maximum dose of up to three drugs of the above mentioned groups.

Group –C Included 24 patients in whom the HbA1c was below 9 mg% and they were given the maximum dose of two oral drugs as mentioned in group –B plus adding a bed time basal insulin 10 to 20 unites.

All groups were given the medications regularly for 3 months and doses are adjusted every 3 weeks according to blood sugar readings

Statistical analysis

The data was analyzed with the program Statistical Package for Social Science (SPSS) under windows version 11.0.1. The following tests were used: Calculation of the mean value, Student t-test, Chi-square test (χ^2).

The probability of error (P) was expressed as following:

p - value > 0.05: non-significant (NS).

p - value ≤ 0.05: significant (S).

p - value < 0.001: highly significant (HS).

3. Results

Ninety six patients with uncontrolled (T2 DM) and HCV receiving a single weekly INF SC injection - there age ranged from 35 to 45 years old, 51 males and 43 females whom HbA1c ranged from 7.9 to 10.3 mg % there age ranged from 35 to 45 years divided into three groups, group A included 36 patients and were given premixed insulin and group – B included 36 patients given up to the maximum dose of up to 3 drug from metformin, SU, DPP4I & TZDs and group –C included 24 patients given two oral drugs up to their maximum dose plus a bed time 10-20 unites of basal insulin. in all patients measurement of weight, Hb1ic, AST & ALT was done before intervention 3 months later and the results are:

All patients included in the study initially have uncontrolled diabetes and have nearly similar AST AND ALT & body weight

Table-1 Summery of patients data before and after treatment (Mean ± SD)

	No	Before intervention					3 months after intervention				
		Weight (kg) Mean± SD	BMI Mean± SD	HbA1c (gm%) Mean± SD	AST (mg %) Mean± SD	ALT mg % Mean± SD	Weight (kg) Mean± SD	BMI Mean± SD	HbA1c (mg %) Mean± SD	AST (mg %) Mean± SD	ALT (mg%) Mean± SD
Group-A	36	61.5± 2.4	22.3±1.5	8.95±0.8	34.2±2.1	50.1±2.3	62.8± 2.8	22.9 ±1.7	7.50±0.8	32.27± 2.3	45.09±2.5
Group-B	36	61.6±2.6	22.34± 1.6	8.88±0.9	34.3±1.9	49.5±2.6	60.3±3.1	21.8 ±2.1	8.15±o.6	37.72± 2.6	51.60±2.8
Group-C	24	61.8±3.1	22.4± 1.3	8.13±1.1	35.7±2.1	49.8±3.1	62.1±2.4	22.6 ±1.9	7.57±o.9	37.27± 2.9	50.1±3.2

Table -1 shows descriptive date of all the studied population in the three groups both at the start of the study – before intervention - and at the end of the study – 3 months after intervention.

Table -2 patient that achieved the target glycemic control (HbA1c less than 7 mg % in different groups

	Total number	NUMBER OF PATIENTS (HbA1c 7 mg% or less)	%
Group - A	36	22	6.1 %
Group - B	36	6	16..7 %
Group - C	24	9	37.5 %

This table showed that 61% of patients on insulin achieved glycemic control after 3 month while only 17 % of those on oral therapy achieved control and the difference between the two groups A and B is statistically highly significant ($p < 0.001$) and around 38 % of group –C patients achieved control and when comparing group –C to group – B the differences are statistically significant (p= 0.03) also the differences between group –A and C are statistically significant (p=0.04)

Table -3 Comparison between different groups regarding to HbA1c values

Group	HbA1c before intervention	HbA1c 3-months after intervention	P - value
Group-A	8.95	7.50	0.003
Group-B	8.88	8.15	0.04
Group-C	8.13	7.57	0.03
		A compared to B	0.O2
		A compared to C	0.8
		C compared to B	0.02

This table showed that patients on insulin therapy - group A - and patients on oral drugs plus bed time insulin – group C- achieved better HbA1c compared to those on oral drugs only - group B- and the differences are statistically significant (p=0.02). And patients on insulin therapy - group A - achieved

nearly the same HbA1c compared to patients on oral drugs plus bed time insulin – group C and the differences are statistically not significant (p=0.8)

Table -4 comparisons between different groups regarding body weight

Group	Weight before intervention	Weight 3-months after intervention	*P* - value
Group-A	61.5	62.8	0.3
Group-B	61.6	60.3	0.3
Group-C	61.8	62.1	03
		A compared to B	0.06
		A compared to C	0.4
		C compared to B	0.06

This table showed that patients on insulin therapy - group A - and patients on oral drugs plus bed time insulin – group C- achieved better weight gain compared to those on oral drug s only - group B- and the differences are statistically not significant (p=0.06). And patients on insulin therapy - group A - achieved better weight gain compared to patients on oral drugs plus bed time insulin – group C - and the differences are statistically not significant (p =0.4)

Table -5 comparisons between different groups regarding AST values

group	AST before intervention	ALT 3- months after intervention	*P* - value
Group-A	34.2	32.27	0.009
Group-B	34.3	37.72	0.005
Group-C	35.7	37.27	0.05
		A compared to B	0.001
		A compared to C	0.001
		C compared to B	0.5

This table showed that patients on insulin therapy - group A - achieved greater AST reduction compared to the other groups (those on oral drug s only - group B- and those on oral therapy and basal insulin the differences are statistically highly significant (p=0.0001). And patients on oral drugs plus basal insulin - group C - achieved nearly the same AST level compared to patients on oral drugs only– group B – (AST increased in both groups) and the differences are statistically not significant (p =0.5)

This table showed that patients on insulin therapy - group A - achieved greater ALT reduction compared to the other groups (those on oral drug s only - group B- and those on oral therapy and basal insulin the differences are statistically significant (p =0.002 and 0.003 respectively). And patients on oral drugs plus basal insulin - group C - achieved nearly the same ALT level compared to patients on oral drugs only– group B – (ALT increased in both groups) and the differences are statistically not significant (p =0.2) m69-262-764

Table- 6 comparison between different groups regarding ALT values

group	ALT before intervention	ALT 3- months after intervention	*p* - value
Group-A	50.1	45.09	0.005
Group-B	49.5	51.60	0.3
Group-C	49.8	50.1	0.5
		A compared to B	0.002
		A compared to C	0.003
		C compared to B	0.2

Table -7: Comparing all groups as regard the hypoglycemic events

	Total number	Number of hypoglycemic events	Total
Group -A	36	2 sever and 5 mild	7
Group -B	36	3 sever and 7 mild	10
Group -C	24	0 sever and 6 mild	6

From this table it is clear that 2 sever plus 5 mild hypoglycemic attacks were reported in patients on insulin therapy - group –A-, while 3 sever and 7 mild attacks were reported in patients on oral therapy - group- B- especially when triple therapy is used but in group – C whom were given one or two oral drugs and a bedtime basal insulin no sever hypoglycemic events were detected while six mild hypoglycemic events were reported and the differences between the groups are statistically non significant

4. Discusion

This study included 96 HCV patients receiving INF in whom diabetes is badly controlled on a single oral hypoglycemic agent or two drug combination in the maximum allowed doses including 51 males and 42 females and their age ranged from 35 to 45 years old and their HbA1c ranged from 7.9 - 10.3 mg % and their AST AND ALT values were normal or slightly elevated, their weight and height are measured and the BMI was calculated and ranged from 19.1 to 22.8 as INF and hyperglycemia affected their weight Trying to control their hyperglycemia by either stopping the oral drugs and shifting to premixed insulin in two doses before breakfast and dinner (group – A) or adding a third drug (group-B) or adding a bed time basal insulin (group-C)

All patients are regularly followed up and their doses were re- adjusted every 3 weeks according to

their blood sugar readings and t the end of the study - after 3 months- HbA1c, AST, ALT and body weight were re-measured and data were analyzed and we found that 61% of patients on insulin achieved glycemic control after 3 month while only 17 % of those on oral therapy achieved control and the difference between the two groups A and B is statistically highly significant ($p < 0.001$) and around 38 % of group –C patients achieved control and when comparing group –C to group – B the differences are statistically significant ($p= 0.03$) also the differences between group –A and C are statistically significant ($p=0.04$)

Patients on insulin therapy - group A - and patients on oral drugs plus bed time insulin – group C- achieved better HbA1c compared to those on oral drugs only - group B- and the differences are statistically significant ($p=0.02$). And patients on insulin therapy - group A - achieved nearly the same HbA1c compared to patients on oral drugs plus bed time insulin – group C - and the differences are statistically not significant ($p=0.8$)

Patients on insulin therapy - group A - and patients on oral drugs plus bed time insulin – group C- achieved better weight gain compared to those on oral drug s only - group B- and the differences are statistically not significant ($p=0.06$). And patients on insulin therapy - group A - achieved better weight gain compared to patients on oral drugs plus bed time insulin – group C - and the differences are statistically not significant ($p=0.4$)

Patients on insulin therapy - group A - achieved greater ALT reduction compared to the other groups (those on oral drug s only - group B- and those on oral therapy and basal insulin the differences are statistically significant ($p=0.002$ and 0.003 respectively). And patients on oral drugs plus basal insulin - group C - achieved nearly the same ALT level compared to patients on oral drugs only– group B – (ALT increased in both groups) and the differences are statistically not significant ($p=0.2$)

Patients on insulin therapy - group A - achieved greater AST reduction compared to the other groups (those on oral drug s only - group B- and those on oral therapy and basal insulin the differences are statistically highly significant ($p=0.0001$). And patients on oral drugs plus basal insulin - group C - achieved nearly the same AST level compared to patients on oral drugs only– group B – (AST increased in both groups) and the differences are statistically not significant ($p =0.5$)

Two sever & 5 mild hypoglycemic attacks were reported in patients on insulin therapy (group –A), while 3 sever and 7 mild attacks were reported in patients on oral therapy - (group- B) especially when triple therapy is used but in (group – C) whom were given one or two oral drugs and a bedtime basal insulin no sever hypoglycemic events were detected while six mild hypoglycemic events were reported and the differences between the groups are statistically non significant

Our results are consistent with Higgins et al. who reported that insulin is preferred to oral hypoglycemic drugs in hepatic patients (13)

United Kingdom Prospective Diabetes Study (UKPDS) in 1998 also stated that insulin gives better and greater Hba1c reduction if the initial Hba1c is higher (14). Also Narhan who stated that insulin gives better results in type -2 diabetic patients that oral drug combination (15)

Roaid et al. stated that oral hypoglycemic drugs are effective in treating diabetes in HCV patients but insulin is preferred during anti viral treatment (12)

An ongoing research in the National Taiwan university with early results published in the university web in 2009 stating that oral drug may not be effective in treating diabetic patients receiving interferon therapy (16)

The ADA report (2011) stated that all oral drugs are contraindicated if liver enzymes are highly elevated

Defranzo et al., (18) and Sherifali et al.,(19) studied the HbA1c lowering effect of the currently used anti diabetic agents and found that insulin had the highest power followed by combining insulin and oral and lastly oral agents alone

Harrison concluded that pioglitazone may improve glycemic control in insulin-resistant HCV patients (20).

Conclusion

Insulin therapy is more effective in controlling hyperglycemia in T2DM and HCV during interferon therapy with also improvement of liver enzymes and stoppage of weight loss noticed in those patients compared to oral hypoglycemic drugs even if insulin is given once daily with oral drugs patients will get better glycemic control.

References

1- WHO report 2008 HCV in Egypt reached alarming levels

2 Grimbert S, Valensi P, Levy-Marchal C, Perret G, Richardet JP, Raffoux C, Trinchet JC, *et al.,* High prevalence of diabetes mellitus in patients with chronic Hepatitis C. A case control study. Gastroenterol Clin Biol., 1996;20:544-548

3 - Abd El-Satar H, Mahfouz M, Rashed L, Ahmed D. Insulin Resistance in Patients with Chronic Hepatitis C Infection. Aust. J. Basic & Appl. Sci. 2010; 4: 4554-4558

4- Betterle C, Fabris P, Zanchetta R, Pedini B, Tositti G, Bosi E *et al.* Autoimmunity against pancreatic islets and other tissues before and after interferon-a therapy in patients with hepatitis C virus chronic infection. Diabetes Care 2000; 23(8):1177-1181.

5- Lecube A, Hernandez C, Genesca J, Simo R. Proinflammatory cytokines, insulin resistance, and insulin secretion in chronic hepatitis C patients. Diabetes Care 2006; 29: 1096-1101.

6- Piquer S, Hernández C, Enriquez J, Ross A, Esteban JI, Genescá J et al. Islet cell and thyroid antibody prevalence in patients with hepatitis C virus infection: Effect of treatment with interferon. J Lab Clin Med., 2001; 137(1):38-42.

7-- Wesche B, Jaeckel E, Trautwein C, Wedemeyer H, Falorni A, Frank H *et al.* Induction of autoantibodies to the adrenal cortex and pancreatic islet cells by interferon alpha therapy for chronic hepatitis C. Gut 2001; 48(3):378-383.

8 - Brandman D, Bacchetti P, Ayala CE, Maher JJ, Khalili M. Impact of insulin resistance on HCV treatment response and impact of HCV treatment on insulin sensitivity using direct measurements of insulin action. Diabetes Care. 2012 ;35(5):1090-4.

9 - Elgouhari HM, Zein CO, Hanouneh I, Feldstein AE, Zein NN. Diabetes mellitus is associated with impaired response to antiviral therapy in chronic hepatitis C infection. Dig Dis Sci 2009; 54: 2699-2705.

10 -Konishi I, Horiike N, Hiasa Y, Tokumoto Y, Mashiba T, Michitaka K., et al. Diabetes mellitus reduces the therapeutic effectiveness of interferon-α2b plus ribavirin therapy in patients with chronic hepatitis C. Hepatology Research 2007; 37: 331–336.

11 - Eslam M., Aparcero R., Kawaguchi, T., *et al.* Meta-analysis: insulin resistance and sustained virological response in hepatitis C. *Alimentary Pharmacology and Therapeutics* (2011)34(3): 297-305

12- Roaid Khan, ; Graham R. Foster, ; Tahseen A. Chowdhury, Managing Diabetes in Patients with Chronic Liver Disease Diabetes Care 2000; 23(8):1155-1161

13- Higgins J., Deeks j. and Atram D Eds (2011) chapter 16 :special topics in statistics, Cochrane Handbook for systematic review of intervention

14- United kingdom prospective diabetes study group (UKPDS 24) a six year randomized controlled trial comparing SU insulin and metformin therapy in patients with newly diagnosed type -2 diabetes that could not be controlled with diet therapy. Ann. Int.Med.1998 128:165-1175

15-Narhan DM finding new treatment of diabetes – how many, how fast, how good? N.Eng.J.Med.2007, 356:437-440

16-National Taiwan University Hospital (2009): The Effects of Oral Hypoglycemic Agents on Chronic Hepatitis C Patients Receiving Peg-Intron Plus Ribavirin ClinicalTrials.gov Identifier:

17- America Diabetes Association, Standard of medical care in diabetes 2011. Diabetes Care 2011: 34 (supp. 1):511-61

18- Defranzo RA., Stonehouse AH, Hanj J. *et al.* Relationship of baseline HbA1c and efficacy of current glucose lowering therapeutics.A meta – analysis of randomized clinical trials. Diab. Med 2010, 27 :309-17

19 –Sherifali A., Dnerenberg k.. Cheng e *et al.* the effect of oral antidiabetic agents on A1C levels a systematic review and meta- analysis Diabetes Care 2010. 33:1859-64

20 -Harrison SA. Pioglitazone may improve glycemic control in insulin-resistant HCV patients *Hepatology*. 2012; 56:464-473.

11/10/2012

Meta Malmquist Index Based On Trade Offs Models in Data Envelopment Analysis

Parisa Firoozi shahmirzadi; Gholamreza Jahanshahloo

[1, 2] Department of Mathematics, Karaj Branch, Islamic Azad University, Karaj, Iran
Email:Parisa.Firoozi@gmail.com

Abstract: The Trade Offs approach is an advanced tool for the improvement of the discrimination of Data Envelopment Analysis (DEA) models, Meta Malmquist Index was defined by Maria Portella and et. al (2008). In this paper we compute the Meta Malmquist Index in Trade Offs model in DEA and we compare, obtaining results, of Meta Malmquist Index in different models of DEA, Variable Return to Scale (VRS), Constant Return to Scale (CRS) and Trade Offs (T-O). Numerical example is given for the purpose of illustration and we will show the management science is effective on efficiency of Decision Making Units (DMUs). The main advantage this index is that, it is circular.

[Paris Firoozi shahmirzadi, Gholamreza Jahanshahloo. **Meta Malmquist Index Based On Trade Offs Models in Data Envelopment Analysis.** *Life Sci J* 2012;9(4):2875-2883] (ISSN:1097-8135). http://www.lifesciencesite.com. 422

Keywords: Data Envelopment analysis, Trade Offs, Meta Malmquist Index, Meta Efficiency, Meta Frontier.

1. Introduction

Data Envelopment Analysis (DEA) is a mathematical programing technique that measures the relative efficiency of decision making units (DMUs) with multiple inputs and outputs, Charnes et. al (1978). First proposed DEA as an evaluation tool to measure and compare the relative efficiency of DMUs, their model assumed constant return to scale (CRS, the CCR model). It was developed for variable return to scale (VRS, the BCC model) by Banker et. al (1984). Podinovski suggests the incorporation of production Trade Offs in to DEA models, under this circumstance (Podinovski 2004), when we use Trade Offs in our models, the original technology expands to include the new area, Podinovski and et. al (2004) show that the production possibility set (PPS), generated by the traditional DEA axioms, may not include all the producible production points, the PPS generated by the DEA models is only the subset of the PPS with Trade Offs. Podinovski also describes the theatrical development of Trade Offs and demonstrated that Trade Offs can improve the traditional meaning of efficiency as a radial impronment factor for input or outputs (Podinovski, 2007a, 2007b). The Malmquist Index is the most important index for measuring the relative productivity change of DMUs in multiple time periods by DEA, for the first time the Malmquist Index was introduced by Caves et al (1982) for measuring the Malmquist Index. Fare et. al (1992, 1994), they computed the Malmquist index in CRS and VRS of DEA models. Also Maria Portella and Thanassoulis, defined Meta Efficiency and based on Meta Malmquist Index, they computed Meta Malmquist Index in CRS and VRS models of DEA. Meta Malmquist computes change of Meta Efficiency. The structure of the paper is as follows. In section 2 Trade Offs model of DEA is described. Section 3, we introduce Meta Malmquist Index in different models of DEA. In section 4, we explain advantage of Meta Malmquist Index and in the section 5 using the Meta frontier to compare productivities of DMUs. In section 6 we explained comparing two units at two different point in time To illustrate numerical example is brought in section 7. The last section summarizes and concludes.

2. Trade Offs in DEA models

Considering the observed output vector as $Y_j \in R^s$ and the input vector as $X_j \in R^m$, we assume that the inputs and outputs are nonnegative and $X_j \neq 0$, $Y_j \neq 0$ for DMU_j, j=1,2,…,n.

A Trade Off is a judment of possible variation in some input and or output levels, with which DMU can work without changing the other inputs and or outputs. For example, in the case of two inputs and a single output, the trade-off (P, Q) = (2,−1, 0) indicates that the DMU can work by increasing the first input by two and decreasing the second input one without changing its output (for more details, see Podinovski, 2004).

Now, suppose we have k Trade Offs. We shall represent the Trade Offs in the following form: (P_r, Q_r), where r = 1, 2 ,…, k. Also, the vector $P_r \in R^m$ and $Q_r \in R^s$ modify the inputs and outputs, respectively.For using Trade Offs in DEA models, Podinovski makes some assumptions and extends the axioms of PPS in the following manner:

Assumption:

1-All the DMUs should accept the Trade Offs.

2- Each Trade Off can be used repetitively by the DMUs.

Extended axioms:
1- (Nonempty). The observed $(X_j, Y_j) \in T$; j = 1, 2, ..., n.
2- (Proportionality). If $(X,Y) \in T$, then $(\lambda X, \lambda Y) \in T$ for all $\lambda \geq 0$.
3- (Convexity). The set T is convex.
4- (Free disposability). If $(X, Y) \in T$, $\bar{X} \geq X$, $\bar{Y} \geq Y$,then $(\bar{X}, \bar{Y}) \in T$.
5- (Feasibility of Trade Offs). Let $(X, Y) \in T$. Then for any Trade Off r in the form of $(P_r, Q_r) \in T$ and any $\pi_r \geq 0$, the unit $(X + \pi_r P_r, Y + \pi_r Q_r) \in T$, provided that $X + \pi_r P_r \geq 0$ and $Y + \pi_r Q_r \geq 0$.
6- (Closeness). The set T is closed.
7- (Minimum extrapolation). T is the smallest set that satisfies axiom 1-6. (Where T is, $T = \{(X, Y) |$ output vector $Y \geq 0$ can produced from input vector $X \geq 0\}$).
Now, the PPS can be defined on the basis of the following.
The minimal PPS (PPS_{TO}) that satisfies axioms (1) – (7) is:
$PPS_{TO} = \{(X,Y)|Y = \bar{Y}\lambda + \sum_{t=1}^{k} \pi_t Q_t - e, X = \bar{X}\lambda + \sum_{t=1}^{k} \pi_t P_t + d, \lambda \in R_+^n, \pi \in R_+^k, d \in R_+^m$ and $e \in R_+^s\}$, (see Podinovski (2004)).
Based on PPSTO, for assessing the relative efficiency of DMUP (p = 1, 2, ..., n) that is defined from this PPS, we have the following model:
DEA model with trade-offs technology and input orientation

$$\begin{aligned} &\text{Min } \theta_p \\ &\text{S.t} \quad \bar{X}\lambda + \textstyle\sum_{t=1}^{k} \pi_t P_t \leq \theta_p X_p \\ &\qquad \bar{Y}\lambda + \sum_{t=1}^{k} \pi_t Q_t \geq Y_p \qquad (1) \\ &\qquad \lambda, \pi \geq 0,\ \theta_p \text{ sign free} \end{aligned}$$

DEA model with trade-offs technology and output orientation

$$\begin{aligned} &\text{Max } \theta_p \\ &\text{S.t} \quad \bar{X}\lambda + \textstyle\sum_{t=1}^{k} \pi_t P_t \leq X_p \\ &\qquad \bar{Y}\lambda + \sum_{t=1}^{k} \pi_t Q_t \geq \theta_p Y_p \qquad (2) \\ &\qquad \lambda, \pi \geq 0,\ \theta_p \text{ sign free} \end{aligned}$$

Now, by considering the definition of PPS_{TO}^t, we have the following problem with different frontiers (t = 1, 2):
DEA model with Trade Offs technology and input orientation
Frontier-period=t, DMUp-period=t

$$\begin{aligned} &\text{Min } \theta_p^t \\ &\text{S.t} \quad \bar{X}^t\lambda^t + \textstyle\sum_{t=1}^{k} \pi_r P_r^t \leq \theta_p^t X_p^t \\ &\qquad \bar{Y}^t\lambda^t + \sum_{t=1}^{k} \pi_r Q_r^t \geq Y_p^{t+1} \qquad (3) \\ &\qquad \lambda^t, \pi \geq 0, \theta_p^t \text{ sign free} \end{aligned}$$

DEA model with Trade Offs technology and input orientation
Frontier-period=t + 1 DMUp-period=t + 1

$$\begin{aligned} &\text{Min } \theta_p^{t+1} \\ &\text{S.t} \quad \bar{X}^{t+1}\lambda^{t+1} + \textstyle\sum_{t=1}^{k} \pi_r P_r^{t+1} \leq \theta_p^{t+1} X_p^{t+1} \\ &\qquad \bar{Y}^{t+1}\lambda^{t+1} + \sum_{t=1}^{k} \pi_r Q_r^{t+1} \\ &\qquad\qquad \geq Y_p^{t+1} \qquad (4) \\ &\qquad \lambda^t, \pi \geq 0, \theta_p^{t+1} \text{ sign free} \end{aligned}$$

DEA model with Trade Offs technology and input orientation
Frontier-period=t DMUp-period=t + 1

$$\begin{aligned} &\text{Min } \theta_p^t \\ &\text{S.t} \quad \bar{X}^t\lambda^t + \textstyle\sum_{t=1}^{k} \pi_r P_r^t \leq \theta_p^t X_p^{t+1} \\ &\qquad \bar{Y}^t\lambda^t + \sum_{t=1}^{k} \pi_r Q_r^t \geq Y_p^{t+1} \qquad (5) \\ &\qquad \lambda^t, \pi \geq 0, \theta_p^t \text{ sign free} \end{aligned}$$

DEA model with Trade Offs technology and input orientation
Frontier-period=t + 1 DMUp-period=t

$$\begin{aligned} &\text{Min } \theta_p^{t+1} \\ &\text{S.t} \quad \bar{X}^{t+1}\lambda^{t+1} + \textstyle\sum_{t=1}^{k} \pi_r P_r^{t+1} \leq \theta_p^{t+1} X_p^t \\ &\qquad \bar{Y}^{t+1}\lambda^{t+1} + \sum_{t=1}^{k} \pi_r Q_r^{t+1} \\ &\qquad\qquad \geq Y_p^t \qquad (6) \\ &\qquad \lambda^t, \pi \geq 0, \theta_p^{t+1} \text{ sign free} \end{aligned}$$

Where X_p^t is the input vector and Y_p^t is the output vector for DMUp (p = 1, 2 ,…, n) in period t.
First, we define EEC and ETC, consider the following equations:

$$EEC = \frac{\theta_{(t+1)}^{t+1(TO)}}{\theta_{(t)}^{t(TO)}} \qquad (7) \qquad \text{and}$$

$$ETC = \left[\frac{\theta_{(t)}^{t(TO)}}{\theta_{(t)}^{t+1(TO)}} \times \frac{\theta_{(t+1)}^{t(TO)}}{\theta_{(t+1)}^{t+1(TO)}}\right]^{\frac{1}{2}} \qquad (8)$$

EEC define the changes of efficiencies for DMUp between two periods based on Trade Off

technology. ETC define the change of Trade Off frontiers for DMUp between two periods.

These two definitions can present a decomposition of the EMI (Expanded Malmquist Index) as follows:

$$EMI = EEC \times ETC \quad (9)$$

Consider another equation:

REC define the changes of efficiencies for DMUp between two periods, which includes any change that come from rules and regulations based trade offs. Then,

$$EMI = EC \times REC \times ETC \quad (10)$$

or $$EMI = PEC \times SEC \times REC \times ETC \quad (11)$$

Where

$$EC = \frac{\theta_{(t+1)}^{t+1(CRS)}}{\theta_{(t)}^{t(CRS)}} \quad (12) \quad \text{and}$$

$$TC = \left[\frac{\theta_{(t)}^{t(CRS)}}{\theta_{(t)}^{t+1(CRS)}} \times \frac{\theta_{(t+1)}^{t(CRS)}}{\theta_{(t+1)}^{t+1(CRS)}}\right]^{\frac{1}{2}} \quad (13)$$

$$PEC = \frac{\theta_{(t+1)}^{t+1(VRS)}}{\theta_{(t)}^{t(VRS)}} \quad (14) \quad \text{and}$$

$$SEC = \left[\frac{\theta_{(t)}^{t(VRS)}}{\theta_{(t)}^{t+1(CRS)}} \times \frac{\theta_{(t+1)}^{t(CRS)}}{\theta_{(t+1)}^{t+1(VRS)}}\right]^{\frac{1}{2}} \quad (15)$$

So we have

$$\text{Malmquist Index} = EC \times TC \quad (16)$$

or $$\text{Malmquist Index} = PEC \times SEC \times TC \quad (17)$$

We now, DEA models for measuring efficiency of DMUp(p = 1, 2, ..., n) with problems below:

DEA model with CRS technology and input orientation

$$\begin{aligned} &\text{Min } \theta_p \\ &\text{S.t } \bar{X}\lambda \leq \theta_p X_p \\ &\quad \bar{Y}\lambda \geq Y_p \\ &\quad \lambda \geq 0,\ \theta_p \text{ sign free} \end{aligned} \quad (18)$$

DEA model with VRS technology and input orientation

$$\begin{aligned} &\text{Min } \theta_p \\ &\text{S.t } \bar{X}\lambda \leq \theta_p X_p \\ &\quad \bar{Y}\lambda \geq Y_p \\ &\quad 1.\lambda = 1 \\ &\quad \lambda \geq 0,\ \theta_p \text{ sign free} \end{aligned} \quad (19)$$

Thus, if $\theta_{j(t)}^{T}$ is the efficiency measure of unit j observed at time t relative to the technology boundary of time period T, then a Malmquist Index of the change of its productivity between period t and t + 1 is given by Malmquist productivity change index j equivalent $\frac{\theta_{j(t+1)}^{T}}{\theta_{j(t)}^{T}}$ (20) and the traditional Malmquist index is computed by $MI = \frac{\theta_{j(t+1)}^{T+1}}{\theta_{j(t)}^{T}} \times \left[\frac{\theta_{j(t+1)}^{T}}{\theta_{j(t+1)}^{T+1}} \times \frac{\theta_{j(t)}^{T}}{\theta_{j(t)}^{T+1}}\right]^{\frac{1}{2}}$ (21) where $\frac{\theta_{j(t+1)}^{T+1}}{\theta_{j(t)}^{T}}$ (22) is an efficiency change and $\left[\frac{\theta_{j(t+1)}^{T}}{\theta_{j(t+1)}^{T+1}} \times \frac{\theta_{j(t)}^{T}}{\theta_{j(t)}^{T+1}}\right]^{\frac{1}{2}}$ (23) is a technological change or boundary shift.

$$EC = \frac{\theta_{j(t+1)}^{T+1(CRS)}}{\theta_{j(t)}^{T(CRS)}} \quad (24)$$

$$P\,EC = \frac{\theta_{j(t+1)}^{T+1(VRS)}}{\theta_{j(t)}^{T(VRS)}} \quad (25)$$

$$TC = \left[\frac{\theta_{j(t)}^{T(CRS)}}{\theta_{j(t)}^{T+1(CRS)}} \times \frac{\theta_{j(t+1)}^{T(CRS)}}{\theta_{j(t+1)}^{T+1(CRS)}}\right]^{\frac{1}{2}} \quad (26)$$

$$SEC = \left[\frac{\theta_{j(t)}^{T(VRS)}}{\theta_{j(t)}^{t(CRS)}} \times \frac{\theta_{j(t+1)}^{T+1(CRS)}}{\theta_{j(t+1)}^{T+1(VRS)}}\right]^{\frac{1}{2}} \quad (27)$$

$$EEC = \frac{\theta_{j(t+1)}^{T+1(TO)}}{\theta_{j(t)}^{T(TO)}} \quad (28)$$

$$ETC = \left[\frac{\theta_{j(t)}^{T(TO)}}{\theta_{j(t)}^{T+1(TO)}} \times \frac{\theta_{j(t+1)}^{T(TO)}}{\theta_{j(t+1)}^{T+1(TO)}}\right]^{\frac{1}{2}} \quad (29)$$

$$MI = EC \times TC \quad (30)$$

$$MI = PEC \times SEC \times TC \quad (31)$$

$$MI = EEC \times ETC \quad (32)$$

$$EMI = EC \times REC \times ETC \quad (33)$$

$$EMI = PEC \times SEC \times REC \times ETC \quad (34)$$

3. Meta Malmquist Index

Consider DMUs (1, 2, ..., n) observed over time period t, t = 1, 2, ..., T so that meta period covers T periods. Let (X_{ij}^{t}, Y_{rj}^{t}) be respectively the ith input and rth output level of DMUj in period t within the meta period, The meta efficiency of DMUj0 and j0 $\in$ 2 (1, 2, ..., n) observed in some period $\tau \in$

$(1, 2, \ldots, T)$ is $\theta^{m}_{j0(\tau)}$, where $\theta^{m}_{j0(\tau)}$, is the optimal value of k_{j0} in model (35) below:

$$\theta^{m}_{j0(\tau)} = \min k_{j0}$$
$$\text{S.t} \quad \sum_{t=1}^{T}\sum_{j=1}^{n}\lambda_{jt}\, x^{t}_{ij} \le k_{j0}x^{\tau}_{ij0} \quad i = 1,2,\ldots,m$$
$$\sum_{t=1}^{T}\sum_{j=1}^{n}\lambda_{jt}\, y^{t}_{rj} \ge y^{\tau}_{rj0} \quad r = 1,2,\ldots,s \qquad (35)$$
$$\lambda_{jt} \ge 0 \;, j = 1,2,..,n \qquad k_{j0} \quad \text{free}$$

Model (35) relates to constant return to scale technologies and has input orientation. Now let θ^{m}_{jt} be the Meta efficiency of unit j as observed in period t and computed using a model such as (35). Then we have:

Meta efficiency of unit j observed in period t = within period t efficiency of unit j ×technological gap between period t boundary and the Meta frontier.

Putting the foregoing decomposition in symbols we have $\theta^{m}_{jt} = \theta^{T}_{jt} \times TG_{jt}$ where θ^{T}_{jt} is obtained for each unit j0 as the optimal value of k_{j0} in (35) after dropping all instances apart from those occurring in period t, and TG_{jt} is retrieved residually as $TG_{jt} = \frac{\theta^{m(CRS)}_{jt}}{\theta^{T(CRS)}_{jt}}$ thus $\theta^{m(CRS)}_{jt} = \theta^{T(CRS)}_{jt} \times TG^{CRS}_{jt}$ (36)

In this paper, we obtain θ^{m}_{jt} by solving Trade Offs model. First, we introduce Meta Malmquist Index for DMUj between period t and t + 1.

Meta Malmquist Index=$MI^{j}_{t,t+1}=\frac{\theta^{m}_{j(t+1)}}{\theta^{m}_{jt}}$ (Maria Portela and Thanassoulis(2008)). So

$$MI^{j(CRS)}_{t,t+1} = \frac{\theta^{m}_{j(t+1)}}{\theta^{m}_{jt}} = \frac{\theta^{T+1(CRS)}_{j(t+1)}}{\theta^{T(CRS)}_{j(t)}} \times \frac{TG^{CRS}_{j(t+1)}}{TG^{CRS}_{j(t)}} \qquad (37)$$

The term $\frac{\theta^{T+1}_{j(t+1)}}{\theta^{T}_{j(t)}}$ captures the efficiency change of unit j from year t + 1 as in traditional Malmquist Index of productivity change.

The term $\frac{TG_{j(t+1)}}{TG_{j(t)}}$ captures frontier shift between period t and t+1, $\frac{TG_{j(t+1)}}{TG_{j(t)}} = \frac{\theta^{m}_{j(t+1)}}{\theta^{T+1}_{j(t+1)}} \Big/ \frac{\theta^{m}_{j(t)}}{\theta^{T}_{j(t)}}$.

For computing VRS efficiency scores all that is to add to DEA models (such as (35)) the convexity constraint imposing the sum of all lambdas to be 1, $\sum_{t=1}^{T}\sum_{j=1}^{n}\lambda_{jt} = 1$, which in the case of (35). Would yield the Meta efficiency VRS score of unit j0. Now, we write DEA model with Trade Offs technology and input orientation. Suppose we have k Trade Offs, and we show (P_h, Q_h) where h = 1, 2, ..., k, then the meta efficiency of DMU_{j0} and j0 ∈ (1, 2, ..., n) observed in some period τ, $\tau \in (1,2,..,T)$ is $\theta^{m}_{j0(\tau)}$, where $\theta^{m}_{j0(\tau)}$ is the optimal value of k_{j0} in model (38) below:

$$\theta^{m}_{j0(\tau)} = \min k_{j0}$$
$$\text{S.t} \quad \sum_{t=1}^{T}\Big(\sum_{j=1}^{n}\lambda_{jt}\, x^{t}_{ij} + \sum_{h=1}^{k}\pi_{ht}\, P^{t}_{ih}\Big) \le k_{j0}x^{\tau}_{ij0} \quad i = 1,2,\ldots,m$$
$$\sum_{t=1}^{T}\Big(\sum_{j=1}^{n}\lambda_{jt}\, y^{t}_{rj} + \sum_{h=1}^{k}\pi_{ht}\, Q^{t}_{rh}\Big) \ge y^{\tau}_{rj0} \quad r = 1,2,\ldots,s \qquad (38)$$
$$\lambda_{jt} \ge 0 \;, j = 1,2,..,n \qquad k_{j0} \quad \text{free} \quad \pi_{ht} \ge 0 \;\; h = 1,2,\ldots k$$

Model (38) relates to Trade Offs technologies and has an input orientation. Thus $\theta^{m(TO)}_{jt}$ is the Meta efficiency of unit j as observed in period t and computed using a model such as (38). $\theta^{m(TO)}_{jt} = \theta^{T(TO)}_{jt} \times TG^{TO}_{jt}$ is obtained for each unit j0 as the optimal value of k_{j0} in (38) after dropping all instances apart from those occurring in period t, then $TG^{TO}_{jt} = \frac{\theta^{m}_{jt}}{\theta^{T(TO)}_{jt}}$ and we obtain $\theta^{T(TO)}_{j0\tau}$ from solving this program:

$$\theta^{T}_{j0(\tau)} = \min k_{j0}$$
$$\text{S.t} \quad \sum_{j=1}^{n}\lambda_{jt}\, x^{T}_{ij} + \sum_{h=1}^{k}\pi_{ht}\, P^{T}_{ih} \le k_{j0}x^{\tau}_{ij0} \quad i = 1,2,\ldots,m$$
$$\sum_{j=1}^{n}\lambda_{jt}\, y^{T}_{rj} + \sum_{h=1}^{k}\pi_{ht}\, Q^{T}_{rh} \ge y^{\tau}_{rj0} \quad r = 1,2,\ldots,s \qquad (39)$$
$$\lambda_{jt} \ge 0 \;, j = 1,2,..,n \qquad k_{j0} \quad \text{free} \quad \pi_{ht} \ge 0 \;\; h = 1,2,\ldots k$$

Then $MI^{j(TO)}_{t,t+1} = \frac{\theta^{m(TO)}_{j(t+1)}}{\theta^{m(TO)}_{jt}} = \frac{\theta^{T+1(TO)}_{j(t+1)}}{\theta^{T(TO)}_{j(t)}} \times \frac{TG^{TO}_{j(t+1)}}{TG^{TO}_{j(t)}}$ (40)

Therefor $\frac{TG^{TO}_{j(t+1)}}{TG^{TO}_{j(t)}} = \frac{\theta^{m(TO)}_{j(t+1)}}{\theta^{m(TO)}_{jt}} \times \frac{\theta^{T(TO)}_{j(t)}}{\theta^{T+1(TO)}_{j(t+1)}}$ (41)

$$MI^{j(TO)}_{t,t+1} = EEC \times \frac{TG^{TO}_{j(t+1)}}{TG^{TO}_{j(t)}} = EC \times REC \times \frac{TG^{TO}_{j(t+1)}}{TG^{TO}_{j(t)}} = PEC \times SEC \times REC \times \frac{TG^{TO}_{j(t+1)}}{TG^{TO}_{j(t)}} \qquad (42)$$

Thus $MI^{j(TO)}_{t,t+1} = \frac{EMI}{ETC} \times \frac{TG^{TO}_{j(t+1)}}{TG^{TO}_{j(t)}}$ (43)

4. Advantage of the Circular Meta Malmquist Index

To see that note that $\frac{\theta^{m}_{j(t+2)}}{\theta^{m}_{jt}} = \frac{\theta^{m}_{j(t+2)}}{\theta^{m}_{j(t+1)}} \times \frac{\theta^{m}_{j(t+1)}}{\theta^{m}_{j(t)}}$. That is the productivity change between period t and t+2 is the product of the successive productivity change from period t to t + 1 and from period t + 1 to t + 2.

$$\frac{\theta^{m(TO)}_{j(t+2)}}{\theta^{m(TO)}_{jt}} = \frac{\theta^{m(TO)}_{j(t+2)}}{\theta^{m(TO)}_{j(t+1)}} \times \frac{\theta^{m(TO)}_{j(t+1)}}{\theta^{m(TO)}_{j(t)}} \quad (44)$$

Similarly, we will want $\frac{\theta^{T+2(TO)}_{j(t+2)}}{\theta^{T(TO)}_{jt}} = \frac{\theta^{T+2(TO)}_{j(t+2)}}{\theta^{T+1(TO)}_{j(t+1)}} \times \frac{\theta^{T+1(TO)}_{j(t+1)}}{\theta^{T(TO)}_{j(t)}}$ is an efficiency change from period t to t + 2 and $\frac{TG^{T+2(TO)}_{j(t+2)}}{TG^{T(TO)}_{jt}} = \frac{TG^{T+2(TO)}_{j(t+2)}}{TG^{T+1(TO)}_{j(t+1)}} \times \frac{TG^{T+1(TO)}_{j(t+1)}}{TG^{T(TO)}_{j(t)}}$ is a boundary shift from period t to t + 2. And meta efficiency VRS score of unit j0 is $\theta^{m(TO)}_{j(t)} = \theta^{T(VRS)}_{j(t)} \times \frac{\theta^{m(VRS)}_{j(t)}}{\theta^{T(VRS)}_{jt}} \times \frac{\theta^{m(TO)}_{j(t)}}{\theta^{m(VRS)}_{jt}} = \theta^{T(VRS)}_{j(t)} \times TGV_{jt} \times MSET_{jt}$ that is meta efficiency decomposes in to within period efficiency in relation to a VRS frontier $\theta^{T(VRS)}_{j(t)}$, technological gap between the VRS frontier in t and the VRS meta frontier $\frac{\theta^{m(VRS)}_{j(t)}}{\theta^{T(VRS)}_{jt}}$, labeled TGV and meta scale efficiency $\frac{\theta^{m(TO)}_{j(t)}}{\theta^{m(VRS)}_{jt}}$ labeled MSET. Note that MSET capture the distance between the TO and V RS meta frontiers, at the input output mix of unit j as observed in period t, thus the circular Meta Malmquist Index, defined asn $MI^{j(TO)}_{t,t+1} = \frac{\theta^{m(TO)}_{j(t+1)}}{\theta^{m(TO)}_{jt}}$ can be decomposed as shown:

$$MI^{j(TO)}_{t,t+1} = \frac{\theta^{T+1(VRS)}_{j(t+1)}}{\theta^{T(VRS)}_{jt}} \times \frac{TGV_{j(t+1)}}{TGV_{j(t)}} \times \frac{MSET_{j(t+1)}}{MSET_{j(t)}} \quad (45)$$

$$MI^{j(TO)}_{t,t+1} = PEC \times \frac{TGV_{j(t+1)}}{TGV_{j(t)}} \times \frac{MSET_{j(t+1)}}{MSET_{j(t)}} \quad (46)$$

Pure technical efficiency change $\frac{\theta^{T+1(VRS)}_{j(t+1)}}{\theta^{T(VRS)}_{jt}}$, frontier shift between VRS frontiers $\frac{TGV_{j(t+1)}}{TGV_{j(t)}}$ and Meta scale efficiency change $\frac{MSET_{j(t+1)}}{MSET_{j(t)}}$.

5. Using the meta frontier to compare productivities of units

Using now the unit specific boundaries we can compute two efficiency scores for each unit instance jt (i.e unit j observed in year t). One efficiency will be relative to the meta frontier as before and denoted θ^{m}_{jt} , while the second will be relative to the unit specific boundary as defined above and it is denoted $\theta^{U_j}_{jt}$, where the index U_j relates to the unit specific boundary of unit j, and $\theta^{U_j}_{jt}$ in relation to unit j0 ∈ (1, 2, ..., n) observed in period $\tau \in$(1, 2, ..., T) is obtained buy solving model (49) (M. Portela and et.al (2008)).

$$\theta^{U_j}_{j0(\tau)} = min\ k_{j0}$$
$$\text{S.t} \quad \sum^{T}_{t=1} \lambda_{j0t}\, x^{t}_{ij0} \le k_{j0} x^{\tau}_{ij0} \qquad i = 1,2,\dots,m$$
$$\sum^{T}_{t=1} \lambda_{j0t}\, y^{t}_{rj0} \ge y^{\tau}_{rj0} \qquad r = 1,2,\dots,s \quad (49)$$
$$\lambda_{jt} \ge 0 \ , j = 1,2,..,n \qquad k_{j0} \quad free$$

Notation in (49) is as in (35). Note now that we have $\theta^{m}_{jt} = \theta^{U_j}_{jt} \times UG_{jt}$ where is retrieved residually and it measure the distance from the unit specific frontier to the Meta frontier, we shall refer to UG_{jt} as the unit frontier gap for unit j, measured at the units input-output mix in time period t.

Now we will obtain $\theta^{U_j}_{jt}$ in Trade Offs model in DEA, therefore we will have $\theta^{U_j}_{jt}$ by solving model (50). Suppose we have k Trade Offs, and we show (P_h, Q_h) where h = 1, 2, ..., k, then DMU_{j0} and j0 ∈ (1, 2, ..., n) observed in some period τ, $\tau \in (1,2,..,T)$ is $\theta^{m}_{j0(\tau)}$ where $\theta^{m}_{j0(\tau)}$ is the optimal value of k_{j0} in model (50) below:

$$\theta^{U_j}_{j0(\tau)} = min\ k_{j0}$$
$$\text{S.t} \quad \sum^{T}_{t=1}(\lambda_{j0t}\, x^{t}_{ij0} + \sum^{k}_{h=1} \pi_{ht}\, P^{T}_{ih}) \le k_{j0} x^{\tau}_{ij0} \qquad i = 1,2,\dots,m$$
$$\sum^{T}_{t=1}(\lambda_{j0t}\, t + \sum^{k}_{h=1} \pi_{ht}\, Q^{T}_{rh}) \ge y^{\tau}_{rj0} \qquad r = 1,2,\dots,s \quad (50)$$
$$\lambda_{j0t} \ge 0 \ , j = 1,2,..,n \qquad k_{j0} \quad free \quad \pi_{ht} \ge 0 \ \ h = 1,2,\dots k$$

The $\theta^{m}_{jt} = \theta^{U_{j(TO)}}_{jt} \times UG^{TO}_{jt}$ where UG^{TO}_{jt} is retrieved residually and it measures the distance from unit specific frontier to the Meta frontier. We shall refer to UG_{jt} as the unit frontier gap for unit j, measured at the units input-output mix in time period t. We can

now the Meta efficiency of two units at the same period in time to compare their productivities. Let us consider unit j and k and let us take their instances in period t. A measure of their relative productivity is given by the ratio of their Meta efficiencies, $MI_{kj}^{t}=\frac{\theta_{jt}^{m}}{\theta_{kt}^{m}}$. When MI_{kj}^{t} is greater than 1 it means that productivity at unit j is higher than that of unit k in period t. Values lower than 1 mean the converse.

By Using this definition which decomposes Meta efficiency in to within unit and unit frontier gap we can decompose the index of comparative unit productivity MI_{kj}^{t} of unit j and k as observed in period t as follows (Maria Portela and Thanassoulis (2008)):

$$MI_{kj}^{t}=\frac{\theta_{jt}^{m}}{\theta_{kt}^{m}}=\frac{\theta_{jt}^{U_j}}{\theta_{kt}^{U_k}}\times\frac{UG_{jt}}{UG_{kt}} \qquad (52)$$

The term $\frac{\theta_{jta}^{U_j}}{\theta_{kt}^{U_k}}$ captures the component of the relative productivity of units j and k accounted for by the distance of unit j in period t from its unit specific boundary U_j compared to the corresponding distance of unit k in period t from its own unit specific boundary U_k. This term will be referred to the general as within unit efficiency difference between j and k at time t. The term $\frac{UG_{jt}}{UG_{kt}}$ captures the component of the relative productivity of units j and k at time t accounted for by the distance of the unit specific boundary of unit j from the meta frontier, taken at the input-output mix of unit j at time t, compared to the corresponding distance of unit specific boundary of unit k taken at its input-output mix in period t. Given that the Meta frontier is stationary the ratio in question reflects the distance between the unit specific boundaries taken at their respective input-output mixes in period t. Thus the term $\frac{UG_{jt}}{UG_{kt}}$ is analogous to the Frontier Shift component in the Meta Malmquist Index of productivity change over time as defined in

$$MI_{t,t+1}^{j}=\frac{\theta_{j(t+1)}^{m}}{\theta_{jt}^{m}}=\frac{\theta_{j(t+1)}^{T+1}}{\theta_{jt}^{T}}\times\frac{TG_{j(t+1)}}{TG_{j(t)}} \qquad (53)$$

But here the frontier shift is not over time but rather between production units. So we shall refer to the term $\frac{UG_{jt}}{UG_{kt}}$ as unit frontier shift between k and j at time t. Similarly, suppose we have k Trade Offs then we will observe:

$$MI_{kj}^{t(TO)}=\frac{\theta_{jt}^{m(TO)}}{\theta_{kt}^{m(TO)}}=\frac{\theta_{jt}^{U_j(TO)}}{\theta_{kt}^{U_k(TO)}}\times\frac{UG_{jt}^{(TO)}}{UG_{kt}^{(TO)}} \qquad (54)$$

6. Comparing two units at two different point in time

We know generalize the above concepts to compare and decompose the productivities of two units at two different points in time. Let us consider units j and k and let us take their instance in period s and t respectively. A measure of the relative productivity is given by the ratio of their meta efficiencies, $MI_{kj}^{ts}=\frac{\theta_{js}^{m}}{\theta_{kt}^{m}}$ and we will have (for more details seeMaria Portela and Thanassoulis (2008)):

$$MI_{kj}^{ts}=\frac{\theta_{js}^{m}}{\theta_{kt}^{m}}=\frac{\theta_{js}^{m}}{\theta_{jt}^{m}}\times\frac{\theta_{jt}^{m}}{\theta_{kt}^{m}} \qquad (55)$$

That is MI_{kj}^{ts} decomposes in two indices, The first index is $\frac{\theta_{js}^{m}}{\theta_{jt}^{m}}$, This will be referred to as productivity change over time. Here it captures the change in the productivity of unit j between period t and s. The second index is $\frac{\theta_{jt}^{m}}{\theta_{kt}^{m}}$ this will be referred to as productivity difference between contemporaneous units. Here it captures the difference in the productivity of units j and k in period t Note that a similar decomposition to that in MI_{kj}^{ts} , but using unit k rather than j as a reference is also possible. That is we could have:

$$MI_{kj}^{ts}=\frac{\theta_{js}^{m}}{\theta_{kt}^{m}}=\frac{\theta_{ks}^{m}}{\theta_{kt}^{m}}\times\frac{\theta_{js}^{m}}{\theta_{ks}^{m}} \qquad (56)$$

By using all of formulation in this paper we will have:

$$MI_{kj}^{ts}=\frac{\theta_{js}^{S}}{\theta_{kt}^{T}}\times\frac{TG_{js}}{TG_{jt}}\times\frac{\theta_{jt}^{U_j}}{\theta_{kt}^{U_k}}\times\frac{UG_{jt}}{UG_{kt}} \qquad (57)$$

That is the difference in productivity between units k and j observed in period t and s decomposes in to efficiency change $\frac{\theta_{js}^{S}}{\theta_{kt}^{T}}$ for unit j between periods t and s, period frontier shift $\frac{TG_{js}}{TG_{jt}}$ between s and t, at the input-output mix of unit j, within unit efficiency difference $\frac{\theta_{jt}^{U_j}}{\theta_{kt}^{U_k}}$ between j and k at time t and unit frontier shift $\frac{UG_{jt}}{UG_{kt}}$between units j and k at their input-output mix in period t. Similarly, with having k Trade Offs we will have:

$$MI_{kj}^{ts(TO)}=\frac{\theta_{js}^{m(TO)}}{\theta_{kt}^{m(TO)}}=\frac{\theta_{ks}^{m(TO)}}{\theta_{kt}^{m(TO)}}\times\frac{\theta_{js}^{m(TO)}}{\theta_{ks}^{m(TO)}} \quad (58)$$

$$MI_{kj}^{ts} = \frac{\theta_{js}^{S(TO)}}{\theta_{kt}^{T(TO)}}\times\frac{TG_{js}{}^{TO}}{TG_{jt}{}^{TO}}\times\frac{\theta_{jt}^{U_j(TO)}}{\theta_{kt}^{U_k(TO)}}\times\frac{UG_{jt}{}^{TO}}{UG_{kt}{}^{TO}} \quad (59)$$

7. Example

Example 1: Consider Table (1)... (6) in this Tables, we have ten DMUs with three inputs and five outputs at three periods. Data have been taken from a commercial Bank in IRAN for seven branches. Assume that all DMUs agree as being true for the following judgments at two periods (we have three Trade Offs in each period).

1.$(P_1^t, Q_1^t)= (P_1^{t+1}, Q_1^{t+1}) =(P_1^{t+2}, Q_1^{t+2}) =(p_{11}^t, p_{12}^t, p_{13}^t, q_{11}^t, q_{12}^t, q_{13}^t, q_{14}^t, q_{15}^t)=$
$(-10,10000000,1000000000,100000000,10000000000,1000000000,1100000000,10000000000)$
2 .$(P_2^t, Q_2^t)= (P_2^{t+1}, Q_2^{t+1}) =(P_2^{t+2}, Q_2^{t+2}) =(p_{21}^t, p_{22}^t, p_{23}^t, q_{21}^t, q_{22}^t, q_{23}^t, q_{24}^t, q_{25}^t)=$
$(-14, 20000000, 2000000000, 11100000000, 10000000000, 100000000000, 9000000000, 900000000000)$
3. $(P_3^t, Q_3^t)= (P_3^{t+1}, Q_3^{t+1}) =(P_3^{t+2}, Q_3^{t+2}) =(p_{31}^t, p_{32}^t, p_{33}^t, q_{31}^t, q_{32}^t, q_{33}^t, q_{34}^t, q_{35}^t)=(0,0,0,0,0,0,0,0)$
$(-10, 10000000, 2000000000, 100000000000, 120000000000, 100000000000, 80000000000,-30000000)$

Table (1), Inputs in period$t$

Unit	x_1	x_2	x_3
DMU_1	24.6	1163006699	21214797126
DMU_2	26.51	433148930	586933516
DMU_3	14.69	2338234805	2423898801
DMU_4	20.15	1344914230	4260524118
DMU_5	19.74	488806775	3658263944
DMU_6	16.32	1506571113	1700726564
DMU_7	16.3	575541160	4931297789
DMU_8	38.64	687401632	9892984883
DMU_9	30.54	1052621363	10850597644
DMU_{10}	20.04	620789783	4005818426

Table (2), Inputs in period$t+1$

Unit	x_1	x_2	x_3
DMU_1	24.6	2195224416	20705682078
DMU_2	26.51	859703238	573439627
DMU_3	14.69	4686245937	2419191001
DMU_4	20.15	2716258762	5708905141
DMU_5	19.74	965343887	3510322663
DMU_6	16.32	2957622923	1767161564
DMU_7	16.3	1169632952	5089852841
DMU_8	38.64	1380459532	9688488055
DMU_9	30.54	2156060329	11187719906
DMU_{10}	20.04	1257857335	4003741426

Table (3), Inputs in period $t+2$

Unit	x_1	x_2	x_3
DMU_1	24.6	3161147138	17899623576
DMU_2	26.51	1268741030	1310517912
DMU_3	14.69	7030453173	2270066109
DMU_4	20.15	4110060766	5708955141
DMU_5	19.74	1437235127	3509804663
DMU_6	16.32	4396171175	1823653154
DMU_7	16.3	1794807344	5284876078
DMU_8	38.64	2076989680	10217822041
DMU_9	30.54	3307801816	11216072885
DMU_{10}	20.04	1892438197	2509333739

Table (4), Outputs in period t.

Unit	y_1	y_2	y_3	y_4	y_5
DMU_1	242241992696	149927581688	739255995	137914144	428667943
DMU_2	107238188475	86355903094	9516959	230075940	80728098
DMU_3	277898251065	219123202540	270049146	19573201	532701000
DMU_4	88180358515	173092885271	74637180	625952459	5860810117
DMU_5	128834133115	88264150018	235995190	906927396	7805587173
DMU_6	298359497990	184328871243	1712460544	1213573293	11308531095
DMU_7	85714984119	125413342055	54632177	385747036	5669053062
DMU_8	135956919734	119648993075	29280821	102535073	5155800956
DMU_9	333510866500	137294730996	79558096	112179147	666055008
DMU_{10}	234535258794	116487806490	85936562	152512990	453380535

Table (5), Outputs in period $t+1$.

Unit	y_1	y_2	y_3	y_4	y_5
DMU_1	249623342159	117399292537	1540543984	178683273	428667943
DMU_2	112562861469	86202028391	25345126	345083696	84628098
DMU_3	276955477174	195761787737	466977957	48703328	537701000
DMU_4	89769875594	175034650015	85423893	711106298	6140099086
DMU_5	126452729455	81056170548	1021865861	1097224634	7975379183
DMU_6	313515525726	180595350698	4678292867	1420994153	12549446009
DMU_7	88201054771	115220570013	59465117	737973247	5788081726
DMU_8	146533627624	113094425933	396985110	168979756	5150091667
DMU_9	328457006339	153646949485	160072278	180257561	656055008
DMU_{10}	239480060054	119637603603	153267220	232276956	468380535

Table (6), Outputs in period $t+2$.

Unit	y_1	y_2	y_3	y_4	y_5
DMU_1	293867028198	140441085515	1761926627	219200982	417867943
DMU_2	115139451138	87285197519	24844888	435539236	165778098
DMU_3	278333223405	206467052805	791923009	64527873	537701000
DMU_4	93698153403	174197607935	320187997	767855712	5878898037
DMU_5	141765332119	91751175208	1144343535	1405955598	8089357778
DMU_6	318100978977	188236536110	6433265613	1601266241	12025630507
DMU_7	90693221404	131524255400	141621574	906022389	6897553226
DMU_8	145024864957	117506091612	636944528	234797904	5138375112
DMU_9	347376530595	156528383470	167954127	203958539	661772204
DMU_{10}	242826874768	114773321947	208500176	268924230	368380535

Table (7), Meta Efficiency and Meta Malmquist Index for $DMUs$ in CRS models of DEA.

Unit	$\theta_{jt}^{m(CRS)}$	$\theta_{jt+1}^{m(CRS)}$	$\theta_{jt+2}^{m(CRS)}$	$MI_{t,t+1}^{j(CRS)}$	$MI_{t+1,t+2}^{j(CRS)}$	$MI_{t,t+2}^{j(CRS)}$
DMU_1	0.8494	0.5976	0.6402	0.7036	1.0712	0.7537
DMU_2	1.0000	1.0000	0.5536	1.0000	0.5536	0.5536
DMU_3	1.0000	0.9844	0.9946	0.9844	1.0103	0.9946
DMU_4	0.8875	0.6896	0.6726	0.7771	0.9753	0.7579
DMU_5	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
DMU_6	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
DMU_7	1.0000	0.7384	0.7228	0.7384	0.9788	0.7228
DMU_8	0.8586	0.4812	0.3739	0.5604	0.7771	0.4355
DMU_9	0.9042	0.6742	0.6165	0.7456	0.9145	0.6819
DMU_{10}	1.0000	0.7907	0.6620	0.7907	0.8372	0.6620

Table (8), Meta Efficiency and Meta Malmquist Index for DMUs in Trade Offs models of DEA.

Unit	$\theta_{jt}^{m(TO)}$	$\theta_{jt+1}^{m(TO)}$	$\theta_{jt+2}^{m(TO)}$	$MI_{t,t+1}^{j(TO)}$	$MI_{t+1,t+2}^{j(TO)}$	$MI_{t,t+2}^{j(TO)}$
DMU_1	0.1935	0.1779	0.2130	0.9196	1.1971	1.1009
DMU_2	1.0000	1.0000	0.5536	1.0000	0.5536	0.5536
DMU_3	0.9352	0.8368	0.9278	0.8948	1.1088	0.9921
DMU_4	0.4920	0.3534	0.3457	0.7183	0.9781	0.7026
DMU_5	0.4835	0.3891	0.3667	0.8048	0.9423	0.7584
DMU_6	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
DMU_7	0.3490	0.2920	0.3063	0.8366	1.0489	0.8775
DMU_8	0.2237	0.2035	0.1728	0.9097	0.8495	0.7727
DMU_9	0.4612	0.3662	0.3314	0.7940	0.9050	0.7185
DMU_{10}	0.7609	0.6124	0.6160	0.8049	1.0057	0.8095

8. Conclusion

Trade Off technology is used o evaluate in Malmquist, Expanded Malmquist and Meta Malmquist productivity the validity of models is shown by numerical example and a set of data from a commercial bank is used and the result from the point board of directory is quite satisfactory.

The above mation models may be extended for multicative models and the models for non redial efficiency also the Malmquist and Expanded meta Malmquist may be used for cost efficiency and revenue efficiency.

References

[1]. Banker R. D., Charnes A. and Cooper W.W., (1984) Some models for estimating echnical and scale inefficies in Data Envelopment Analysis, Management Science 30, 1078-1092.

[2]. Charnes, A., Cooper, W.W., Rhodes, E., 1978. Measuring the efficiency of the decision making units.European Journal of Operational Research 2, 429-444.

[3]. Cooper, W.W., Seiford, L.M., Tone, K., 2000. Data envelopment analysis: A comprehensive text with models, applications, references, and DEA − solver software . Kluwer Academic Publisher, Dordrecht.

[4]. Fare, R., Grosskopf, S., Lindgren, B., Roose, P., 1992. Productivity change in Swedish analysis pharmacies 19801989: A nonparametric Malmquist approach. Journal of Productivity 3, 85-102.

[5]. Fare, R., Grosskopf, S., Norris, M., Zhang, A., 1994. Productivity growth, technical progress,
and efficiency changes in industrial country. American Economic Review 84, 66-83.

[6]. Farrell. M.T. (1957), "The Measurement of Productive Efficiency," Journal of the Royal Statistical Society Series A , 120, III, pp.253-281.

[7]. Podinovski, V.V., 2004. Production trade-offs and weight restrictions in data envelopment analysis. Journal of the Operational Research Society 55, 1311-1322.

[8]. Podinovski, V.V., 2007a. Improving data envelopment analysis by the use of production trade-offs. Journal of the Operational Research Society 58, 1261-1270.

[9]. Podinovski, V.V., 2007b. Computation of effcient targets in DEA models with production trade-offs and weight restrictions. European Journal of Operational Research 181, 586-591.

[10]. Podinovski, V.V., Thanassoulis, E., 2007. Improving discrimination in data envelopment analysis: Some practical suggestions. Journal of the Operational Research Society 28, 117-126.

[11]. Portela, M.C.A.S and Thanassoulis, E.(2006), Malmquist index using geometric distance function (GDF). Application to a sample of Portuguese bank branches, Journal of Productivity Analysis 25, 25-41.

[12]. Portela, M.C.A.S and Thanassoulis, E.(2001), Decomposing school type efficiency, European Journal of Oprational Research, 132/2, 114-130.

[13]. Portela, M.C.A.S and Thanassoulis, E.(2008), A circular meta malmquist index for measuring productivity, Journal of Aston Business School research, ISBN NO :978 − 1 − 85446 − 724 − 6.

[14]. Thanassoulis E. and Portela, M.C.A.S (2002) School Outcomes: Sharing the responsibility between pupil and school, Education Economics 10/2, 183-207.

11/10/2012

The Outcome of Surgical Interference in Patients with Chronic Obstructive Renal Failure

Tamer A. Ali, Mohamed A. Abd Elaal, Ashraf H. Abd-Eltif, Sabry M. Khalid, Ibrahim A. El Sotohy
Ahmed F. Abd El Rahim and Tarek M. El Salamony

Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
Dr_tamer_ali@yahoo.com

Abstract: Objective: To evaluate some of the morphological, functional and clinical impacts of surgical management of chronic obstructive renal failure. We will try to assess some of the factors that may predict favorable outcomes. **Patients and methods:** Eighty six patients clinically diagnosed as having chronic obstructive renal failure (53 men 61.63% and 33 women 38.37% ranging in age between 25 and 69 years, mean 47 years) in the period from October 2007 to January 2012. The patients on this study were divided according to past history of renal impairment and/or regular dialysis into two groups as follow: ***Group (A):*** Patients with chronic renal failure with no regular dialysis (46 patients) Males: 28 (60.86%) Females: 18 (39.14%). ***Group (B):*** Patients with chronic renal failure with regular dialysis (40 patients) Males: 25 (62.5%) Females: 15 (37.5%). All patients have been evaluated according to the protocol of obstructive uropathy. Clinically most patients presented by anuria 28 (32.65%) patients (16 group A and 12 group B), oliguria 25 (29.07%) patients (13 group A and 12 group B), loin pain 40 (46.5%) patients (25 group A and 15 group B), nausea and vomiting 29 (33.72%) patients (12 group A and 17 group B). 58 Patients underwent direct intervention and 28 patients were managed by temporary drainage until improvement of the general condition then definitive surgical procedure. **Results:** In our series patients with chronic obstructive renal failure (group A), showed improvement in 33 patients (71.74%), equivocal improvement in7 patients (15.21%) and did not improve in 6 patients (13.04). Out of the 6 patients who did not improve after management 2 patients (4.35%) remained unchanged and 4 patients (8.68%) continued to have progressive renal failure up to regular dialysis. In patients with chronic obstructive renal failure (group B), renal functions showed different degrees of improvement as follow: In 14 patients (35%) good improvement and subsequent complete weaning from dialysis occurred, while in 16 patients (40%) there was a decrease in weekly dialysis sessions from 3 to 2 sessions/week. In the remaining 10 patients (25%) there was no improvement and patients continued to have regular dialysis as preintervention. The overall complications in this series were (12.79%). The incidence was much more in the chronic cases group B. The mortality rate in our series is (2.33%) which is not high if compared with other series dealing with corrective surgery in obstructive renal failure. **Conclusion:** There is evidence of reversibility of renal function after long standing obstruction which provides justification for efforts to identify and treat urinary tract obstruction even if a patient with an obstruction requires dialysis to avoid the dialysis or kidney transplantation or helping patients under dialysis for complete weaning form dialysis or decrease their number of weekly sessions, and in all cases the risk of the procedures should be weighed against the chances of improvement .

[Tamer A. Ali, Mohamed A. Abd Elaal, Ashraf H. Abd-Eltif, Sabry M. Khalid, Ahmed F. Abd El Rahim and Tarek M. El Salamony. **The Outcome of Surgical Interference in Patients with Chronic Obstructive Renal Failure**.*Life Sci J* 2012;9(4):2884-2890]. (ISSN: 1097-8135). http://www.lifesciencesite.com. 423

Key words: Obstructive, Renal Failure

1. Introduction

Renal insufficiency describes a measurable reduction in renal function with normal serum biochemical values. Renal failure is an advanced stage of renal insufficiency in which renal function deteriorates to the extent that homeostatic mechanisms are impaired and serum biochemical parameters are disturbed ***(Dooley and Mazze, 1996).***

Obstructive uropathy refers to the functional or anatomic obstruction of urinary flow at any level of the urinary tract. Obstructive nephropathy is present when the obstruction causes functional or anatomic renal damage ***(Vernon et al., 2007).***

The diagnosis of obstruction as the cause of renal failure is important, as it is correctable. Relief of such obstruction may cure acute renal failure due to post-renal etiology or convert the situation in cases of chronic renal failure from advancing progressive disease to stable renal insufficiency compatible with comfortable life ***(Mathew, 1996).***

Having preoperative predictors of renal recovery may ensure optimal patients selection, reducing the number of procedures and economic burden on the patient who does not require intervention ***(Ramanthan et al., 1998).***

2. Patients and Methods

This prospective study was conducted at Al-Azhar University Hospitals. The study included 86 patients clinically diagnosed as having chronic obstructive renal failure (53 men 61.63% and 33

women 38.37% ranging in age between 25 and 69years, mean±SD 47 years) in the period from October 2007 to January 2012. The patients in this study were divided into two groups as follow:

Group (A): Patients with chronic renal failure with no regular dialysis (46 patients) Males: 28 (60.86%) Females: 18 (39.14%).

Group (B): Patients with chronic renal failure with regular dialysis (40 patients) Males: 25 (62.5%) Females: 15 (37.5%).

Preoperative evaluation:

All patients underwent the following preoperative evaluation in the form of:

A- Clinical assessment:

1- Full medical history

2- Complete general and urologic examination.

Including systemic, abdominal, perineal, digital rectal examination in males and vaginal examination in females.

B- Laboratory investigations: These included:

Complete urine analysis, urine culture and sensitivity in presence of urinary tract infection guided by colony count > 100,000 micro organism/ ml, Creatinine clearance, Fluid input /24 hours, Urine output /24 hours, Blood chemistry with special request for: Serum creatinine, Serum sodium (Na), Serum potassium (K) and Serum bicarbonate (HCO3).

C- Imaging studies

a- Plain X-ray urinary tract (PUT): PUT was done to all the patients.

b- Abdominal ultrasonography (US):

Abdominal US was carried out in all patients. It had a special value for those who had chronic renal insufficiency. Ultrasonography was done with special request for measuring the paranchymal thickness, grade of echogenicity, corticomedullary differentiation and the degree of hydronephrosis.

c- Diuretic renography:

Technetium-99m diethylenetriamine penataacetic acid (^{99m}Tc DTPA) was used for diuretic renography according to the standard protocol with 40 mg of furosemide injected 20 minutes after injection of the radiotracer. Half-time drainage was calculated using computer generated curve and the GFR was calculated by the accumulated tracer in the kidney between 2 and 3 minutes after radiopharmaceutical injection. Sequential images were obtained by gamma camera computer system.

Obstructive response was considered when after collecting system filling and furosemide administration, the collecting system activity kept rising, peaked and remained at this level, or the half time clearance of radionuclide was greater than 20 minutes.

***d- Magnetic resonance urography (MRU)*:**

MRU was done to some patients who had no clear cause of hydronephrosis to diagnose the possible cause of obstruction.

Treatment:

1- Preliminary Procedures

A- Preintervention percutaneus nephrostomy (PCN) fixation

Eighteen patients (20.93%) 10 cases (21.74%) of group A and 8 patients (20%) of group B underwent preliminary ultrasonic guided percutaneous nephrostomy (PCN).

B- Preintervention dialysis

Preintervention dialysis was performed urgently to 10 patients of group A and all patients of group B to improve the general condition and physical fitness of those patients for anesthesia and surgery.

2- Definitive treatment

Types of surgical intervention

Some patients receive one type of surgical intervention, but others receive two or more types of surgical intervention together as follow**:**

1- **Ureterolithotomy** was performed to 36 patients {19 group A (41.3%) and 17 group B (42.5%)}.
2- **Pyelolithotomy** was performed to 24 patients {14 group A (30.43%) and 10 group B (25%)}.
3- **Ureteroscopy (URS)** was performed to 18 patients {10 group A (21.74%) and 8 group B (20%)}.
4- **Endoscopic endodilatation** of the lower ureter was performed to 8 patients {5 group A (10.87%) and 3 group B (7.5%)}.

Postoperative follow up

All patients were put under strict clinical surveillance during the early postoperative days with the following assessments performed on day +1 and +3; urine output, serum creatinine, serum electrolytes (K, Na & HCO_3) and blood gases. In addition to PUT and creatinine clearance were performed on day +3.

Late follow up

The duration of follow up ranged from two weeks to six months after definitive procedures. All patients were followed after a period of two weeks and six months by the following: urine analysis with culture and sensitivity test (when indicated), serum creatinine, serum electrolytes (K, Na & HCO_3), creatinine clearance, abdominal ultrasonography (US), diuretic renography and state of redialysis to evaluate the end results of our surgical intervention.

Improvement evaluation

Evident improvement was judged if one or more of the following criteria were fulfilled: Creatinine returned to the normal as matched to the patient's age and gender, creatinine clearance increased by 20

ml/min or more or complete weaning from dialysis occurred.

Equivocal improvement was judged if one or more of the following criteria were fulfilled: Creatinine decreased but still above the normal as matched to the patient's age and gender or the number of weekly dialysis sessions decreased. Otherwise, patients were considered as having no improvement.

3. Results

Improvement

Improvement ratio:

Table (1): The incidence of improvement among the studied groups

Groups	Improvement		
	Good improvement	Equivocal improvement	No improvement
A (n = 46)	33 (71.74%)	7 (15.22%)	6 (13.04%)
B (n = 40)	14 (35%)	16 (40%)	10 (25%)

Prognostic criteria

Age distribution

Table (2): Correlation between age distribution and improvement among studied groups.

	Mean age	No of patients	Improvement	No improvement	P value
Group A (n = 46)	Age ≤ 47	22	19 (86.36%)	3 (13.63%)	> 0.05 NS
	Age > 47	24	21 (87.5%)	3 (12.5%)	
Group B (n = 40)	Age ≤ 47	18	14 (77.78%)	4 (22.22%)	> 0.05 NS
	Age > 47	22	16 (72.73%)	6 (27.27%)	

2- Sex distribution

Table (3): Correlation between sex distribution and improvement among studied groups.

	Sex	No of patients	Improvement	No improvement	P value
Group A (n = 46)	Males	28	24 (82.14%)	4 (17.86%)	> 0.05 NS
	Females	18	16 (88.89%)	2 (11.11%)	
Group B (n = 40)	Males	25	19 (76%)	6 (24%)	> 0.05 NS
	Females	15	11 (73.33%)	4 (26.67%)	

3- Laboratory investigations

The correlation between preoperative laboratory investigations and improvement among studied groups are shown in tables from 5 to 11.

Table (4): Correlation between preoperative creatinine and improvement among studied groups.

	Mean preoperative creatinine(mg/dl)	No of patients	Improvement	No improvement	P value
Group A (n = 46)	Cr ≤ 4	22	19 (86.36%)	3 (13.63%)	> 0.05 NS
	Cr > 4	24	21 (87.5%)	3 (12.5%)	
Group B (n = 40)	Cr ≤ 4	19	15 (78.95%)	4 (21.05%)	> 0.05 NS
	Cr > 4	21	11 (71.43%)	6 (28.57%)	

Table (5): Correlation between preoperative creatinine clearance and improvement among studied groups.

	Mean preoperative CcR (ml/min)	No of patients	Improvement	No improvement	P value
Group A (n = 46)	CcR ≤ 30	29	25 (86.21%)	4 (13.79%)	> 0.05 NS
	CcR > 30	19	17 (89.47%)	2 (10.53%)	
Group B (n = 40)	CcR ≤ 30	23	17 (73.91%)	6 (26.09%)	> 0.05 NS
	CcR > 30	17	13 (76.47%)	4 (23.53%)	

Table (6): Correlation between preoperative K+ and improvement among studied groups.

	Mean preoperative K+	No of patients	Improvement	No improvement	P value
Group A (n = 46)	K+ ≤ 5	19	17 (89.47%)	2 (10.53%)	> 0.05 NS
	K+ > 5	27	22 (85.19%)	4 (14.81%)	
Group B (n = 40)	K+ ≤ 5	14	10 (71.43%)	4 (28.57%)	> 0.05 NS
	K+ > 5	26	20 (76.92%)	6 (23.08%)	

Table (7): Correlation between preoperative Na+ and improvement among studied groups.

	Mean preoperative Na+	No of patients	Improvement	No improvement	P value
Group A (n = 46)	**Na+ ≤ 135**	22	20 (90.91%)	2 (9.09%)	> 0.05 NS
	Na+ > 135	24	20 (83.33%)	4 (16.67%)	
Group B (n = 40)	**Na+ ≤ 135**	19	15 (78.95%)	4 (21.05%)	> 0.05 NS
	Na+ > 135	21	11 (71.43%)	6 (28.57%)	

Table (8): Correlation between preoperative HCO_3 and improvement among studied groups.

	Mean preoperative HCO_3	No of patients	Improvement	No improvement	P value
Group A (n = 46)	**$HCO_3 \leq 15$**	29	25 (86.21%)	4 (13.79%)	> 0.05 NS
	$HCO_3 > 15$	19	17 (89.47%)	2 (10.53%)	
Group B (n = 40)	**$HCO_3 \leq 15$**	23	18 (78.26%)	5 (21.74%)	> 0.05 NS
	$HCO_3 > 15$	17	12 (70.59%)	5 (29.41%)	

Table (9): Correlation between preoperative UTI and improvement among studied groups.

	preoperative UTI	No of patients	Improvement	No improvement	P value
Group A (n = 46)	Positive UTI	22	19 (86.36%)	3 (13.64%)	> 0.05 NS
	Negative UTI	24	21 (87.5%)	3(12.5%)	
Group B (n = 40)	Positive UTI	20	15 (75%)	5 (25%)	> 0.05 NS
	Negative UTI	20	15 (75%)	5(25%)	

3- U/S findings

A- Parenchymal thickness

Table (10): Correlation between preoperative parenchymal thickness and improvement among studied groups.

	Mean preoperative Parenchymal thickness(mm)	No of patients	Improvement	No improvement	P value
Group A (n = 46)	P. thickness ≤ 10	18	12 (66.67%)	6 (33.33%)	< 0.01 HS
	P. thickness > 10	28	28 (100%)	0	
Group B (n = 40)	P. thickness ≤ 10	29	19 (65.52%)	10 (34.48%)	< 0.01 HS
	P. thickness > 10	11	20 (100%)	0	

B- Corticomedullary differentiation

Table (11): Correlation between preoperative corticomedullary differentiation and improvement among studied groups.

	preoperative Corticomedullary differentiation	No of patients	Improvement	No improvement	P value
Group A (n = 46)	Good	30	30 (100%)	0	< 0.01 HS
	Poor	16	10 (62.5%)	6 (37.5%)	
Group B (n = 40)	Good	14	14 (100%)	0	< 0.01 HS
	Poor	26	16 (61.54)	10 (38.46%)	

C- Parenchymal echogenicity

Table (12): Correlation between preoperative parenchymal echogenicity and improvement among studied groups.

	preoperative Parenchymal echogenicity	No of patients	Improvement	No improvement	P value
Group A (n = 46)	**Normal**	19	19 (100%)	0	< 0.01 HS
	Grade I	20	20 (100%)	0	
	Grade II	7	1 (14.28%)	6 (85.72%)	
Group B (n = 40)	**Normal**	0	0	0	< 0.01 HS
	Grade I	21	21 (100%)	0	
	Grade II	19	9 (47.37%)	10 (52.63%)	

5- Renal isotopic GFR

Table (13): Correlation between preoperative GFR of target kidney and improvement among studied groups.

	Mean preoperative GFR(ml/min)	No of patients	Improvement	No improvement	P value
Group A (n = 46)	GFR ≤ 30	17	11 (58.3%)	6 (41.7%)	< 0.01 HS
	GFR > 30	29	29 (100%)	0	
Group B (n = 40)	GFR ≤ 30	15	5 (33.33%)	10 (66.67%)	< 0.01 HS
	GFR > 30	25	25 (100%)	0	

6- Etiology of obstruction

Table (14): Correlation between etiologies of obstruction and improvement among studied groups.

	Cause of obstruction	No of patients	Improvement	No improvement	P value
Group A (n = 46)	**Calcular obstruction**	27	24 (88.89%)	3 (11.11%)	> 0.05 NS
	Stricture	19	11 (57.89%)	3 (42.11%)	
Group B (n = 40)	**Calcular obstruction**	24	19 (79.17%)	5 (20.83%)	> 0.05 NS
	Stricture	16	11 (68.75%)	5 (31.25%)	

7- Types of intervention

Table (15): Correlation between types of intervention and improvement among studied groups.

	Types of intervention	No of patients	Improvement	No improvement	P value
Group A (n = 46)	**Direct**	26	22 (84.62%)	4 (15.38%)	> 0.05 NS
	Staged	20	18 (90%)	2 (10%)	
Group B (n = 40)	**Direct**	32	24 (75%)	8 (25%)	> 0.05 NS
	Staged	8	6 (75%)	2 (25%)	

Morbidity

Table (16): Incidence of postoperative morbidity among the studied groups.

		Morbidity						
		Bleeding from nephrostomy	Wound gaping	Pyelonephritis	Perinephric abscess	Myocardial infarction	Wound infection	Septic shock
A (n = 46)	**Number**	0	0	1	0	0	1	0
B (n = 40)	**Number**	2	1	1	1	1	2	1
P value		0.0001 (HS)						

4. Discussion

The main step in the treatment of obstructive renal failure is drainage. Drainage of the obstructed tract could be as simple as catheter drainage of the bladder or a definitive operation to remove the cause of obstruction. Intermediate steps as bypassing ureteric obstruction by a catheter or proximal diversion by percutaneous nephrostomy (PCN) have their indications. However an initial medical treatment may be required particularly in cases of advanced degrees of renal failure where hypervolemia, hyperkalemia and acidosis may necessitate appropriate treatment. In severely affected patients (urgent cases) we tried to relief obstruction by simple short procedure as many patients in this group were had poor general conditions and this agree with *Mokhmalji et al. (2001)* who recommended that before any procedure patients must be euhydrated, controlled electrolytes and acid base balance.

The replacement therapy with fluids, electrolyte and acid base monitoring after stenting are very essential for uremic patients to compensate post obstructive diuresis and this was recommended by *Gulmi et al. (1995).*

In patients with chronic obstructive renal failure, the major goals were to establish euvolemia, to correct hypertension, hyperkalemia and acidosis to minimize the uremic bleeding tendency. Dialysis could be utilized to prepare the patient for definitive treatment. In this work dialysis was performed urgently preoperative to 10 patients of group A and all patients of group B to improve the general condition and physical fitness of those patients for anesthesia and surgery.

Direct definitive intervention in this work was applicable in 58 (67.44%) patients 26 (44.83%) of group A and 32 (80%) patients of group B. Staged treatment was done in 28 (32.56%) patients 20 cases (43.48%) of group A and 8 patients (20%) of group B. We tried to compare the results of direct intervention with staged intervention as regards recovery of renal function. No significant difference was noticed between both types of intervention either in patients with chronic obstructive renal failure.

Improvement

In 1982 Singh et al. reported renal function improvement in 86%, while 6% showed no improvement and they were given regular dialysis

after surgical management of 50 patients with renal and ureteric calculi and renal failure (31 acute renal failures and 19 chronic renal failures).

In 1985 Gupta et al. reported renal function improvement in 40 patients (67.8%), 8 cases (13.6%) showed no improvement and 11 cases (18.6%) continued to have progressive renal failure in management of 59 patients with renal and ureteric calculi presented with chronic renal failure.

In 1992 Cohen et al. reported that relief of obstruction in 3 patients with end stage renal disease led to discontinuation of dialysis.

In 2001 Gharbi et al. reported improvement of renal function in 16 (58%) cases with acute obstructive renal failure, remained unchanged in 6 (21%) and 3 cases (10.5%) continued to have progressive renal failure.

Witheraw and Wickham (2003) reported different degrees of improvement in 17 cases (89.5%), 2 cases (10.5%) remained stable, while no patient required long term dialysis after nephrolithotomy on 19 patients with chronic renal failure.

In 2004 Goel et al. reported improvement of renal function in 18 (90%) cases with chronic renal failure, and nephrolithiasis, remained unchanged in 1 (5%) and 1 case (5%) continued to have progressive renal failure.

In our series patients with chronic obstructive renal failure (group A), showed improvement in 33 patients (71.74%), equivocal improvement in7 patients (15.21%) and did not improve in 6 patients (13.04). Out of the 6 patients who did not improve after management 2 patients (4.35%) remained unchanged and 4 patients (8.68%) continued to have progressive renal failure up to regular dialysis. In patients with chronic obstructive renal failure (group B), renal functions showed different degrees of improvement as follow: In 14 patients (35%) good improvement and subsequent complete weaning from dialysis occurred, while in 16 patients (40%) there was a decrease in weekly dialysis sessions from 3 to 2 sessions/week. In the remaining 10 patients (25%) there was no improvement and patients continued to have regular dialysis as preintervention.

Morbidity

The overall complications in this series were (13.79%) %. There was significant difference between the incidence of morbidity in patients with chronic renal failure. The incidence was much more in the chronic cases group B.

Bleeding from nephrostomy in this series occurred in 2 patients (2%), while *Singh et al. (1982)* sighted 3 cases (6%) of operative hemorrhage that need blood transfusion. Perinephric collection occurred in 2 patients (2%).

Bedair (1983) reported 4 (5%) cases of septicemia in his series. Catheter problems (obstruction or dislodgement) are the most frequent minor complication met with *(Bedair, 1983; Stables, 2001).*

Stables, (2001) reported that bacteremic reaction occurred in 1.9% after placement of percutaneous nephrostorny.

In this series wound gaping occurred in 1 patient (1.16%) and wound infection in 3 patients (3.48%).

Witheraw and Wickham (2003) reported 2 patients (4%) with delayed wound healing and 4 with wound infection. Delayed wound healing and infection are probably seen more in patients with renal failure. This may result in part from uremic immunosuppression.

Pyelonephritis in this series occurred in 2 patients (2.32%) and perinephric abscess occurred in 1 patient (1.16%). *Gupta et al. (1985)* reported 12 cases (24%) with positive urine culture postoperatively.

Mortality

The mortality rate in our series is (2.32%) which is not high if compared with other series dealing with corrective surgery in obstructive renal failure. *Singh et al. (1982) reported* (8%), *Gupta et al. (1985)* reported overall mortality rate of (17%), while *Witheraw and Wickham (2003)* reported (10.5%).

The urologist must have a high index of suspicion to detect septicemia in patients with obstructive renal failure because uremic patients usually do not have the classic signs of this condition *(Ansong and Smith, 2003).*

In this series septic shock occurred in 1 patient (1.16%) and myocardial infarction occurred in 1 patient (1.16%) after direct surgery in group B. While in group A, no mortality occurs.

This figure is lesser than the figure reported by *Stables (2001)* which was (1.9%) after replacement of percutaneous nephrostomy. However *Bedair (1983)* reported 4 cases (5%), a figure higher than ours because of the low incidence of infected obstructed systems in our series.

Conclusion

No significant difference was noticed between both types of intervention (direct or staged) as regarding renal improvement in patients with chronic obstructive renal failure under regular dialysis or not.

There was no correlation between the degree of improvement of renal function and the degree of renal failure according to preoperative creatinine clearance, preoperative urinary tract infection, methods of

intervention, age, sex, biochemical state of the patient, or to etiology of obstruction in patients with chronic obstructive renal failure under regular dialysis or not.

The degree of improvement of renal function found to be correlated to preoperative residual parenchymal thickness, parenchmal echogenicity, corticomedullary differentiation, and radioisotope GFR.

Finally there is evidence of reversibility of renal function after long standing obstruction which provides justification for efforts to identify and treat urinary tract obstruction even if a patient with an obstruction requires dialysis to avoid the dialysis or kidney transplantation or helping patients under dialysis for complete weaning form dialysis or decrease their number of weekly sessions, and in all cases the risk of the procedures should be weighed against the chances of improvement as renal dysfunction due to chronic obstructive uropathy is not always reversible.

Corresponding author
Tamer A. Ali
Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
Dr_tamer_ali@yahoo.com

References

1. **Ansong K And Smith AD:** Emergency Management Of Obstructive Uropathy Urol Clin North Am 2003; 10:161.
2. **Bedair AS:** Ultrasonically Guided Percutaneous Kidney Puncture In Diagnosis And Management Of Upper Urinary Tract Problems. MD Thesis (Urology) Faculty Of Medicine, Cairo University 1983.
3. **Cohen EP, Sobrero M, Roxe DM, *Et Al.*:** Reversibility Of Long Standing Urinary Tract Obstruction Requiring Long-Term Dialysis. Arch Intern Med., 1992; 152:177.
4. **Dooley JR And Mazze RI:** Oliguria. In: Orkin FK, Cooper NLH (Eds): Complications In Anesthesiology, (2nd Ed.) Edited By Nikolaus Gravenstein And Report R Kirby. Philadelphia, Lippincott-Raven Publishers 1996; Chapter 23: P 373.
5. **Gharbi BM, Ramdani B, Hachin K, *Et Al.*:** Acute Obstructive Renal Failure. Analysis Of 28 Cases. J Urol., 2001; 102:220 (Abstract).
6. **Goel Mc, Ahlawat R, Kumar M, *Et Al.*:** Chronic Renal Failure And Nephrolithiasis In A Solitary Kidney: Role Of Intervention. J Urol 2004; 57:1574.
7. **Gulmi FA, Matthews GJ, Marion D, *Et Al.*:** Volume Expansion Enhances The Recovery Of Renal Function And Prolongs The Diuresis And Natriuresis After Release Of Bilateral Ureteral Obstruction: A Possible Role For Atrial Natriuretic Peptide. J Urol 1995; 153:1276.
8. **Gupta NP, Koeliar GS, Wadhwa SN, *Et Al.*:** Management Of Patients With Renal And Ureteric Calculi Presenting With Chronic Renal Insufficiency. Br J Urol 1985; 97:130.
9. **Mathew TH:** Urinary Obstruction. Med Inter., 1996; 33:1351.
10. **Mokhmalji H, Braun PM, Martinez Portillo FJ, *Et Al.*:** Percutaneous Nephrostomy Versus Ureteral Stents For Diversion Of Hydronephrosis Caused By Stones: A Prospective, Randomized Clinical Trial. J Urol., 2001; 165:1088.
11. **Ramanathan R, Kumar A, Kapoor R, *Et Al.*:** Relief Of Urinary Tract Obstruction In Tuberculosis To Improve Renal Function: Analysis Of Predictive Factors. Br J Urol., 1998; 81:199.
12. **Singh SM, Yaday R, Gupta NP, *Et Al.*:** The Management Of Renal And Ureteric Calculi In Renal Failure. Br J Urol., 1982; 54:455.
13. **Stables DP:** Percutaneous Nephrostomy: Technique, Indications And Results. Urol Clin North Am 2001; 9:15.
14. **Vernon M, Pais JR, Jack WS, *Et Al.*:** Pathophysiology Of Urinary Tract Obstruction. In: Walsh PC, Retik AB, Vaughan ED, Wein AJ (Eds): Campblell's Urology, Vol 2, (9th Ed.) Philadelphia, W.B. Saunders 2007; P 993.
15. **Witheraw RO And Wickham JE:** Nephrolithotomy In chornic Renal Failure, Saved From Dialysis. Br J Urol., 2003; 52:419.

11/10/2012

The Role of the International Monetary Fund in the Global Financial System as an International Lender of Last Resort

Hossein Kazemi[1], Vahid Rafiei[2] (Corresponding author)

[1.] Assistant professor and faculty of Raja University, Qazvin, Iran
[2.] Master of Accounting Raja University, Qazvin, Iran/ PGD in International Accounting and Finance University of East London

Abstract: International monetary fund (IMF) manages and supervises the global financial system. Its purpose is to facilitate development and stabilize international exchange rates. The present study has been conducted to examine the role of the International monetary fund (IMF) in the global financial system as an International lender of last resort. In this, we have determined the importance of IMF as well as its current status, function and objectives were discussed.The analysis showed that IMF plays a vital role in the global financial assistance. It is called as the lender of the last resort so financial crisis.
[Hossein kazemi, Vahid rafiei. **The Role of the International Monetary Fund in Global Financial System as an International Lender of Last Resort**. *Life Sci J* 2012;9(4):2891-2894] (ISSN:1097-8135). http://www.lifesciencesite.com. 424

Key words: International Monetary Fund (IMF)

Introduction:

An international financial organization which manages and supervises the global financial system is known as The International Monetary Fund (IMF). IMF came into existence in 1944, during the United Nations Monetary and Financial Conference. In the United States IMF's head office is in Washington, D.C. (Teunissen and Akkerman, 2005, pp. 78 - 96).

The purpose of existence of IMF is to facilitate development and to stabilize international exchange rates. By keeping track of its member countries' macroeconomic policies, balance of payments and exchange rates, IMF administers global financial system. Currently IMF has 186 members. Other then North Korea, Monaco, Cuba, Taiwan, Tuvalu, Andorra, Nauru, and Liechtenstein all member of United Nations are direct participants in IMF. (Dreher, 2004, pp. 445 – 464).

Especially to poor and underdeveloped countries, IMF provides long-term high leveraged loans. The global influence of IMF is consistently increasing. In order to ensure that IMF's member counties' perspective financial requirements are fulfilled during the current global credit crunch, recently it was decided that additional financial resources would be provided to IMF. Therefore, International Monetary Fund plays a vital role of the in the Global Financial System and often works as an international lender of last resort. (Teunissen and Akkerman, 2005, pp. 78 – 96).

In this essay we will critically evaluate the role of International Monetary Fund in the global financial system as an international lender of the last resort. Moreover, we will determine the importance and significance of IMF as well as its current status, functions and objectives will be discussed.

The Role of the International Monetary Fund in the Global Financial System

IMF's Purpose of Existence and Functions

Great depression of 1930's cased an extraordinary fall down in the global financial activates. It is also considered as one of the reasons which triggered the disastrous World War II. In order to prevent such disaster from happening again, in 1944, world famous leaders met in Bretton Woods to develop financial and economic cooperation amongst counties. As a result of this conference IMF came into existence. IMF was based on macroeconomic, multilateral and global financial cooperation. (Barnett, Finnemore, 2004, pp. 134 – 170).

The prime purpose of its existence was to look after global financial system and to be a lender of the last resort. Therefore, it provides loans even in the global financial crisis and credit crunch situations. Besides providing loans and financial assistance IMF provides early warnings regarding potential finical crisis of a county as well as global ones. It helps countries in formulation of financial policy by giving expert advices according to each individual country's situation and socio-political-economic conditions. (McLeod, 1983, pp. 44 – 61)

One of the prime purposes of IMF is to provide timely loans to countries when their balance of payment is imbalanced due to trade deficits. To ensure that their loans are repaid to them by their creditors (countries obtaining loans) IMF intervene and give advices regarding country's financial and economic policies. Since IMF is created the rate of

international financial integration and globalization has increased and constantly increasing. (Calomiris, 1998, pp. 12 – 28).

At the time of creation there were only 45 members of IMF. They all had common goals toward reformation of international payment system, stabilization of exchange rates globally. The most importantly purpose of IMF creation was to stabilize economic system worldwide. The International Monetary Fund is a financial reserve or pool created as a result of investments or contributions made by all member counties. Member counties can borrow money from this pool when their balance of payment for a year does not balance. (Rapkin, and Jonathan R, 2005, pp. 26 - 39).

Presently 186 counties are present members of IMF striving towards achieving global financial stability, international trade enhancement, higher employment generation, poverty reduction, economic growth stability and international monetary cooperation. (Sakbani, 2005, pp. 11 – 25).

IMF as a Lender of the Last Resort

In a situation of financial crisis where availability of credit becomes extinct, financial institutions do not want to provide credit due to fair of creditor's bankruptcy. In such a situation, a financial institution which is willing to provide credit is called as lender of the last resort. As IMF was created with the intention of creating global financial cooperation and harmony therefore, it provides credit and long-term loans to needy countries even during global financial crisis and economic instable situations such as recession and depression. (Calomiris, 1998, pp. 12 – 28).

When most borrowers and lenders become insolvent as a result of fractional reserve banking panic withdrawal of deposited money in the bank can occur. In such a situation IMF prevent panic withdrawal from speeding and hence protect depositors from closing their accounts (Niskanen, 1998, pp. 6-7). So in this way IMF saves entire economy and prevents numerous businesses and financial institutions from collapsing. In severe financial crisis situation State Banks and other institutions can also borrow money from IMF. IMF is considered as a lender of the last resort because it also provides loans even when the borrowers' financial conditions are poor and there is a possibility of their collapse. (Dreher, 2004, pp. 445 - 464).

Importance and Significance of IMF

IMF consistently concentrates and works to improve its member countries' economies. IMF funds are used to providing financial assistance to countries facing severe financial crisis or whose balance of trade shows deficit. Moreover, when stoppage occurs in global market liquidity and capital inflows, IMF provide assistance so that economies can survive. When banking sector of a country reaches bankruptcy for instance due to recession or severe economic crisis then in such situations IMF provides support to the banking sector by supplying required financial support. (Arthur, Sheffrin, 2003, pp. 478 – 488).

Low-income countries especially under developed ones already facing problems due to food, energy and fuel price increase. It is causing decline in remittances, industrial activities and trade. Moreover, due to this social unrest and political instability will increase further. According to World Bank report, this year approximately fifty million further people will be poverty. Till 2015, three million children may further die if the required financial assistance is not provided to such poor countries. Therefore, to give financial assistance to low-income countries additional six billion dollars were announced to be provided by IMF. (Barnett, Finnemore, 2004, pp. 134 – 170).

IMF when provide loans and requisite financial assistance in return it levies certain reforms on the borrowing country. Those reforms are known as Washington Consensus. These reforms or conditions can result in strict price control, fixed exchange rate policies and under or over-valuation of currency. Therefore, financial crisis prevention is merely the intended objective of IMF rather than providing funds carelessly. So by levying conditions over borrowing country's monetary, fiscal, trade, exchange rate and tax collection policies IMF ensures the economic stability of the country as well as return over its investment. (Griffith-Jones, Bhattacharya, 2001, pp. 49 - 109).

Some times when a country consistently suffers trade deficit and financial instability it becomes difficult to repay the borrowed money in the allocated time duration, therefore in such situation IMF reschedule old loans and grant additional time to the country to repay the debt.

Current Status of IMF

IMF still working towards achieving global economic stability as it was working the time it was created. The increased number of IMF member has strengthened IMF and purpose of its existence. In 2008, the recession even affected the liquidity of IMF. Therefore, in order to meet credit shortfall, part of IMF's gold reserves were sold according to the agreed of International Monetary Fund's executive board. (Sakbani, 2005, pp. 11 – 25).

At G-20 London summit, in 2009, it was stated that to meet its member counties' prospective financial needs so that they can sustain current global

financial crunch, additional financial resources will be required by IMF. During the London summit, the G-20 leaders promised that IMF's supplementary cash will be increase to $500 billion. Moreover, they granted member countries special drawing rights, which allowed them to draw further $250 billion. (Griffith-Jones, Bhattacharya, 2001, pp. 49 - 109).

Critical Analysis of IMF and its Functions

Economists often make two criticisms on IMF aid. First of all along with financial support, IMF's conditionalities come also which includes Structural Adjustment Programs (SAP). Main objective of levying conditions is to ensure protection of investment by achieving target performance therefore conditionalities results in social unrest and instability. On the other hand, poverty further increases in the borrowing country due to the SAP. (Williamson, 1982, pp. 11 - 25).

IMF is a financial reserves fund in which world most rich and developed countries, people, institutions and organizations invest and earn return over their investment in the form of interest. Some people critics that rather than making suggestions and providing advices, IMF start instructing and dictating borrowing country's economic policies and financial matters to ensure safety of their investment. Moreover, they use their power and influence for gaining non-financial benefits. It is also said that the purpose of creation of IMF was to ensure solidarity and power of certain dominant countries by offering loans so that they can control and suppress needy countries economically and politically. (Dreher, Axel, 2004, pp. 53 - 75).

Although, it provide timely loans and financial stability but at the same time it exploits its creditor countries. IMF is not like a charitable trust, who just gives money without any interest. IMF is a specialized financial institution and even though it provides timely and flexible loans it does not mean that they are not interested in earning interest or non financial benefits. (Dreher, 2003, pp. 101 - 120).

IMF conditionality may result in rising direct and indirect taxes so that budget deficit can be balanced and government revenues can be generated. But when such condition is imposed in a country it further weakens its economy. So in this way rather than making economic conditions better it actually works other way around. As in the case of Pakistan, even though Pakistan was facing hyper inflation but still IMF's conditionality resulted in utility, electric and fuel prices increase. As a result prices of commodities further increased and industrial production declined. (DeRosa, 2001, pp. 17 – 28).

IMF conditionality has great impact on public health of borrowing country. According to a research made in 2008 by two analysts of Cambridge and Yale universities, thousands of deaths in Eastern Europe has caused due to tuberculosis as a result of strict conditions imposed by IMF on international loans borrowers (Chomsky, 2009). It was an indirect effect of IMF conditionality because fewer funds were allocated to public health care due to which tuberculosis cases increased which ultimately lead to thousands of deaths. The countries which have obtained loans from IMF, the deaths caused by tuberculosis have increased to 16.6%. (Teunissen and Akkerman, 2005, pp. 78 - 96).

Conclusion

After analyzing the whole essay it is clear that IMF plays a vital role in the global financial assistance. IMF is called as the lender of the last resort because it lends money to countries facing financial crisis in such a situation when there is no one to give them loans. By providing timely loans to countries facing financial crisis IMF saves them from destabilizing.

References

1. Teunissen, Jan Joost. and Akkerman, Age., (eds.) (2005). Helping the Poor? The IMF and Low-Income Countries. FONDAD. ISBN 90-74208-25-8. 78-96
2. Dreher, Axel (2004). "A Public Choice Perspective of IMF and World Bank Lending and Conditionality". Public Choice 119 (3–4): 445–464.
3. Dreher, Axel (2004). "The Influence of IMF Programs on the Re-election of Debtor Governments". Economics & Politics 16 (1): 53–75.
4. Dreher, Axel (2003). "The Influence of Elections on IMF Programme Interruptions". The Journal of Development Studies 39 (6): 101–120.
5. Rapkin, David P. and Jonathan R. Strand (2005) "Developing Country Representation and Governance of the International Monetary Fund," World Development 33, 12: 1993–2011, pp. 26 – 39
6. Williamson, John. (August 1982). The Lending Policies of the International Monetary Fund, Policy Analyses in International Economics 1, Washington D.C., Institute for International Economics. ISBN 0-88132-000-5, pp. 11-25
7. Griffith-Jones, Stephany., Bhattacharya, Amar., 2001 Developing Countries and the Global Financial System, Commonwealth Secretariat, ISBN-13: 978-0850926750, pp. 49 – 109

8. Niskanen, William A., "Reshaping the Global Financial Architecture: A Comment," Paper presented at Cato Institute's 16th Annual Monetary Conference cosponsored with the Economist, October 22, 1998, Washington, DC. See also Anna Schwartz, "Time to Terminate the ESF and the IMF," Foreign Policy Briefing, Cato Institute, August 26, 1998, pp. 6-7.
9. DeRosa, David. In Defense of Free Capital Markets: The Case against the New International Financial Architecture. Princeton, N.J.: Bloomberg, 2001, pp.
10. Calomiris, Charles W. ‘‘The IMF’s Imprudent Role as Lender of Last Resort.’’ Cato Journal 17, no. 3, page: 12 - 28 (Winter 1998)
11. McLeod, A.N., Reforming the International Monetary System, International Journal of Social Economics, MCB UP Ltd, 1983, Volume: 10, Issue: 2, Page: 44 - 61.
12. Sakbani, Michael., The global economic system: asymmetries and inconsistencies, journal: foresight, Emerald Group Publishing Limited, Year: 2005, Volume: 7, Issue: 1, Page: 11 - 25
13. Arthur, Sullivan., Sheffrin, Steven M., (2003). Economics: Principles in action. Upper Saddle River, New Jersey 07458: Pearson Prentice Hall. pp. 478-488. ISBN 0-13-063085-3. http://www.pearsonschool.com/index.cfm?locator=PSZ3R9&PMDbSiteId=2781&PMDbSolutionId=6724&PMDbCategoryId=&PMDbProgramId=12881&level=4.
14. Barnett, Michael; Finnemore, Martha (2004), Rules for the World: International Organisations in Global Politics, Ithaca: Cornell University Press, ISBN 9780801488238, 134 - 170
15. Chomsky, Noam. Interview with Amy Goodman. Noam Chomsky on the Global Economic Crisis, Healthcare, US Foreign Policy and Resistance to American Empire. Democracy Now!. New York. April 13, 2009.

9/29/2012

Receptor Activator of Nuclear Factor-Kappa B Ligand, Osteoprotegerin and Interleukin-17 Levels in GCF of Chronic, Aggressive Periodontitis and Type 2 Diabetes

Riham Omar Ibrahim

Department of Oral Medicine, Periodontology and Oral Diagnosis, Faculty of Oral and Dental Medicine, Cairo University, Cairo, Egypt
riham_omar2003@yahoo.com

Abstract: Background: The aim of this study is to compare the levels of osteoclastogenesis-related factors sRANKL and OPG and their ratios as well as the level of IL-17 in gingival crevicular fluid (GCF) from subjects with chronic periodontitis, generalized aggressive periodontitis and controlled type 2 DM patients with chronic periodontitis. Methods: GCF samples and clinical periodontal parameters were randomly obtained from sixteen patients with chronic periodontitis, 16 patients with aggressive periodontitis, 16 patients with controlled diabetes type II and 12 healthy controls. Concentrations of sRANKL, OPG, and IL-17 in GCF were analyzed by enzyme-linked immunosorbent assay (ELISA). Results: Higher concentration levels of sRANKL, OPG, RANKL/OPG ratios and IL-17 in the three diseased (experimental) periodontitis groups compared to the control group. Aggressive periodontitis group showed higher concentration level of GCF IL-17 in GCF significantly higher than both chronic periodontitis and diabetic groups. Significant There was positive correlation of sRANKL, IL-17, and sRANKL/OPG ratio in GCF with the clinical parameters ($P < 0.01$). Conclusion: GCF total amount of sRANKL, OPG were significantly increased in periodontal disease, supporting its role in the alveolar bone changes developed in this disease. Th17 responses may be characteristic of AgP, and IL-17 may play a role in the pathogenesis of aggressive periodontitis.

[Riham Omar Ibrahim **Receptor Activator of Nuclear Factor-Kappa B Ligand, Osteoprotegerin and Interleukin-17 Levels in GCF of Chronic, Aggressive Periodontitis and Type 2 Diabetes**] Life Science Journal 2012; 9(4):2895-2903]. (ISSN: 1097-8135). http://www.lifesciencesite.com.425

Key words: Periodontitis, Diabetes type 2, RANKL, OPG, IL-17, GCF, ELISA.

1. Introduction:

Chronic periodontitis (CP) and aggressive periodontitis (AgP) are bacteria-induced infections affecting the periodontium and resulting in the loss of tooth attachment and bone resorption. Aggressive periodontitis is characterized by a rapid and severe periodontal destruction in young systemically healthy subjects, and can be subdivided into localized and generalized forms according to the extension of the periodontal destruction.[1] Lipopolysaccharides and other virulence factors of periodontal pathogens have been shown to promote a host-mediated, tissue-destructive immune response. The nature of tissue destructin may be influenced by microbial, environmental, behavioral and genetic factors.[2] There is evidence that a local autoimmune reaction may participate in the onset and persistence of the aggressive periodontitis.[3] Systemic diseases that affect the host response, such as diabetes mellitus (DM) either type 1 or type 2 may potentiate the severity of periodontal disease and accelerate bone resorption.[4] Considerable evidence supports DM as a risk factor for periodontal diseases because the incidence, progression, and severity of periodontal diseases are higher in subjects with type 2 DM than in those without DM.[5]

The hallmark of periodontal diseases is bone resorption. This is mainly an action of the innate and adaptive immune mechanisms.[6] The mechanism of bone resorption and remodeling is coordinated by the interaction among the receptor activator of nuclear factor-kappa B (RANK), RANK ligand (RANKL), and its decoy soluble receptor osteoprotegerin (OPG). The expression of these receptors is regulated by several inflammatory mediators and bacterial products. RANK protein expression has been detected in normal dendritic cells, CD4 and CD8 T lymphocytes, osteoclast monocytic precursors, and endothelial cells. RANK remains expressed on osteoclast lineage cells throughout their life span.[7] RANKL is a homotrimeric transmembrane protein that is expressed as a membrane-bound and a secreted protein, which is derived from the membrane form as a result of either proteolytic cleavage or alternative splicing.[8] Many cell types express RANKL, including osteoblasts, periodontal ligament fibroblasts, gingival fibroblasts and endothelial cells. More than 50% of T cells and 90% of B cells express RANKL in periodontitis tissue, whereas less than 20% of either B cells or T cells showed RANKL expression in healthy gingival tissue.[9]

RANKL functions both as a membrane anchored molecule and as a soluble molecule, both forms bind to RANK. The binding of RANKL to RANK elicits osteoclastogenesis and promotes the activation and survival of osteoclast cells, which, in turn, results in bone resorption.[10]

Osteoprotegerin (OPG), also known as osteoclastogenesis inhibitory factor (OCIF), is a secreted TNF receptor member that is expressed ubiquitously by many types of cells and tissues. OPG is produced by osteoblasts,[11] endothelial cells and vascular smooth muscle cells.[12] OPG binds RANKL and thereby prevents activation of its single cognate RANK. Osteoclast activity is likely to depend, at least in part, on the relative balance of RANKL and OPG.[13] Serum OPG is significantly increased in both type 1 and type 2 diabetic patients.[14] There is growing evidence that Interleukin-17 (IL-17), produced by a subset of T-helper cells (Th17) play a role in inflammatory reaction, autoimmunity, and antimicrobial responses in a variety of infectious and inflammatory diseases at mucosal surfaces.[15] IL-17 has been found in patients with relatively severe periodontitis, where it could potentially contribute to bone destruction.[16] Also, IL-17 and RANKL were positively correlated to each other and to RAR-related orphan receptor gamma(RORγt) in inflamed tissue of periodontitis patients.[17]

There was a positive correlation between the level of gingival crevicular fluid RANKL/OPG ratio and clinical parameters; periodontal pocket depth and clinical attachment loss suggesting that elevated levels of local RANKL is responsible for periodontal bone resorption.[18]

Therefore, the aim of this study is to compare the levels of sRANKL and OPG and their ratios as well as the level of IL-17 in gingival crevicular fluid (GCF) from subjects with chronic periodontitis, generalized aggressive periodontitis and in type 2 DM patients with chronic periodontitis. Our hypothesis is that aggressive periodontitis may be associated with an autoimmune reaction and increased IL-17 expression. Also, RANKL/OPG ratio may be altered in diabetic individuals. It has been proposed that individuals with type 2 DM display certain features of inflammation and immunity that can alter the pathogenesis of periodontal diseases.

2. Materials and Methods:

Study Population:

Sixty subjects (age range: 26-70 years) were selected from those attending the outpatient clinic, Department of Oral Medicine, Periodontology and Oral Diagnosis, Faculty of Oral and Dental Medicine, Cairo University, Cairo, Egypt, between April 2011 and February 2012. It was a clinical randomized controlled study which included four groups: 16 patients with chronic periodontitis, 16 patients with aggressive periodontitis, 16 patients with controlled diabetes type 2 and 12 controls. Subjects were randomly assigned using a coin toss. The assignment of subjects to the groups was carried out by the clinic coordinator remote from the study. The randomization code was held centrally by the clinic coordinator and was not broken until completion of the data analysis. Detailed medical history of each subject was obtained according to the detailed questionnaire of the modified Cornell Medical Index.[19]

Inclusion Criteria:

Patients were diagnosed with moderate-to-advanced generalized chronic periodontitis, or generalized aggressive periodontitis based on the clinical and radiographic criteria proposed by the 1999 World Workshop for Classification of Periodontal Diseases and Conditions. [20] The criteria for entry were a minimum of 14 natural teeth, excluding third molars, with at least five to six teeth had sites with probing depth =6 mm and attachment loss =5 mm and radiographically determined bone loss.

Data concerning the duration and medication were obtained from diabetic patient's medical record. All subjects had presented with type 2 DM diagnosis for =5 years and under a controlled therapy.

A blood sample from each subject was taken to measure glycated hemoglobin (HbA1c). Blood samples were collected in a single laboratory and expressed as, a percentage with a normal healthy range of 4.5% to 8%. Therefore, subjects who had HbA1c values =8% were assigned to be well-controlled. Patients who presented HbA1c levels >8% were assigned to be poorly controlled and were excluded from the study.

Exclusion Criteria

Exclusion criteria were: pregnancy, lactation, current smoking or even within the last 5 years. All patients did not have any systemic illness that could affect the progression of periodontal disease and had not received any periodontal therapy and/or antibiotic, non-steroidal anti-inflammatory therapies during the previous 6 months prior to the study. Subjects with periapical pathology, orthodontic appliances, and multiple systemic complications of DM were also excluded from the study.

Twelve patients were selected from periodontally healthy volunteers who either patients were presenting for other dental treatment or University staff members. The study protocol was approved by the Ethic Committee of Faculty of Oral

and Dental Medicine. And it was explained to all participants, and informed consent forms were signed.

Clinical Monitoring

Clinical examination was performed by one calibrated examiner. For each patient, individual number of teeth presents and the clinical parameters were documented, excluding the third molar. The following periodontal parameters were evaluated on study sites: plaque index (PI),[21] gingival index (GI),[22] probing depth (PD), clinical attachment loss (CAL) using William's graduated periodontal probe to the nearest 0.5 mm.

Collection of Gingival Crevicular Fluid (GCF)

GCF was sampled one week after clinical examination so as not to alter its nature and to decide the most affected sites to collect GCF. After isolating the tooth with a cotton roll, supragingival plaque was removed with a curette without touching the gingival margin and dried gently with an air syringe. GCF was collected using standard filter paper strips (PerioPaper, Oraflow, Smithtown, NY) which were placed into the deepest sulci/pocket until mild resistance was felt and left in place for 30 seconds. Strips visually contaminated by blood were excluded. After GCF collection, the strips were immediately placed in Eppendorf vials containing 250 µl of phosphate buffered saline (PBS). The samples were left at 4◦C for 2 hrs and, then, they were frozen at −70◦C and stored until cytokine analysis by ELISA.

Quantification of Cytokine sRANKL, OPG and IL-17

Results were reported as concentrations of related factors in each GCF sample (as picograms per microliter) (pg/µl) per site in 30 seconds.

Aliquots of each GCF sample were assayed by ELISA to determine the level of sRANK-L, OPG, and IL-17 according to the manufacturer's recommendations. GCF was eluted from each filter paper strip into PBS as follows: each strip was lifted to the surface of the eluent, and another 350 µL of PBS was added to the strip (600 µL final volume). Samples were, refrigerated at 4◦C for another 20min and centrifuged at 10,000 rpm for 10 min. Finally, the strips were discarded. Commercial ELISA kits for sRANKL (Koma Biotech Inc., biotechnology) (Catalog No. K0331187) OPG and IL-17, (R and D systems, Quantikine, Minneapolis, MN, USA) (Catalog Number: DY805 for OPG and Catalog Number D1700 for IL-17) were used to analyze sRANKL, OPG, &IL-17. The kit employs a quantitative "sandwich" enzyme immunoassay technique. Briefly, antihuman monoclonal antibody specific for sRANKL, OPG, and IL-17 was precoated onto a 96-well microplate. Any sRANKL, OPG, and IL-17 present was bound by the immobilised antibody. After washing of unbound proteins, an enzyme-linked Horseradish Peroxidase (HRP) polyclonal antibody specific for sRANKL, OPG, and IL-17 was added to each microplate well and incubated. Then, a tetramethylbenzidine (TMB) substrate solution was added to each well. Any color developed was proportional to the amount of sRANKL, OPG, and IL-17 respectively. The enzyme-substrate reaction is terminated by the addition of a sulphuric acid solution. The intensity of the color (optical density) was measured by spectrophotometer at a wavelength of 450nm (wavelength correction set to 540 nm) within 30min. A standard curve was prepared against their optical density and the concentration sRANKL, OPG, and IL-17 were determined. Sites with sRANKL, OPG or IL-17 levels below the detection limit of assay were scored as negative. The minimum detectable dose limit of human RANKL is typically less than 66 pg/µl, anti-human OPG is 36 pg/µl and the minimum detectable doses for IL-17 were less than 15 pg/µl.

Statistical Analysis

Statistical analyses were performed using SPSS 20 (Statistical Package for Scientific Studies) software program. Data were first examined for normality by the Kolmogorov-Smirnov test, and data that did not achieve normality were analyzed using non-parametric methods.

The study unit for sRANKL, OPG and IL-17 levels was the site rather than the subject because periodontitis is a site-specific disease. The primary variables were differences in the levels of sRANKL, OPG and IL-17 and the RANKL/OPG ratio. The secondary variables were clinical parameters, and plasma levels of HbA1c. The percentage of sites with PI, GI, the mean PD, CAL, and the levels of HbA1c were computed for each subject. One way ANOVA was used to asses significant of age, CAL, and IL-17 between groups. When there were significant differences by the ANOVA test, a pairwise comparison was performed by the Tukey test. Kruskal-Wallis test used to assess significance of PI, GI, PD, sRANKL, OPG, and sRANKL/OPG ratio between groups. When there were significant differences by Kruskal-Wallis test, a pair wise comparison was performed by Mann-Whitney with Bonferroni correction. Chi square test was used to detect the difference in frequencies of gender between groups. The possible correlation between the levels of sRANKL, OPG, IL-17, and sRANKL/OPG ratio and clinical parameters of sampled sites and

HbA1c% were tested by the Spearman rank correlation. The significance level established for all analyses was 5%. Except for pair wise comparison was performed by Mann-Whitney p value was adjusted by Bonferroni correction to 0.008.

3. Results

There were no subject and site dropouts during the course of the study period. Thus, a total of 60 subjects completed the study and a total of 180 GCF samples were analyzed.

Table 1: Demographic characteristic and Clinical parameters of study population

Characteristics	Chronic (n=16)	Aggressive (n=16)	Diabetic patients (n=16)	Control (n=12)
Age(years)				
- Mean ±Sd	48.37 ±6.88	33.68 ± 4.6[a]	56.56 ±7.2	33.08 ±5.68[a]
- Range	38 to 60	26 to 42	45 to 70	26 to 42
Gender (n)				
- Male	7	6	7	5
- Female	9	10	9	7
Controlled treatment regimen (n)			16	
Clinical parameters per site in 4 groups and glycemic parameters (HbA1c value) in treated diabetic type II patients				
PI median (Iq range)	2(1)a	2 (1)a	1 (0)b	1(1)b
GI median (Iq range)	2 (0.75)ab	2 (0)a	1 (1)b	1 (0.75)
PD (mm) mean ±Sd	5.06 ±0.57	6.8 ±1.22	3.75 ±1	1.42 ±0.52
CAL (mm) mean±Sd	6.31 ±1.19	8.69 ±1.92	4.06 ±1.06	0.5 ±0.52
HbA1c % mean ±Sd			7.13 ± 0.62	

Similar superscript, lowercase letters indicate statistically non significant differences by analysis of variance and Tukey test (P <0.05) within each experimental group

There was no statistically significant differences between aggressive periodontitis and control groups as regards age and gender (P >0.05).

No statistically significant differences in plaque index between chronic and aggressive periodontitis, also, between controlled type II DM and controls. As regards the gingival index, statistically significant differences were recorded between aggressive periodontitis group and type II diabetic group and between control group and other groups (P <0.05). Pd and CAL showed significant difference between all studied groups.

sRANKL, OPG and IL-17 Levels:

The concentrations (picograms per microliter) (pg/µl) of sRANKL, OPG and IL-17 levels (mean ±Sd) in the GCF per site of the 4 groups are presented in Figures 1, 2 and 3 respectively.

There was statistically significant higher level of sRANKL, OPG and IL17 in the three diseased (experimental) groups compared to control group. Diabetic group showed higher concentration of sRANKL 525 ±49.67 than both CP 437.5 ±68.26[a] and AgP groups 380 ±83.7[a] with no statistically significant differences between the mean recorded of chronic and aggressive periodontitis groups (P >0.05). Diabetic group showed statistically significant higher level of sRANKL than non-diabetic groups (P <0.05).

In the mean time OPG level in the diabetic group 425.63 ±25.55[b] was statistically significant higher than in AgP group 328 ±38.96[a] (P <0.05).

The level of IL-17 was extremely low in the GCF of control group 35 ±18.83. Aggressive periodontitis group showed higher level of GCF IL-17 significantly higher 179.38 ±52.34 than that in both CP 114.38 ±58.65[a] and diabetic groups 128.75 ±44.1[a] (P <0.05) where there was no statistically significant difference between chronic periodontitis group and type II diabetic group (P >0.05).

Figure 4 presents the GCF sRANKL/OPG ratios in the 4 groups per site. There was no statistically significant difference in the mean sRANKL/OPG ratios between the three experimental groups (AgP 1.17±0.32[a], CP 1.18±0.26[a], and DM 1.24±0.16[a] (P >0.05), but was significantly higher than the control group 0.52± 0.11

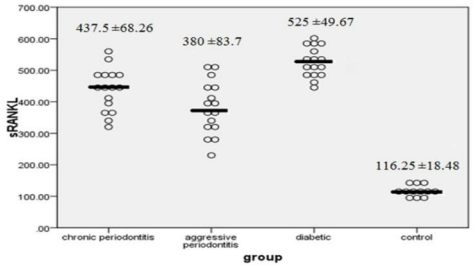


Figure 1: Distribution of concentration (pg/µl) of sRANKL in the GCF per site in the 4 groups

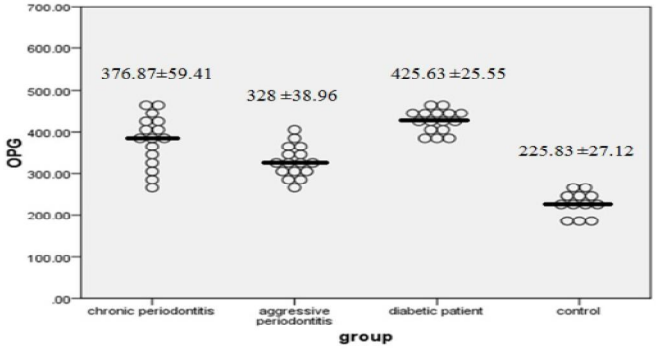


Figure 2: Distribution of concentration (pg/µl) of OPG in the GCF per site in the 4 groups

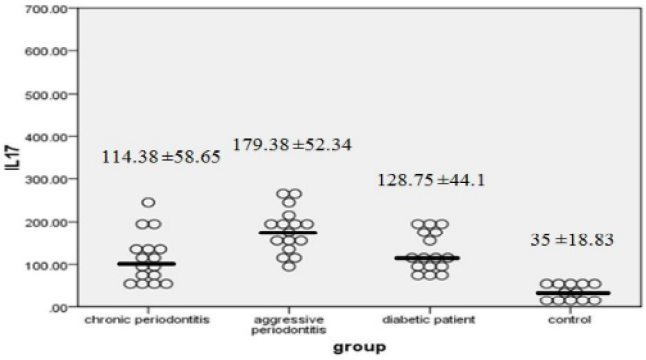


Figure 3: Distribution of concentration (pg/µl) of IL-17 in the GCF per site in the 4 groups

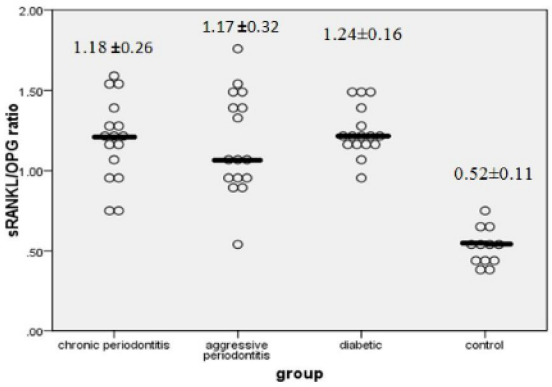


Figure 4: The ratios of RANKL/OPG in the 4 groups in GCF per site.

Correlations

Table 2 presents the correlation coefficients for total amounts and concentrations of osteoclastogenesis-related factors and clinical parameters of the sampled sites and HbA1c. The present study demonstrates significant positive correlation of sRANKL, IL-17, and sRANKL/OPG ratio in GCF with PI, GI, PD, and CAL (P <0.01).

Table 2: Correlation coefficients for the osteoclastogenesis-related factors and the clinical parameters per site and HbA1c levels

Clinical and glycemic parameter	Concentration			Ratio **sRANKL/OPG**
	sRANKL	**OPG**	**IL-17**	
PI	0.321*	0.15	0.343*	0.479*
GI	0.375*	0.192	0.373*	0.515*
PD	0.285*	0.182	0.672*	0.506*
CAL	0.286*	0.191	0.602*	0.499*
HbA1c	0.709*	-0.232	-0.18	0.609*

Significant at P <0.05 by the Spearman rank correlation test- * Significant

4. Discussion

This study compared the levels of bone-related factors (sRANKL and OPG) and cytokine (IL-17) in the gingival crevicular fluid (GCF) of systemically healthy, chronic periodontitis, aggressive periodontitis and controlled Type 2 DM patients with chronic periodontitis. We hypothesized that these three groups could exhibit different dysregulations of bone-related factors and proinflammatory cytokine profile which could affect their susceptibility to periodontal breakdown. It is important to understand the immunoinflamatory mechanisms that determine the higher susceptibility to periodontitis in patients with diabetes, compared to individuals without diabetes, as only minor periodontal microbiologic differences have been found between patients with and without diabetes.[23]

The results of the present study showed that the concentrations of sRANKL, OPG were elevated in the GCF of CP, AgP and were significantly higher in periodontitis lesions of type II diabetic patients in comparison to non diabetic groups.

These results run parallel to that reported by Ribeiro *et al.,* 2011[24] who found that Type 2 diabetes mellitus, as a whole, upregulates the levels of OPG, sRANKL and IL-17 in sites with CP. It was thought that controlling the glycemic level in type II DM patients modulate the levels of biomarkers sRANKL, OPG.[25] They found that total amounts and concentrations of sRANKL and RANKL/OPG ratios were higher in GCF of poorly controlled subjects than in well-controlled subjects. The interaction between AGE and its receptor (RAGE), which is present in different types of cells, enhances the expression of proinflammatory cytokines including interleukin (IL)-1 and -17 and tumor necrosis factor-alpha.[26]

Earlier studies reported that OPG protein was significantly lower (P < 0.05) in the periodontitis tissues [27] and in GCF of patients with periodontitis.[28] In the present study OPG concentration was elevated in all periodontitis groups. This is in accordance with the findings that found that OPG expression from gingival tissue was higher in chronic periodontitis than in healthy patients.[29] This could be explained by the observation that human periodontal ligament cells stimulated with lipopolysaccharide could inhibit osteoclastogenesis by producing higher levels of OPG than RANKL via the induction of IL-1β and TNF-α.[30] Porphyromonas gingivalis upregulated the expression of OPG by human gingival fibroblasts and in human microvascular endothelial cells via a nuclear factor-Kappa B dependent pathway; thus these cells may act as a source of OPG and thereby may play a role in regulating bone metabolism in periodontitis.[31,32] So, the regulation of the balance between bone breakdown and reformation is modulated, to a large extent, by the secreted soluble receptor OPG.

In the present study there was no statistically significant difference in sRANKL/OPG ratio among the three studied groups but were significantly higher than the control group (P<0.01) (Fig.4). Periodontal ligament fibroblasts are a source of RANKL, but concurrently produce OPG, in response to IL-1 stimulation. Periodontal ligament fibroblasts and osteoblasts express RANKL and OPG mRNA via PKA and PKC signalling, respectively.[33] Furthermore, there was increased in OPG production by human gingival fibroblasts when stimulated by lipopolysaccharide (LPS) from Aggregatibacter actinomycetemcomitans and Porphyromonas gingivalis.[32]

In this study, IL-17 was present at significantly higher concentrations in GCF from those with GAgP (179± 52.34pg/μL) than CP and diabetic patients with CP. The presence of IL-17 has been documented in sera of GAgP patients in significantly higher level than CP patients and healthy controls.[34] This may be explained in part by the autoimmune reaction in AgP.

High levels of autoantibodies directed to extracellular matrix components (type I collagen, fibronectin and laminin) were detected in the sera of AgP patients.[3] Autoantibody binding to native and ROS -modified type I and type III collagens and citrullinated peptides CCP) were observed exclusively in the sera of patients with AgP and not in those with chronic periodontitis or gingivitis.[35] Citrulline is a non-standard amino acid generated by post-translational modification of arginine residues by peptidylarginine deiminase (PAD). P. gingivalis, one of putative pathogens in AgP is the only bacterium known to express a PAD enzyme.[36]

Although the role of IL-17 in the pathogenesis of periodontal disease is poorly understood, the presence of IL-17 has been documented in GCF of periodontitis patients [37] and in periodontal tissues biopsied during periodontal surgery.[10] Elevated levels of IL-17 and bone resorptive factors RANKL, IL-1β, and IL-6 (messenger RNA and protein) as well as the presence of Th17 cells has been found in periodontal tissues from patients with periodontitis.[17,38] This suggests that IL-17 may be the link between the adaptive immune system and the innate immune system to amplify inflammation and mobilize neutrophils.

Other studies suggested dual role of IL 17, thus, in a sterile inflammatory state such as rheumatoid arthritis or other autoimmune diseases, IL-17 signalling contributes to tissue damage, whereas in bacterial infections such as periodontal diseases, IL-17 may be critical for recruiting neutrophils and/or other immune cells required to limit the spread of infection. However, IL-17RA exerts a profound bone-protective effect on PD bone loss.[39,40]

On the contrary of these results, two investigators failed to detect IL-17 in GCF samples from Japanese patients with periodontitis and from Indian patients.[41,42]

Our results showed significant positive correlations between sRANKL, IL-17, and sRANKL/OPG ratio and PI, GI, PD, and CAL (P <0.01). This result is in accordance with Bostanci *et al.,* [18] who reported a positive correlation between the GCF RANKL/OPG ratio and PD in patients with periodontitis. Other two investigators failed to report significant correlations between GCF RANKL and/or OPG concentrations and clinical measurements of disease severity in terms of PD, CAL, and inflammation with regard to bleeding on probing in patients with chronic periodontitis.[28,43]

Conclusions

High levels of bone-related factors sRANKL and OPG and cytokine IL-17 were observed in the GCF of patients with CP, GAgP and in type 2diabetic patients with CP. Patients with type 2 DM display certain features of inflammation and immune reaction that can alter the pathogenesis of periodontal diseases.

The author reports no conflicts of interest related to the study.

Corresponding author
Riham Omar Ibrahim
Department of Oral Medicine, Periodontology and Oral Diagnosis, Faculty of Oral and Dental Medicine, Cairo University, Cairo, Egypt
riham_omar2003@yahoo.com

References:

1. Genco RJ. Host responses in periodontal diseases: current concepts. *J Periodontol,* 1992; 63:338-55.
2. Schenkein, H. & Van-Dyke, T. Early onset periodontitis. Systemic aspects of etiology and pathogenesis. *Periodontology 2000,* 1994;6:7–25.
3. De-Gennaro L., Lopes J. and Mariano M. Autoantibodies Directed to Extracellular Matrix Components in Patients With Different Clinical Forms of Periodontitis. *Journal of Periodontology,* 2006;77: 2025-2030.
4. Kaur, G., Holtfreter, B., Rathmann, W. G., Schwahn, C.,Wallaschofski, H., Schipf, S., Nauck, M. and Kocher, T. Association between type 1 and type 2 diabetes with periodontal disease and tooth loss. *J. Clin. Periodontol.* 2009;36:765–774
5. Novak MJ, Potter RM, Blodgett J, Ebersole JL. Periodontal disease in Hispanic Americans with type 2 diabetes. *J Periodontol* 2008;79:629-636.
6. Berglundh, T. and Donati, M. Aspects of adaptive host response in periodontitis. *J. Clin. Periodontol.* 2005;32 (Suppl. 6): 87–107.
7. Wong BR, Josien R, Choi Y. TRANCE is a TNF family member that regulates dendritic cell and osteoclast function. *J Leukoc Biol,* 1999;65:715–724.
8. Ikeda T, Kasai M, Utsuyama M, Hirokawa K. Determination of three isoforms of the receptor activator of nuclear factor- [kappa]B ligand and their differential expression in bone and thymus. *Endocrinology* 2001;142:1419-1426.
9. Kawai T, Matsuyama T, Hosokawa Y, Makihira S, Seki M, Karimbux NY, *et al.* B and T lymphocytes are the primary sources of RANKL in the bone resorptive lesion of

periodontal disease. *Am J Pathol* 2006; 169: 987-998.
10. Nakashima T, Kobayashi Y, Yamasaki S, Kawakami A, Eguchi K, Sasaki H, Sakai H. Protein expression and functional diff- erence of membrane-bound and soluble receptor activator of NF-kappaB ligand: modulation of the expression by osteotropic factors and cytokines. *Biochem Biophys Res Commun* 2000; 275:768-775.
11. Udagawa N, Takahashi N, Yasuda H, Mizuno A, Itoh K, Ueno Y, Shinki T, Gillespie MT, Martin TJ, Higashio K, Suda T. Osteoprotegerin produced by osteoblasts is an important regulator in osteoclast development and function. *Endocrinology* 2000; 141:3478–3484.
12. Collin-Osdoby P, Rothe L, Anderson F, Nelson M, Maloney W, Osdoby P. Receptor activator of NF-B and osteoprotegerin expression by human microvascular endothelial cells, regulation by inflammatory cytokines, and role in human osteoclastogenesis. *J Biol Chem* 2001; 276:20659–20672.
13. Romas E, Sims NA, Hards DK, Lindsay M, Quinn JWM, Ryan PFJ, Dunstan CR, Martin TJ, Gillespie MT: Osteoprotegerin reduces osteoclast numbers and prevents bone erosion in collageninduced arthritis. *Am J Pathol* 2002;161:1419-1427.
14. Knudsen ST, Foss CH, Poulsen PL, Andersen NH, Mogensen CE Rasmussen LM: Increased plasma concentrations of osteoprotegerin in type 2 diabetic patients with microvascular complications. *Eur J Endocrinol* 2003; 149:39–42.
15. Khader SA, Gaffen SL and Kolls JK. Th17 cells at the crossroads of innate and adaptive immunity against infectious diseases at the mucosa. *Mucosal Immunology* 2009; 5:405-411.
16. Johnson RB, Wood N, Serio FG: Interleukin-11 and IL-17 and the pathogenesis of periodontal disease. *J Periodontol* 2004;75:37-43.
17. Dutzan, N., J. Gamonal, *et al.* Over-expression of forkhead box P3 and its association with receptor activator of nuclear factor-kappa B ligand, interleukin (IL) -17, IL-10 and transforming growth factor-beta during the progression of chronic periodontitis. *J Clin Periodontol* 2009; 36:396-403.
18. Bostanci N, Ilgenli T, Emingil G, Afacan B, Han B, TÖz H, *et al.* Gingival crevicular fluid levels of RANKL and OPG in periodontol diseases : implications of their relative ratio. *J Clin periodontal* 2007; 34: 370-376.
19. Abramson JH. The Cornell Medical Index as an epidemiological tool. *Am J Public Health Nations Health* 1966;56:287-298.
20. Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999; 4:1-6.
21. Silness J and Löe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontol Scand* 1964;22:121-135.
22. Löe H. The gingival index, and the retention index system. *J periodontal* 1967;38:610-616.
23. Hintao J, Teanpaisan R, Chongsuvivatwong V, Ratarasan C, Dahlen G. The microbiological profiles of saliva, supragingival and subgingival plaque and dental caries in adults with and without type 2 diabetes mellitus. *Oral Microbiol Immunol* 2007;22:175-181.
24. Ribeiro F, de Mendoncxa A, Santos V, Bastos M, Figueiredo L, and Duarte P. Cytokines and Bone-Related Factors in Systemically Healthy Patients With Chronic Periodontitis and Patients With Type 2 Diabetes and Chronic Periodontitis. *J Periodontol* 2011;82:1187-1196.
25. Santos VR, Ribeiro FV, Lima JA, Napimoga MH, Bastos MF, Duarte PM. Cytokine levels in sites of chronic periodontitis of poorly controlled and well-controlled type 2 diabetic patients. *J Clin Periodontol* 2010;37:1049-1058.
26. Lalla E, Lamster IB, Drury S, Fu C, Schmidt AM. Hyperglycemia, glycoxidation and receptor for advanced glycation endproducts: Potential mechanisms underlying diabetic complications, including diabetes associated periodontitis. *Periodontol 2000* 2000;23:50-62.
27. Crotti T, Smith MD, Hirsch R, Soukoulis S, Weedon H, Capone M, Ahern MJ, Haynes D. Receptor activator NF KB ligand (RANKL) and osteoprotegerin (OPG) protein expression in periodontitis. *J Periodont Res.* 2003;38:380–387.
28. Mogi M, Otogoto J, Ota N, Togari A. Differential expression of RANKL and osteoprotegerin in gingival crevicular fluid of patient with periodontitis. *J Dent Res.* 2004;83:166–169.
29. Garlet GP, Martins W Jr, Fonseca BA, Ferreira BR, Silva JS. Matrix metalloproteinases, their physiological inhibitors and osteoclast factors are differentially regulated by the cytokine

profile in human periodontal disease. *J Clin Periodontol* 2004; 31:671–679.
30. Wada N, Maeda H, Yoshimine Y, Akamine A. Lipopolysaccharide stimulates expression of osteoprotegerin and receptor activator of NF-Kβ ligand in periodontal ligament fibroblasts through the induction of interleukin-1β and tumor necrosis factor-α. *Bone* 2004;35:629–635.
31. Kobayashi-Sakamoto M, Hirose K, Isogai E, Chiba I. NF-Kβ-dependent induction of osteoprotegerin by Porphyromonas gingivalis in endothelial cells. *Biochem Biophys Res Commun* 2004; 315:107–112.
32. Kiji M, Nagasawa T, Hormdee D, *et al.* Internal prostaglandin synthesis augments osteoprotegerin production in human gingival fibroblasts stimulated by lipopolysaccharide. *Clin Exp Immunol* 2007; 149:327–334.
33. Kanzaki H, Chiba M, Shimizu Y, Mitani H. Dual regulation of osteoclast differentiation by periodontal ligament cells through RANKL stimulation and OPG inhibition. *J Dent Res* 2001; 80: 887–91.
34. Schenkein H.A., Koertge T.E, Brooks C.N, Sabatini R., Purkall, D.E and Tew J.G. IL-17 in Sera from Patients with Aggressive Periodontitis; *J Dent Res* 2010; 89: 943-947.
35. Hendler A., Mulli T.K., Hughes F.J., Perrett D., Bombardieri M., Houri-Haddad Y., Weiss E.I., and Nissim A. Involvement of Autoimmunity in the Pathogenesis of Aggressive Periodontitis. *J Dent Res* 2010; 89:1389-1394.
36. Hendler A, Mulli TK,Hughes FJ, Perrett D,Bomardieri M,Houri-Haddad Y,Weiss EI and Nissim A. Involvement of Autoimmunity in the Pathogenesis of Aggressive Periodontitis. *J Dent Res* 2010; 89:1389-1394.
37. Vernal R, Dutzan N, Chaparro A, Puente J, Valenzuela MA, Gamonal J. Levels of interleukin-17 in gingival crevicular fluid and in supernatants of cellular cultures of gingival tissue from patients with chronic periodontitis. *J Clin Periodontol* 2005; 32:383-389.
38. Cardoso CR, Garlet GP, Crippa GE, Rosa AL, Ju´nior WM, Rossi MA, Silva JS. Evidenceof the presence of T helper type 17 cells in chronic lesions of human periodontal disease. *Oral Microbiol Immunol* 2009: 24: 1–6.
39. O'Shea J, Ma A, Lipsky P. Cytokines and autoimmunity. *Nat Rev Immunol.* 2002;2:37-45
40. Linden A, Laan M, Anderson G. Neutrophils, interleukin-17A and lung disease. *Eur Respir J.* 2005;25:159-172.
41. Takahashi K, Azuma T, Motohira H, Kinane DF, Kitetsu S. The potential role of interleukin-17 in the immunopathology of periodontal disease. *J Clin Periodontol* 2005;32:369-374.
42. Pradeep A.R., Hadge P., Chowdhry S., Patel S.and HappyD; Exploring the role of Th1 cytokines: interleukin-17 and interleukin-18 in periodontal health and disease; *Journal of Oral Science* 2009;51: 261-266.
43. Lu HK, Chen YL, Chang HC, Li CL, Kuo MY. Identification of the osteoprotegerin/receptor activator of nuclear factor-kappa B ligand system in gingival crevicular fluid and tissue of patients with chronic periodontitis. *J Periodontal Res* 2006;41:354-360.

11/10/2012

Investigation of Wire Electro Discharge Machining of Nickel-Titanium Shape Memory Alloys on Surface Roughness and MRR

Saeed Daneshmand[1], Reza Hessami[2], Habib Esfandiar[3]

[1.] Department of Mechanical Engineering, Majlesi Branch, Islamic Azad University, Isfahan, Iran
[2.] Department of Mechanical Engineering, Roudbar Branch, Islamic Azad University, Roudbar, Iran
[3.] Department of Mechanical Engineering, Firuzkooh Branch, Islamic Azad University, Firuzkooh, Iran
s.daneshmand@iaumajlesi.ac.ir

Abstract: Shape memory alloys are kind of smart materials, which have distinctive properties and are superior in compare with other alloys. Severe reactions to thermodynamic and mechanical parameters and ability to return to their original shape make these alloys distinctive from other alloy regarding machining ability. Since these alloys have a very useful application in various fields such as aerospace, automobile, medicine, dentistry, the present paper surveys the effect of wire electrical discharge machining on them. Surface roughness and material removal rate are the most important parameters of machining which influence product quality and machining time. Reducing surface roughness improves fatigue resistance, corrosion and wear resistance of work piece. Increasing the removal rate and reducing machining time decline the production costs and increase production. The present research seeks to investigate the effect of wire electrical discharge machining parameters on surface roughness and removal rate of NiTi60. Results reveal that increasing current pulse, pulse on-time and wire speed increase surface roughness and material removal rate.

[Daneshmand S, Hessami R, Esfandiar H. **Investigation of Wire Electro Discharge Machining of Nickel-Titanium Shape Memory Alloys on Surface Roughness and MRR**. *Life Sci J* 2012; 9(4):2904-2909] (ISSN: 1097-8135). http://www.lifesciencesite.com. 426

Keywords: Wire electrical discharge machining; material removal rate; surface roughness; NiTi60; smart materials.

1. Introduction

The cost reduction, increasing production rate, low surface roughness and high dimensional accuracy are the most important objectives in machining processes. These objectives enjoy a high importance for expensive materials with low machining ability. New developments in the field of material science have led to new engineering metallic materials, composite materials, high tech ceramics and shape memory alloys, having good mechanical properties and thermal characteristics as well as sufficient electrical conductivity so that they can readily be machined by spark erosion. Traditional machining technique is often based on the material removal using tool material harder than the work material and they are unable to machine economically. At the present time, electrical discharge machining (EDM) is a widespread technique using in industry for high precision machining of all types of conductive materials such as: metallic alloys, metals, graphite, or even some ceramic materials of whatsoever hardness. EDM technology has been increasingly used in tool, die and mould making industries, for machining of heat treated tool steels and advanced materials requiring high precision, complex shapes and high surface finish [1, 2]. Development of new advanced engineering materials and need for precise and flexible prototypes and low-volume component production have made wire electrical discharge machining (WEDM) an important manufacturing process to meet such a demand [3]. The three electrical discharge-machining methods, wire, ram, and small whole EDM all work on the principle of spark erosion [4]. As its name represents, material is eroded from the work piece by electrical discharges that create sparks. Ram EDM, also known as conventional EDM, sinker EDM, die sinker, vertical EDM, and plunge EDM are generally used to produce blind cavities. In ram, EDM sparks jump from the electrode to the workpiece. This causes material to be removed from the work piece. Wire EDM uses a traveling wire electrode that passes through the work piece. The wire is monitored precisely by a computer-numerically controlled (CNC) system Figure 1 [5]. The spark theory on a wire EDM is basically the same as that of the vertical EDM process. In wire EDM, the conductive materials are machined with a series of electrical discharges (sparks) that are produced between an accurately positioned moving wire (the electrode) and the work piece. High frequency pulses of alternating or direct current is discharged from the wire to the work piece with a very small spark gap through an insulated dielectric fluid (water). Many sparks can be observed at one time. The volume of metal removed during this short period of spark discharge depends on the desired cutting speed and the surface finish required

[6, 7]. Between the wire and the work piece is a shield of demonized water called dielectric. Pure water is an insulator, but tap water usually contains minerals that cause the water to be too conductive for wire EDM. To control the water conductivity, the water goes through a resin tank to remove much of its conductive elements. This water is called demonized water. The work piece and the wire represent positive and negative terminals in a DC electrical circuit, and are always separated by a controlled gap, constantly maintained by the machine. This gap must always be filled with a dielectric fluid, in this case demonized water, which acts as an insulator and cooling agent. When sufficient voltage is applied, the fluid ionizes. Then a controlled spark precisely erodes a small section of the work piece, causing it to be melted and vaporized. These electrical pulses are repeated thousands of times per second [5]. Shape memory alloys (SMAs) exhibit unique thermal and mechanical properties that have been extensively studied for over fifty years. While they have been well studied, a push for industrial and commercial applications has only begun to grow in the last 15 to 20 years. The ability of SMAs to recover large strains under thermal and mechanical loading has led to the development of many applications in the biomedical, oil, and aerospace industries [8, 9, 10, 11]. The aerospace industry, on the other hand, has taken a closer look to use SMAs for thermally activated actuator applications [12]. Shape memory alloys have wide range of usage such as free recovery, constrained recovery, actuation recovery and super elastic recovery [13]. Characteristic for shape memory materials is an unconventional, unique correlation of strain, stress and temperature, which is based on crystallographic reversible thermo elastic martenstic transformation. The low temperature and the high temperature phases are, analogous to steel technology named martensite and austenite. The transformation start and finish temperatures are A_S (austenite start) and A_f (austenite finish), and M_S (martensite start) and M_f (martensite finish) during heating and cooling, respectively. The temperature-triggered transformation can be accompanied by unusually large strain; if external forces constrain the deformation, the stress can strongly increase (capability to perform mechanical work). At temperatures above A_f but below Md (the highest possible temperature for the formation of stress-induced martensite), the reversible martensitic transformation can be triggered by an increase of stress level. In this case, an unusual large strain accompanied by very small additional stress increase is possible (pseudo elasticity). When unloaded, transformation and shape change in the reverse direction and order take place. Above M_d, plastic transformation would occur before the onset of the martensitic transformation. When martensite is deformed and heated to the austenitic state, the material returns to the shape it had before the pseudoplastic deformation [14]. The pseudoplastic deformation is characterized not by gliding and generation of dislocations but by movement of twin boundaries thereby reducing the number of different martensitic variants. Upon subsequent cooling, the shape remains unchanged. This phenomenon is known as one-way shape memory effect since there is a shape change during heating only and not during cooling. It is a natural crystallographic property of shape memory materials (Fig. 2). Strain values up to 8% can be recovered in polycrystalline NiTi alloys. The most well known shape memory alloy is NiTi with about equiatomic composition. The transformation temperatures decrease strongly with increasing Ni content. The high-temperature phase (austenite) has an ordered BCC structure; the low-temperature phase (martensite) has an ordered monoclinic structure [15].

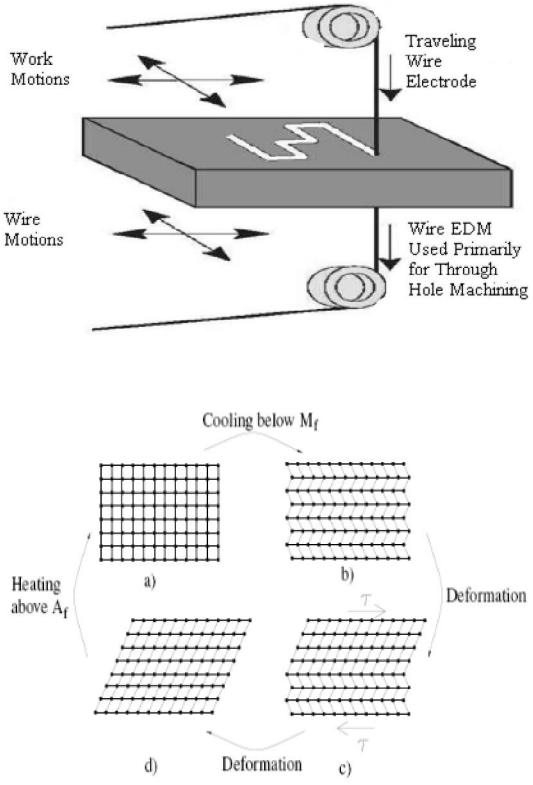


Figure 2. Different phases of a shape memory alloy [12]

Numerous studies have been made for improving machining ability of these materials. Gokler and Ozanozgu conducted some research about three types of steel to improve the surface roughness

[16]. Their research showed that increase of work piece thickness causes more stability and less surface roughness. Kanlayasiri and Boonmung surveyed the effect of pulse on time, pulse off time, pulse current and tension wires on roughness of surface of steel DC53. They concluded that the pulse on time and current are variables, which influence surface quality [17]. Han and Jiang examined the effect of discharge current on surface roughness of steel Cr12 [18]. They conducted the research using different discharge currents and pulse times. Effect of machining parameters such as current, wire speed, pulse on time on surface roughness and effect of current and pulse on time on MRR for NiTi60 alloy has been investigated in their research.

2. Experiments

2.1 Materials

Due to different melting point, evaporation and thermal conductivity, different materials show different surface quality and MRR at the same conditions of machining. NiTi60 is the material, which has been used in the experiments. NiTi considers as a smart materials. The main features of this material are high corrosion resistance, high electrical resistance, good mechanical properties, fatigue resistance, detection and environmental changes [19]. One of the best options to choose NiTi60 for machining is WEDM as it is heat process and toughness of materials doesn't affect it. The work piece dimensions are 47.3 ×30 × 13.3 mm, which was cut in dimensions of 3 × 13.3 ×47.3 mm for different experiments conditions. The mechanical properties of this alloy are shown in table 1.

Table 1. Mechanical and physical properties of Nitinol-60

Density	6.45 G/cc
Tensile strength, ultimate	754 - 960 Mpa
Tensile strength, yield	560 Mpa
Elongation at break	15.5 %
Modulus of elasticity	75.0 Gpa
Poissons ratio	0.300
Shear modulus	28.8 Gpa
Specific heat capacity	0.320 J/g-°c
Thermal conductivity	10.0 W/m-k
Melting point	1240 - 1310 °C

2.2 Test equipment

WEDM, model ONA, series PRLMAS250 was used for experiments. Regarding fixed dimensions of workpiece, machining velocity obtains by measuring machining time through stopwatch and dividing length of workpiece by cutting time. To measure the surface roughness Perthometer M1 made by Mahr Company has been used. Surface roughness has been measured at the longitudinal direction of cutting and perpendicular on it and the average is considered as the surface roughness. To measure machining volume, AND scales, model GR300 with 0.0001 accuracy has been used.

3. Design of experiments (DOE)

Among effective factors in a test, some of them are very important and others are less effective. By using design of experiments, we can obtain some information about factors which effects majorly on responses and select those parameters which need further studies among the large number of them. Manageable input parameters can be changed systematically and their effect on the output parameters can be discussed and evaluated. Taguchi method has been used in the present study as one of the strongest methods of designing and analyzing experiments. WEDM has different input parameters. Variables during the test are pulse current, wire speed and pulse on time [20, 21]. Wires diameter, tension, and other parameters are considered constant. Table 2 shows the test variable parameters. Minimum and maximum amount of discharge current are 1A and 2.5A respectively. Rupture occurs when Amps increase more than 2.5A for 47.3mm of cut length. Pulses on time were chosen 2, 4 and 6 µs. At higher pulse on time, flashing decreases and surface quality and material removal rate are affected. Wire speeds were chosen 0.8, 0.5 and 1.5 mm/s. If wire speed increases more than 1.5 mm/s, the wire will rupture. Material removal rate can be achieved by using weight difference of workpiece before and after machining. Material removal rate is obtained by equation (1) based on gr/min. In this equation, MRR is Material Removal Rate based on gr/min and W_1 and W_2, are weights of workpiece before and after machining.

$$\text{Material Removal Rate (MRR)} = \frac{W_1 - W_2}{T} \quad (1)$$

W_1= initial weight of the workpiece (gr)
W_2= final weight of the workpiece (gr)

Table 2. The operational parameters of WEDM

Wire electrode	Brass		
Current (A)	1	2	-
Pulse on time (µs)	2	4	6
Wire speed (mm/min)	0.5	1	1.5
Flushing pressure (kg/cm^2)		5	
Dielectric	De-ionized water		

4. Evaluation of wire speed, current and pulse on time on surface roughness

Figures 3 and 4 show the effects of input parameters of WEDM including wire speed pulse current and pulse on time on surface roughness (Ra). Figure 3 show that increasing wire speed and discharge current grow surface roughness. Effect of pulse on time on surface roughness has been shown

in figure 4. By increasing discharge current and pulse on time, spark energy, which follows equation 2, is increased and volume of craters on the surface of the workpiece is increased too. Also, surface temperature of workpiece is risen; therefore, larger holes from evaporation and melting are created. Increase of off time decreases surface roughness. Growth of off time reduces the surface temperature by increasing gap flashing. There has been a growth in sparks caused by increasing of off time hence machining velocity is decreased.

$$\Delta E = V_D \times K \times T_{on}^2 \qquad (2)$$

ΔE= Spark energy
T_{on}= Pulse on time
V_D = Gap voltage
K= Current slope increasing

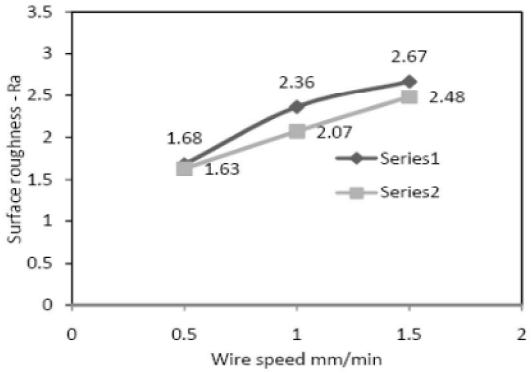


Figure 3. Surface roughness at various wire speed

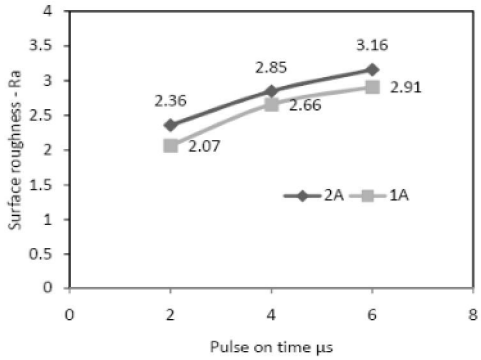


Figure 4. Surface roughness at various pulse on time

5. Evaluation of discharge current and pulse on time on MRR

Figure 5 shows the effect of pulse on time and pulse current on MRR of NiTi alloy by WEDM method. With increasing current and pulse on time in a constant feed of wire, material removal rate increases. When pulse current increases, the spark energy and surface energy increase and melting and MRR increase rapidly at the same time. When pulse current and pulse on time increase, the number of positive ions attacks on workpiece's surface increase too; moreover workpiece's temperature and melting and consequently MRR increase. Pulse current increasing is allowed to a special range, as the wire increasing is being higher than that range subsequently lead to wire tearing. Pulse current can be increase by changing some parameters such as wire speed, wire tension, wire diameter and dielectric pressure.

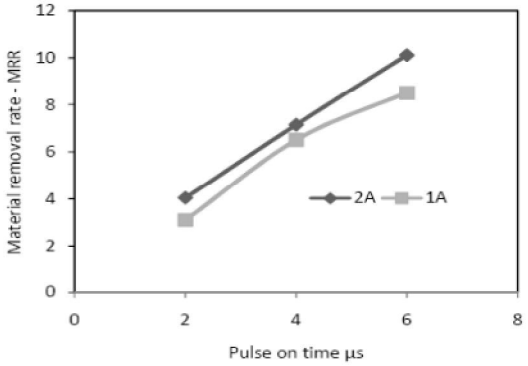


Figure 5. MRR at various pulse on time

6. Effects of various parameters of WEDM on morphology of surface

In this section, cutting surface of NiTi60 by WEDM studies regarding spark behavior and craters on workpiece. In this regard, SEM (Scanning Electronic Microscope), model AIS-2100, made in Seron Company is used. Craters create on the cutting surface at the same time when making spark in a gap between the electrodes. With regard to the optional parameters, different sizes of crater and margin in the shape of rim made by re-melting are existed. Depending on the process, lifting model via volatile and formation of extremely small collapse are the main factor to penetration of wireless materials on the workpiece's surface. Considering the surface morphology of different components and thickness of crater edge, penetration of wireless materials can be seen by microscopic images (Figure 6 to 8). According to the figures craters make over Lap phenomenon by consecutive sparks in small time. Concentration on cutting surface increases when collapse isolation percentage on the wire increased by evaporation mechanism. When power increases due to increase in energy density of pulses and when surrounding temperature increases due to increase in percentage of evaporation, craters should have fewer nesses. However, due to the MRR and increased depth of crater and the higher surface roughness, energy density is raised.

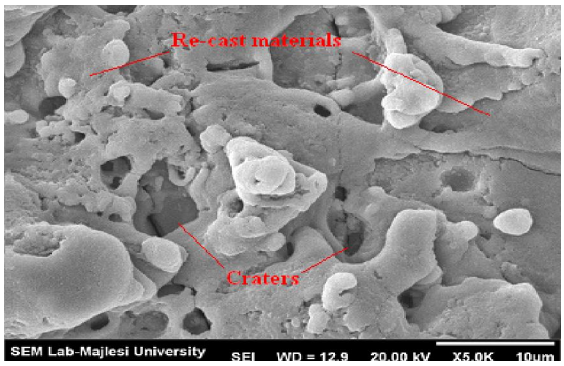


Figure 6. SEM micrograph of the WEDM surface at magnification 5000

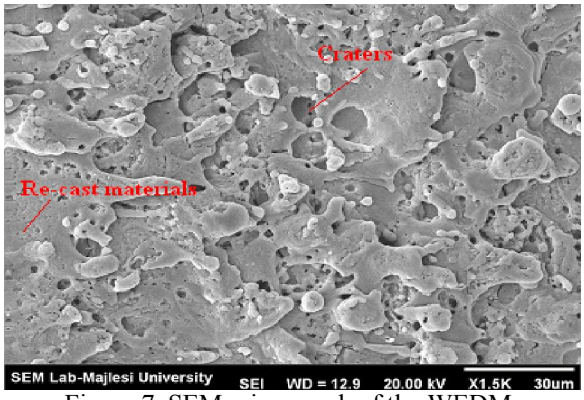


Figure 7. SEM micrograph of the WEDM surface at magnification 1500

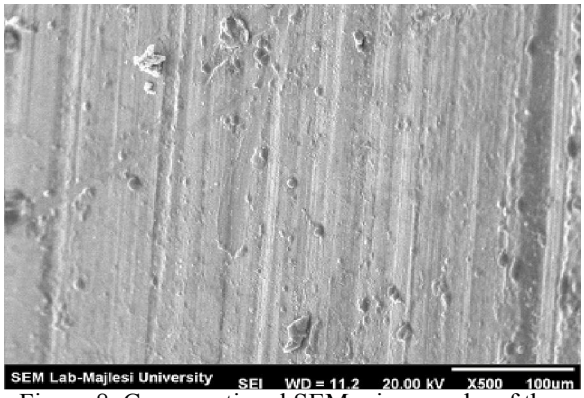


Figure 8. Cross-sectional SEM micrographs of the WEDM specimens NITI60

7. Conclusion

Capabilities of NiTi60 have been studied in the present research. For this purpose, the effect of input parameters of WEDM including wire speed, pulse current and pulse on time on surface roughness and MRR were investigated. Increase of power increases discharge energy and the number of spark which increases the temperature of workpiece and machining speed increases surface roughness rapidly. The study showed that the most affective factor in MRR of NiTi60 alloy is pulse current so that when it increases, MRR increases too. Other factors that increase MRR are wire speed and pulse on time, which increases surface roughness. According to the wire tension and diameter, increases of pulse current are allowed to a special range and over than that range will tears the wire. As cutting process by WEDM is electro thermal, with large number of sparking in NiTi60, lots of craters formed on this smart alloy and due to penetration of isolated materials separated from wire cut on the craters, alloying is done by recast materials. By fast cooling of the melt, a layer with 10-20 μm thickness is formed on the surface of NiTi; this alloy is no more NiTi and has different phases from CuZn, Nio and Cu_2O. These components changed physical and mechanical properties of cutting surface in compared with centre of workpiece.

Acknowledgements:

This study is resulted from a research project in Islamic Azad University, Majlesi Branch. The author is thankful for supportive effort of this research benefactor.

Corresponding Author:
Saeed daneshmand
Department of Mechanical Engineering, Majlesi Branch, Islamic Azad University, Isfahan, Iran
E-mail: s.daneshmand@iaumajlesi.ac.ir

References

1. Mohd Khairul Anuar Bin Mohd Idris. Effects of machining characteristics on electric discharge machine using different electrode materials, Bachelor Thesis, Faculty of Mechanical Engineering University, Malaysia Pahang, 2008.
2. Robert Langlios, Build an EDM electrical discharge machining removing metal by spark erosion, Village Press, 1997.
3. Scott F. Miller, Albert J. Shih, Jun Qu. Investigation of the spark cycle on material removal rate in wire electrical discharge machining of advanced materials, Journal of Machine Tools & Manufacture, 2004; 44(4): 391-400.
4. Sabouni H.R, Daneshmand S. Investigation of the parameters of EDM process performed on smart NiTi alloy using graphite tools. Life Sci J, 2012; 9(4):504-510.
5. Sommer C, Sommer S. Complete EDM handbook, Advance Pub, 2005.
6. Donald, B. Moulton. Wire EDM fundamentals, EDM Network Sugar Grove, IL USA, 2006:1-22.

7. Lotfi A.A, Daneshmand S., Adib Nazari S. The effect of operational cutting parameters in the wire electro discharge machining (WEDM) on micro hardness of alloy surface layer, Journal of Advanced Design and Manufacturing Technology, 2009; 2(4):51-58.
8. Kauffman, G. B., Mayo, I. The story of nitinol: The serendipitous discovery of the memory metal and its applications, The Chemical Educator, 1997; 2(2): 1-12.
9. Duerig, T., Pelton, A., Stoeckel, D., (1999). An overview of nitinol medical applications, Material Science and Engineering A, 1999; 273-275:149-160.
10. Morgan, N. B. Medical shape memory alloy applications - the market and its products, Material Science and Engineering A, 2004; 378:16-23.
11. Hartl, D. J., Lagoudas, D. C. Aerospace applications of shape memory alloys, Proceedings of the Institution of Mechanical Engineers, Part G: Journal of Aerospace Engineering, 2007; 221(4):535-552.
12. Justin Ryan Schick. Transformation induced fatigue of Ni-Rich NiTi shape memory alloy actuators, Texas A&M University, Thesis Master of Science, 2009.
13. Cimpri Darjan, Janez Dolin sek. Shape memory alloys, Seinarska Naloga, Univerza Ljubljani Fakulteta Za Matematiko in Fiziko Oddelek Za Fiziko, Seminarska Naloga, 2007: 1-20.
14. D. Michelle Addington, Daniel L., Schodek. Smart materials and new technologies for the architecture and design professions, Harvard University, Architectural Press An imprint of Elsevier, 2005.
15. Gokler, M. I., Ozanozgu, A. M. Experimental investigation of effects of cutting parameters on surface roughness in the WEDM process, Journal of Machine Tools & Manufacture, 2000; 40(13):1831-1448.
16. Saxena AK, Pandey P, Singh JS. Biological Spectrum and other structural functional attributes of the vegetation of Kumaun Himalaya, Vegetatio 1982; 49(1):111-9.
17. Kanlayasiri, K., and Boonmung, S. An investigation on effects of wire-EDM machining parameters on surface roughness of newly developed DC53 die steel, Journal of Materials Processing Technology, 2007; 187-188:26-29.
18. Han, F., Jiang J., and Yu, D. Influence of machining parameters on surface roughness in finish cut of WEDM, Journal of Advanced Manufacturing Technology, Springer London, 2006; 34(5): 538-546.
19. Carl Sommer. Wire EDM handbook, Advance Publishing (TX); fourth edition. 2000.
20. James Brown. Advanced machining technology handbook, McGraw-Hill Professional; first edition. 1998.
21. Gostimirovic M, Kovac P, Sekulic M, Skoric B. Influence of discharge energy on machining characteristics in EDM, Journal of Mechanical Science and Technology, 2011; 26(1): 173-179.

1/26/2012

Is the financial performance of the National Iranian Oil Company affected by Goals, Structure and Leadership of the Company?

Mohammad Asnaashari, Mehdi Noursina, Afsar Asnaashari, Shahab Shaverdian

Department of Management, Islamic Azad University Tafresh branch, Tafresh, Iran
Email: Asna_2677@yahoo.com

Abstract: By creating a suitable organizational climate, management of an organization can pave the way for growth and development of staff and encourage them to attain their best performance. Creating motivation and enthusiasm can eventually lead to improved organizational performance and consequently to improved financial performance. This study is aimed at investigating the relationship between goals, leadership and structure and the Iranian National Oil Company's financial performance. For this purpose, a descriptive study has been conducted using random sampling from the research population of managers and experts of the National Iranian Oil Company, where 150 persons were selected as samples. Data was collected in this study using a questionnaire. For assessing the reliability of the mentioned questionnaire, the Cronbach's alpha method was used which was equal to 0.92;while its validity was measured on the basis of designing the questionnaire based on the theoretical model and review of literature, and also the validity of the expert judges (confirmation of professors and experts) has been used. For analysis of the collected data, factor analysis and structural equation modeling was used. For this purpose, components of organizational climate were considered based on Weisbord model and three hypotheses were developed based on this model. Results indicate that: (1)the model has a good fit, (2)organizational climate has a significant relationship with financial performance, and (3)all dimensions of the organizational climate, i.e. goals, structure and leadership, have significant relationship with the financial performance; finally, the order of dimensions of organizational climate in terms of significance of their relationship with organizational climate are as follows: leadership, goals and structure. Accordingly, several recommendations have been offered, the most important of which include: involvement of staff in formulation of organizational goals of their unit, directing the organization towards a participatory organization, use of organic structures appropriate to units and work groups, choosing a leadership style suitable for the conditions of the organization, use of appropriate incentive systems to improve employees' performance, improving communications networks of the works, improved and targeted welfare facilities of organization appropriate to the age and experiences of personnel and use of automation technologies, intranet etc.

[Mohammad Asnaashari, Mehdi Noursina, Afsar Asnaashari, Shahab Shaverdian. **Is the financial performance of the National Iranian Oil Company affected by Goals, Structure and Leadership of the Company?** *Life Sci J* 2012; 9(4):2910-2923] (ISSN: 1097-8135). http://www.lifesciencesite.com. 427

Keywords: Organizational climate, Weisbord organizational climate model, performance, financial performance

Introduction

To survive, organizations need flexible organizational environments that encourage creativity and personal responsibility and allow individuals to be responsible for their works. In this context, improving the organizational climate is one of the obvious needs of organizations. Results of researches suggest that satisfaction of members of organizations with the climate of their organizations is a fundamental value itself. It can be said that, among other variables related to organizations, organizational climate is one of the unique factors that can be manipulated so that it would help the realization of organizational goals. The researchers have acknowledged that improvements in organizational climate will result in an increase in job satisfaction (Johnston, 2004:131).Undoubtedly, the corporate culture included into organizational climate can also lead to the emergence of behaviors and attitudes in employees, which in turn will be effective in enhancing the value of organization and providing better results (Lytle & Walker, 2007:318).

Research Reproduction and the Necessity of the Research

Human capital in the present century has become as one of the major challenges for organizations. Human capitals and employees are the very same factors that allow organizations obtain their places, and their job satisfaction will realize the organizations' goals. Now, with regard to the fact that staff should act in an organization and its environment to achieve organizational goals, the conditions and characteristics of organizational climate can be effective in job satisfaction and consequently in realization of organizational goals (financial performance) (Mirkamali,2001:53).

The importance of human resources in management of organizations becomes more and

more. Individuals with high quality, appropriate adaptability, the capability of team work, high motivation, being self-controlled and with professional moral values are the most important resource for any organization to be established(I. Bakir Arabac, 2010:164).

Human Resource Management includes all managerial decisions and actions that affect the nature of the relationship between organization and human resources. One of the methods of human resource management is performance management, by which a single, common language can be created for what the organization should achieve and how to achieve it (Yarmohammadian, 2005:19).In fact, performance management of human resources main activities is effective for achievement of better results by organizations through assessment and performance management. This process will be only possible on the basis of agreed frameworks in terms of goals and skills requirements, evaluation and performance improvement, identification and providing training and development needs. This approach to management will pursue the following goals: objectives such as human resource development and creating the necessary reforms for rehabilitation of human resources, identifying future expectations of employees, determining the criteria and resources for improving organizational processes, creating more motivation in human resources, determining the training needs of staff and improving required educational standards, identifying potentials of employees and creating suitable conditions for their growth and prosperity within the organization (Armstrong, 2007:42).Suitable organizational climate can be effective for creating motivation, improving staff morale, increased participation of individuals in decision making and increasing creativity and innovation; and it can be an important source of job satisfaction of employees and vice versa. So any change in organizational climate can lead to immediate and profound changes in how employees work and in their performance (Sabeti, 1999:42), and ultimately will result in the improved organizational performance and consequently improved financial performance.

Improvement of organizational performance and consequently financial performance is the goal that all organizational efforts are conducted to fulfill it. Achieving this goal, more than anything else, depends on a proper management for full utilization of human and material resource of the organization. Among these resources, human resource is the most important source that has a direct impact on performance. On the other hand, providing and maintaining quality of services can be basically key competitive advantage of many organizations (Albrecht and Zemke, 2006:256). In today's highly competitive and changing environment, companies will most probably evaluate their processes one after another (Auckland, 2007:127) so that the services that they offer would be differentiated from the services of their competitors.

On the Other hand, organizational climate of organizational units can be highly effective in the quality of services, responsiveness to customers and customer satisfaction etc, and this influence can ultimately have an impact on the financial performance of the organization. But this important relationship has not been addressed yet in the National Iranian Oil Company. Considering the benefits due to suitable organizational climate and its impact on other organizational components such as employee satisfaction, customer satisfaction, etc and finally enhancing productivity of the organization intensifies its importance.

Review of Literature

Organizational Climate

In describing the organizational climate, more emphasis has been on interpersonal aspects of situations. Some authors have described it as: the degree of management support, attention to new employees and conflicts between or within the divisions of an organization (Schneider et al, 2005:151). Others have defined organizational climate is such a way that it would include organizational constraints and administrative paperwork, degrees of freedom of employees in decision making, reward type and its frequency, the endeavor, risk, warmth and protection (Fiedler and Chemers, 1993:58).The organizational climate is considered by Kopelmanet al as a change at personal level, where they believe that climate "is neither the work place, nor the way people respond to it; however the climate is a perceptional channel or instrument through which the environment's influences on attitudes and behaviors will be determined (Talebpour, 2001:45).

Halpinand Craft (1970) has defined organizational climate as: "the internal characteristics that distinguishes one organization from other organizations and affects the behavior of its individuals". The organizational climate is measured by the employees' perceptions and their descriptions regarding internal characteristics of organization (Halpin & Craft, 1970:161).

According to the definition of Hoy and Miskel, organizational climate refers to the perceptions of employees of general workplace of an organization and is affected by formal and informal organization, individuals' personality and organizational leadership (Hoy and Miskel, 2003:424).

Campbell et al state that organizational climate shows the organization's way of dealing with its members and therefore it can be assumed as organization's personality (Landy, 1980:156).
Organizational climate refers to a position and subjective content in a place and time and its relationship with thoughts, feelings, and behaviors of members of an organization (Edric, 2010:17).

Organizational climate include employees' perception of policies, practices and procedures of an organization that lead to the formation of employees' behavior in an organization and as a mediator between organization's environment and behaviors of employees, clarifies the experience of organizations' employees (Patterson et al, 2005:385).

In the book titled "Understanding human behavior in organizations," Wendell et al have noted that the organizational climate is a relatively stable set of perceptions of organizational members about the characteristics of organizational culture, and such perceptions affect feelings, attitudes and behavior of individuals (Akram Goodarzi and Vajiheh Gaminiyan, 2002:40).

James and Jones(1974) understand the organizational climate as a set of organizational attributes and characteristics that are perceived by the employees and its manifestation can be described through exerting processes and relationships of members with environment (Jamshidianet al, 1996:51).

George Litwin and Robert Stringer have defined organizational climate as the "perception of an individual regarding the organization where he/she works and his/her feelings towards organization in terms of some aspects like independence, organizational structure, rewards, considerations, intimacy, support and openness" (Dessler, 1994:111).
According to Bloom, the organizational climate includes conditions, forces and external stimuli that affect human beings. He has summarized external stimuli in physical, social and intellectual factors, and has reported the change of climate scope from the innermost social interactions to external cultural and organizational forces (Salehi Hosseini, 1991:45).

Organizational climate is a classified asset that can be of benefit or detriment to a business by describing how the company should use its employees (Hay Groop, 2009:2).

Climate of an organization is the environmental image clearly understood by members of the organization (Noordin & Omar, 2010:151).

Based on another definition, the organizational climate is the "environment where the employees work and it can affect their motivation, performance and job satisfaction" (Seyyed Abbaszadegan, 2005:9).

In the Encyclopedic Dictionary of Management, organizational climate is defined as "the set of view points shared among the majority of senior managers within an organization, particularly with regard to how the organization should behaves towards employees" (Etemadi Ahari, 2006:143).

Dickson has emphasized that the strength of the climate is the agreement between the employees(Dickson et al, 2009:353).

It is inferred from these definitions that organizational climate is a feature that:

1) Makes an organization different from other organizations;
2) Is relatively stable over time; and
3) Can affect people's behaviors.

Organizational Climate Theories

The first study of organizational climate was conducted by Halpin and Craft. They developed the first organizational climate description questionnaire (OCDQ) which was a 100-questions descriptive questionnaire. Through the questionnaire, they identified six main climates in organizations and arranged them along a continuum from closed to open climate that is shown in Figure1(Hoy and Miskel, 2003:426).

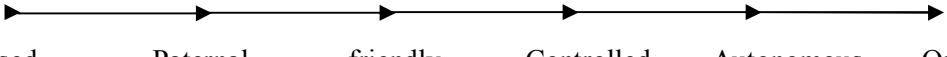


Figure 1: The continuum of organizational climate (Hoy and Miskel, 2003, 426)

In this study and in addition to six major climates in organizations, Halpin and Craftal so identified eight factors affecting the organizational climate including: disengagement, hindrance, spirit, intimacy, production emphasis, aloofness, thrustand consideration (Shirazi, 1994:59).

In 1961, Likert provided a conceptualization similar to the conceptualization of Halpin and Craft for organizational climate. This conceptualization is based on managers and subordinates relations. Based on this conceptualization, the organization is placed on a four-part continuum, i.e. exploitative-authoritarian system, benevolent authoritative system, consultative system and participative system. Likert measurement instrument was based on eight attributes for classification of management systems:

leadership, motivation, communication, interaction-influence process, decision making, goal setting, control and realization of goals Alagheb and, 2005:105).

Litwin and Stringer (1968) have considered eight dimensions for measuring organizational climate including: structure, responsibility, risk, warmth and intimacy, support, standards, conflict and identity (Armstrong, 2007:200).

Donaldet al have considered six dimensions for measuring organizational climate including: organizational support, quality of members of the organization, openness, management style, conflict of organization members and freedom. Their questionnaire has 18questions and each dimension is covered by 3questions (Bowen, 1998:35).

Weisbord (1976) considers 6 dimensions to measure and assess organizational climate which include: purposes, structure, relationships, rewards, leadership and helpful mechanism. These dimensions are shown in Figure 2.

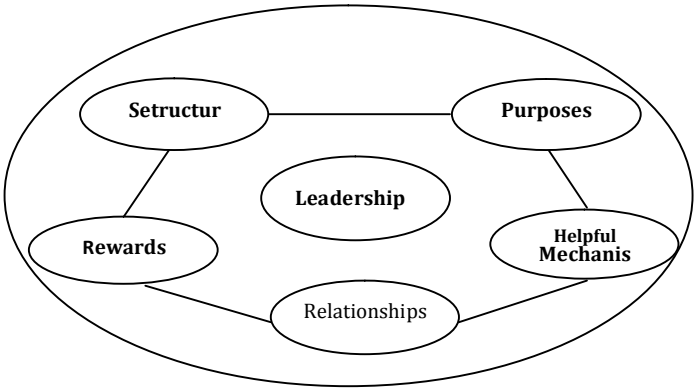


Figure 2: Weisbord Hexagonal Model

Also note that the outer circle is to isolate internal factors and their relationships from environmental factors outside the organization (Jamshidianet al,1996:52). (Jamshidianet al, 1996,52)

Weisbord has identified six critical areas or segments; these segments are the factors that if the organization is seeking to be successful, should properly deal with them (French and H. Bell, 2008:109).

Sergiovanni and Sttarat (1978) in their book titled "Supervision" have considered seven components for measuring organizational climate. These components include: conformity, responsibilities, standards, rewards, organizational clarity, warmth and support and leadership.

Performance

Various definitions have been proposed for "performance" such as: performance is to realize the tasks assigned to human resources by an organization (Cascio, 1995:205).

Performance assessment refers to assessment and measurement process organizations of performance in a specified period so that the expectations and judgment criteria would be clear for assessed organization and it would have been already informed with regard to them (Tabarsa, 1999: 4).

Organizational performance has been attributed to organizational behavior before it would be applied to the branch of management sciences such as production management. Organizational behavior is limited to research in some cases where it affects individuals in an organization and the way in which the individuals affect performance; organizational performance will be studied at three levels (Robbins, 2007:400).

Generally speaking, performance may be studied at three levels, i.e. individual, group and organization; however, according to our research topic, we only investigate organizational performance in this section and will review factors affecting organizational performance and will study existing models for measuring performance.

Factors affecting individual's performance:

1- Capability, 2- personality, 3- learning, 4- perception, 5-motivation and 6- stress

Factors affecting group performance:

1- Relationships, 2- leadership 3- power and policy, 4- inter-group behavior and conflict

Factors affecting organizational performance:

1- Organizational structure, 2- organizational environment, 3- organizational policies and procedures and 4- organizational culture (Mintzberg, 1998:3).

New Models of Organizational Performance Assessment

"Assessment" is one of the widespread discussions engaged by a wide range of disciplines

and experts and there are numerous new reports and papers written about it. In addition, many software applications have been developed in this field. However, despite plenty of models and frameworks in this context, some of conceptual models have had the greatest impact on shaping it. Some of these models are explained below.

A) Performance Matrix (1989)

In 1989, Keegan introduced performance matrix and this matrix is shown in Figure3.The strength of this model is that it covers different aspects of organizational performance, including financial and nonfinancial aspects and internal and external aspects in an integrated manner. However, this model does not show the relationships between different aspects of organizational performance clearly (Karimi, 2006:23).

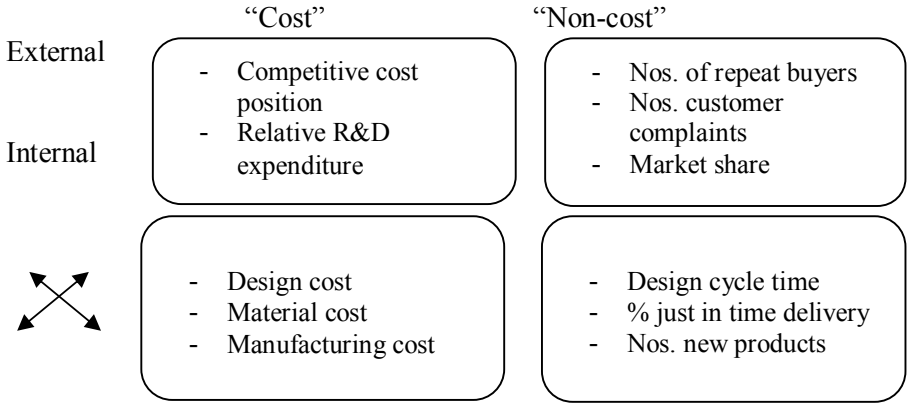


Figure 3: Performance measurement matrix (Karimi, 2006, 23)

B) Performance Pyramid (1991)

One of the requirements of each performance measurement system is a clear relationship between performance criteria and hierarchical levels of an organization, so that each unit would try to achieve the same goals. One of the models which show how to create this relationship is performance pyramid model. The goal of performance pyramid is to establish the relationship between organizational strategy and its operations, as it expresses the effectiveness of an organization and its internal efficiency.

This framework in fact pays attention to the difference between the parameters that are focused on the groups outside the organization (such as customer satisfaction, quality and on-time delivery) and internal business factors (such as productivity, cycle time and waste). An organizational pyramid performance is constructed at the first level by the definition of the vision of the organization which then becomes the objectives of business units. At the second level, business units try to set short-time goals such as profitability and cash flow and long- term goals such as growth and improvement of market share (financial and market).Operational systems of business bridge the gap between daily operational measures (customer satisfaction, flexibility and productivity).Finally, four key performance measures (i.e. quality, delivery, work cycle and waste) are used in units and work centers on a daily basis. The main strength of the performance pyramid is its efforts to integrate organizational goals with operational performance measures. However, this approach does not provide any mechanism for identifying key performance measures and also there is no room for the concept of "continuous improvement" in this model (Karimi,2006:24).

C) Stakeholder Analysis (2001)

The design of performance measurement system begins with understanding the goals and strategies of an organization and that is why the balanced scorecard for design of performance measurement system begins with the question "what are the shareholders' demands?" In fact, the balanced scorecard model implicitly take only shareholders into account and other stakeholders have no role in setting organizations' goals. In other words, this model ignores the impact of other stakeholders on organization. Neglecting the differences of the various stakeholders in different environments is one of the major reasons for failure of some big companies in using this model.

Organizational goals represent key stakeholders' expectations and desires and all key stakeholders exert their powers entirely through the governance structure for setting goals, while non-key stakeholders are not very powerful in setting goals and instead affect the organization's strategies via external mechanisms, and in this way they determine the procedure of attaining goals with regard to

external environment. Therefore, performance measurement system begins with strategies and acts as a bridge between the behaviors of managers and expectations of stakeholders (Karimi,2006:25).

D) Excellence Model

Another widely used known measurement framework is (EFQM) excellence model.

The excellence model has nine criteria, four of which are enables and five criteria are results.

Enablers include: leadership, policy and strategy, employees, partnerships and resources and interests and processes.

Results include: customer results, people results, society results and key performance results.

- Scores and rating logic for performance measurement

Enablers and results each comprises fifty percent of the total value of the model, which indicate similar value of the level at which improvement activities are conducted and the results that are obtained.

Rating logic of excellence model includes four elements:

1- Results, 2- approach 3- deployment 4- assessment and review

The constructive and supportive theory behind this framework is that enablers are like levers that managers can use them to achieve future results faster. One of the weaknesses of this model is that it is difficult to become operational; since the words and concepts used in this model are so general that they can be interpreted in different ways, each organization will be able to use them but will create different assessment criteria (Karimi, 2006: 25).

E) The balanced scorecard model: a model for performance measurement

In early 1990s, Nolan Institute as the research branch of KPMC conducted a study for measuring performance of future organizations. The institute's president David Norton took over the leadership of the research project and Robert Kaplan was appointed as the academic consultant. After a long research program in partnership with the company, the research group achieved a comprehensive framework which was called balanced scorecard in which company's mission and strategic objectives could be converted to an alternative set of performance criteria (Wongrassamee, et al, 2003:18).

This set which includes the process indicators and final results can quickly provide the managers with a comprehensive picture of organizational performance so that the organization's progress in achieving strategic goals can be measured (Ali Ahmadi et al, 2009:336).

The main purpose of the balanced scorecard approach is to provide a practical viewpoint for the managers and to lead them to focus on basic areas and advancement of strategies. Balanced scorecard approach has included an important part of financial goals as criteria to determine how the system works (Kaplan & Norton, 1996:83).Balanced scorecard Model (BSC) is a qualitative and comprehensive model for performance management of organizations. This model focuses on organization's strategies and creates balance between various fields of organization, finance, clients or customers, internal organizational processes and learning and growth, etc and tries to manage and assess complex organizations.

Kaplan and Norton have proposed measurement of organizational performance in the following four key areas:

- Financial
- Customer
- Internal business processes
- Growth and learning

These four areas can be divided into two distinct parts. The first part contains the "current financial criteria" and "operational problems" which are related to customers, internal processes and learning and growth.

Kaplan and Norton have presented some proposals as quantitative criteria for assessment of organizational performance (Kaplan & Norton, 1996:85).

Financial: Financial measures are important components of a balanced assessment system, particularly in profit organizations where these measures indicate success in other fields because they state that the successful implementation in other aspects will lead to what financial results (Kaplan and Norton, 2009:23).The financial area is divided into three parts, i.e. "revenue growth," "cost management" and "asset utilization".

_ Revenue growth:

1- Sales and the market share, 2- Number of new customers and markets and 3- Number of new strategies.

_ Cost Management

1- Revenue per employee and 2- unit cost reduction

_ Asset utilization

1- Inventory reduction, 2- cash-to-cash cycle, 3- return on capital and 4- productivity/efficiency (Kaplan & Norton, 1996:86).

Customer: For choosing objectives and measures related to the customer's perspective, organizations must answer two critical questions: first, who are our target customer? And second, what

are our proposed values to them (Kaplan and Norton, 2009:19).

Kaplan and Norton suggest that organizations must first identify the market segment that they aim to supply. For each segment, they must focus on the type of measure that they use to fit the characteristics of the business.

Market Share

1- Percentage of segment capture, 2- customer retention, 3- number of defections, 4- increase in sales to current customers and 5- Frequency of orders, visits or contacts with customers.

_ Customer Acquisition

1- Number of new customers, 2- ratio of sales to inquires, 3- average cost to acquire a new customer and 4- average order size.

_ Customer Satisfaction

1- Number of complaints, 2- number of customers that express their satisfaction.

_ Customer Profitability

1- The total profit per customer and 2- total cost per customer(Kaplan & Norton, 1996:88).

Internal business processes (organizational processes): From the perspective of internal processes, organizations must identify processes and attain excellence in them so that they can continue creating value for their customers and ultimately their shareholders (Kaplan and Norton,2009:20).Kaplan and Norton acknowledge that, although improvements in internal business processes do not have any bearing on the management of (organization) at the strategic level, they do contribute towards noticeable improvements in business in the long term. They suggest the following measures for these processes:

_ Identify or make market

1- Profitability by segment and 2- percentage of revenue from new customers

_ Design

1- Time to market and 2-break even time

_ Build

1- Number of defects and 2- process time

_ Delivery

1- Percentage of timely delivery 2- percentage of defects

_ After-sales Service

1- Average satisfaction rating, 2- number of orders, and 3- Number of customers who do not reorder(Kaplan& Norton, 1996:92).

Growth and learning: How ambitious goals set out in the perspectives of internal processes, customer and eventually shareholders can be realized? The answer to this question lies in the objectives and measures related to learning and growth perspective (Kaplan and Norton, 2009:21).The learning and growth area is concerned with infrastructure, i.e. the foundations required to achieve objectives in other areas of the business (Kaplan & Norton, 1996: 95). Kaplan and Norton cite three relevant categories: 1- employee capabilities, 2-employee satisfaction and 3- staff turnover.

Research Methodology

Achieving the goals of science or scientific knowledge is not possible except when a methodology is used. Researcher should note that the validity of research results is affected by the method chosen for his/her research (Khaki, 2010:155).This study is an applied research in terms of objective, and a descriptive one in terms of data collection, while it is a survey research in terms of methodology. This study is initiated with a main hypothesis and threesub-hypotheses:

The main hypothesis of the research: there is a significant relationship between goals, structure and leadership (organizational climate)and financial performance in the National Iranian Oil Company.

Sub-hypotheses of the research:

1. It seems that there is a significant relationship between goals and financial performances.
2. It seems that there is a significant relationship between structure and financial performance.
3. It seems that there is a significant relationship between leadership and financial performance.

The research is conducted in the first half of the year 2011 in the National Iranian Oil Company (its central offices in Tehran).Since this study seeks to evaluate the models and relevant variables, based on the stated factors, the research population included all managers and experts of central offices of National Iranian Oil Company in Tehran which are 150 people. In the study the Simple Random Sampling (SRS) method has been used. Our sample size for research population of 150 people is equal to 108 people.

For data collection from samples and in order to test the hypotheses, a questionnaire has been designed considering the research variables.

The reliability test of the questionnaire was conducted for 7 variables and 38 questions of the questionnaire and 40 samples. Cronbach's alpha coefficient was calculated to be 0.701 for the first variable, i.e. "goals", which is comprised of 5 questions. For the second variable, namely the "structure" and for 5 questions of the questionnaire, Cronbach's alpha value is calculated to be 0.778 and similarly, the alpha value is calculated for the remaining variables. Cronbach's alpha coefficient for the whole questionnaire is equal to 0.926.

For analysis of collected data, descriptive statistics were used initially and to test the statistical

hypotheses of the research, factor analysis and structural equation modeling we reemployed. LISREL and SPSS software programs have been used for such analyses.

Conceptual Model of Research

Due to the variety of models for measuring organizational climate like those of Halpin and Craft, Likert, Donald et al, Weisbord, Sergiovanni & Sttarat, etcand since this research is conducted in a large public company, to investigate the organizational climate the researcher has localized six-dimensional model of Weisbordand has used only three major factors, because it is more suitable for large public enterprises that with regard to our research population.In this model the concerned dimensions for studying organizational climate include: goals, structure and leadership.

Meanwhile, there are different models for measuring the financial performance, most of which are based on financial analysis;however, since in this study the financial performance will be measured using a questionnaire and this is only an attitude measurement, Kaplan and Norton model has been used for measuring financial performance and its dimensions, including: revenue growth, cost management and asset utilization.The conceptual model of the research is as follows:

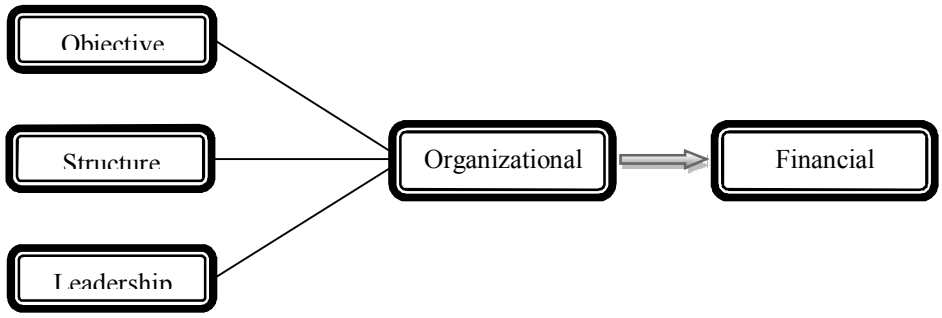


Figure 4: Conceptual model of research

Review of the Conceptual Model of the Research

In this section, we use structural equation modeling to examine the relationship between independent variables (organizational climate variables)and dependent variables (financial performance) of the research.It should be noted that each of the independent variables,i.e. goals, structure and leadership, have been defined using their indicators.Standardized factor loading estimates (standardized regression coefficients) for conceptual model are given in Figure5.

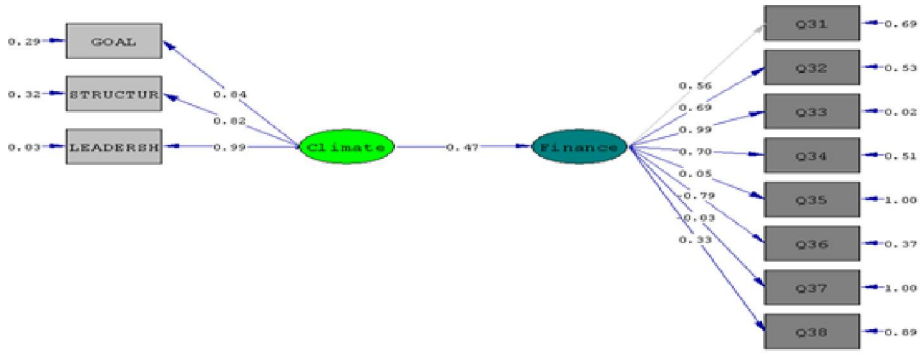


Figure 5: Standardized factor loading estimates for conceptual model of research

It can be observed that there is a nearly strong relationship between the independent variable, i.e. organizational climate, and the dependent variable, i.e. financial performance. This amount is equal to 0.47.Now we turn to examine the relationship between the dependent variable, i.e. financial performance,and the variables that define organizational climate.

Table 1: Strength of the relationship between research variables

Variable name	Strength of relationship withorganizational climate variable	Strength of relationship withthe dependent variable, i.e. financial performance	Significance of relationship
Organizational climate	1	0.47	There is a significant relationship
Financial Performance	0.47	1	There is a significant relationship
Goals	0.84	0.47 * 0.84 = 0.39	There is a significant relationship
Structure	0.82	0.47 * 0.82 = 0.38	There is a significant relationship
Leadership	0.99	0.47 * 0.99 = 0.47	There is a significant relationship

Based on the direct relationship between each of the independent variables with organizational climate variable, and also the direct relationship between organizational climate variable and the dependent variable, i.e. financial performance, the strength of indirect relationship of each of independent variables with the dependent variable, i.e. financial performance can be estimated.The direct and indirect relationships between research variables are shown in Table1.Also the significance of each of relationshipsis shown in Table 1.

Regarding the relationships between the independent variables and the dependent variable, i.e. financial performance, it can be seen that the strongest relationship is between leadership and financial performance with a value of equal to 0.47.

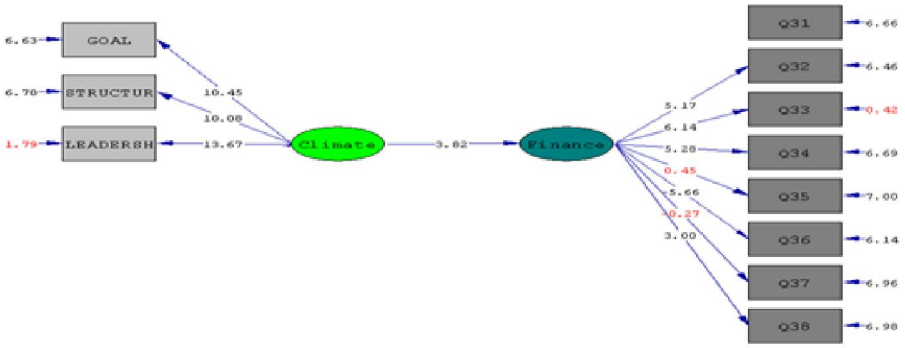


Figure 6: The chart of Student's t-statistic valuesfor conceptual model of research

The relationship between financial performanceindicators can be seen in Figure 6.It can be seen that Q33 has the highest relationship with financial performance variable.The relationship of Q35 and Q37 is very small and even it is zero.The relationship of Q36 and Q37 is negative.

Table 2: Measurement indicators of financial performance variable

Variable	Indicators	Question number
Financial Performance	Sales and the market share	31
	Number of new markets	32
	Number of new strategies	33
	Revenue per employee	34
	Unit costreduction	35
	Inventory reduction	36
	Return on capital	37
	Productivity / efficiency	38

The chart of Student's t-statistic valuesfor conceptual model is given in Figure 6.With regard to the Student's t-statistic values, the relationship between allthevariables,i.e. goal, structure, and leadership (organizationalclimate) and financial performance variable is verified.

Regarding the financial performance indicators,it can be seen that for two indicators of Q35 and Q37, because the Student's t-statistic value is much smaller than the value of 1.96, the significance of this relationship can be rejected.

With regard to Student's t-statistic valuesrelated to errors,it can be seen that the values of this statistic for all indicators and variables except Q33 and leadership variable index is more than 1.96,which indicates that we are faced with a significant level of error,and these errors often occur because of low sample size.But for Q33 and leadership variable,since the Student's t-statistic values are smaller than 1.96, these two errors are not significant.

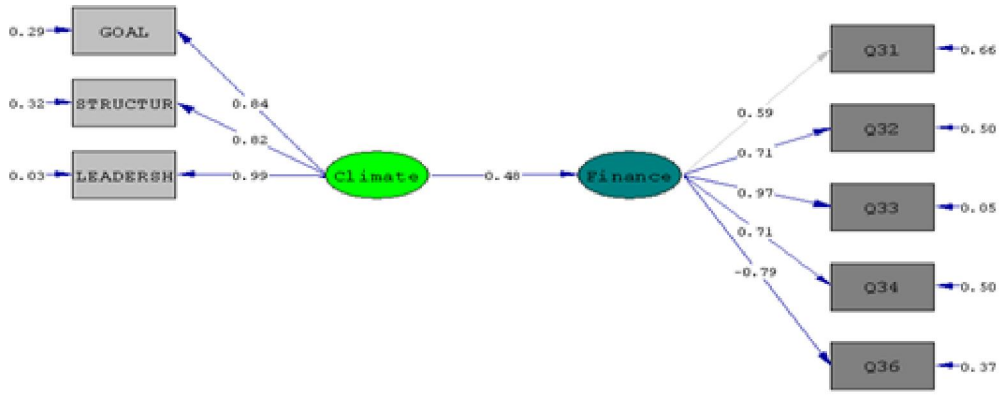


Figure 7: Standardized factor loading estimates for conceptual model of research after excludingnon-significant indicators

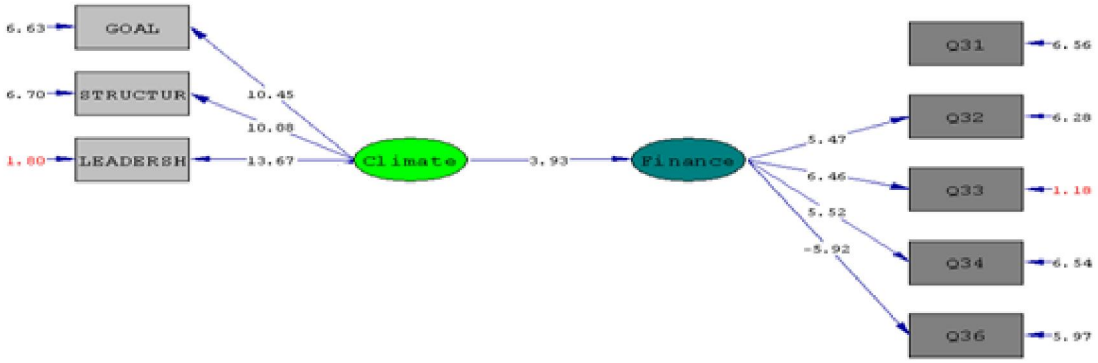


Figure 8: The chart of Student's t-statistic valuesfor conceptual model of research after excluding non-significant indicators

In Figures 7 and 8, factor loading values and Student's t-statistic values of conceptual model have been presented after excluding two indicators,Q35 and Q37. It can be seen that the standardizedfactor loading values have not changed, except for the relationship between organizational climate and financial performance which has changed from 0.47 to 0.48.

The coefficient of multiple determination of the above model is 0.73.This means that the above variables can explain 73% of the dependent variable,i.e. financial performance.Also the coefficients of multiple determinationsfor other variablesare shownin Table3.

Table 3: Coefficient of multiple determinations for financial performance indicators

	Indicator 31	Indicator 32	Indicator 33	Indicator 34	Indicator 35	Indicator 36	Indicator 37	Indicator 38
Coefficient of multiple determination	0.31	0.47	0.98	0.49	0.00	0.63	0.00	0.11

Asit can be seen, indicator 33 can explain financial performance variable more than other indictors; and two indicators,i.e. 35 and 37, cannot explain the financial performance variable.

Table 4: Coefficient of multiple determinations for variables representing organizational climate

	Goal	Structure	Leadership
Coefficient of multiple determination	0.71	0.68	0.97

As it can be seen in Table4,leadership variable can explain organizational climate variable and consequently financial performance more than other variables do.

Results of Tests of Hypotheses

After conducting hypotheses tests (structural equationanalysis), all research hypotheses were confirmed and their significancewere accepted.In other words, allthe mentionedvariableshave significant relationship with the financial performance.

- The main hypothesis of the research: there is a significant relationship between goals, structure and leadership (organizational climate) and financial performance in the National Iranian Oil Company.

Asit can be seenin Table5, organizational climate has a significant relationship with financial performance at the level of 0.05, and the strength of relationship between organizational climate and financial performance is equal to 48 percent.

Table 5: The strength of relationship between research variables and financial performance and the results of hypotheses tests

Variable name	Strength of relationship withdependent variable, i.e. financial performance	Significance ofrelationship	Result of hypothesis test
Organizational climate	0.48	Significant relationship at level of 0.05	Confirmation of the main hypothesis

The first sub-hypothesis: there is a significant relationship between goals and financial performance. As it can be seen in Table6, goal variable has a significant relationship with financial performance at the level of 0.05, and the strength of relationship between organizational climate and financial performance is equal to 39 percent.

Table 6: The strength of relationship between research variables and financial performance and the results of hypotheses tests

Variable name	Strength of relationship withdependent variable, i.e. financial performance	Significance ofrelationship	Result of hypothesis test
Goal	0.39	Significant relationship at level of 0.05	Confirmation of the sub-hypothesis 1

The second sub-hypothesis: there is a significant relationship between structure and financial performance.

As it can be seen in Table7, structure variable has a significant relationship with financial performance at the level of 0.05, and the strength of relationship between organizational climate and financial performance is equal to 38 percent.

Table 7: The strength of relationship between research variables and financial performance and the results of hypotheses tests

Variable name	Strength of relationship withdependent variable, i.e. financial performance	Significance ofrelationship	Result of hypothesis test
Structure	0.38	Significant relationship at level of 0.05	Confirmation of the sub-hypothesis 2

The third sub-hypothesis: there is a significant relationship between leadership and financial performance. As it can be seen in Table 8, leadership variable has a significant relationship with financial performance at the level of 0.05, and the strength of relationship between organizational climate and financial performance is equal to 47 percent.

Table 8: The strength of relationship between research variables and financial performance and the results of hypotheses tests

Variable name	Strength of relationship withdependent variable, i.e. financial performance	Significance ofrelationship	Result of hypothesis test
leadership	0.47	Significant relationship at level of 0.05	Confirmation of the sub-hypothesis 3

Conclusions and Findings

There are several factors that are associated with financial performance and can improve the financial performance of an organization, and can help it for better using of resources; one of the most important of such factors is the organizational climate.Indeed, if the organizational climate would be suitable, organizations can obtain employees' satisfaction and can be successful in achievingtheir goals, which one of them is financial goals.As we observed,among the dimensions of the organizational climate,leadership has the greatest relationship with organizational climate while structure has the lowest relationship. This can be explained by the fact that in large public organizations, and particularly in the Iranian National Oil Company, leadership is much more important than other variables.As organizational behavior scientistsargue, the larger would be the size of an organization, the greater will be the leadership role in achieving organizational goals (such as financial goals).

Meanwhile, all variables of financial performance are related with financial performance, but some of the indicators of these variables were not associated with financial performance and wereexcluded in the final model.Excluded indicators were: unit cost reduction and return on capital.This is also somewhat remarkable.Since the National Iranian Oil Company is a public corporation and is under governmental management,it can be concluded that, like other public companies,the costs of its divisions are not important for managers and employees, and generally there is no such a control on these costs such as private companies.Return on capital is also subject to the same issue;the National Iranian Oil Company is a company that performs its activities based on the natural resources of Iran and has no much planningon return on capital (in fact, the company is not solely an investment company).Although this does not mean that there is no planning at all, but it is much less in comparison with private companies.

Recommendations:

In thisregard, and according to the obtained results,the following recommendations are presented for improving financial performanceto the managers of the National Iranian Oil Company:

1- With regard to the relationship between leadership and financialperformance,it is recommended that a leadership style suitablefor the conditions of organization and appropriate incentive systems to improve employees' performancewould be used.

2- With regard to the relationship between goals and financialperformance,it is recommended that involvement of employees in the formulation of organizational goals of the units, elaboration of organizational goals and mission,and eliminating work barriers would be taken into consideration.

3- With regard to the relationship between structure and financialperformance, it is recommended thatdirecting the organization towards a participatory organization and use of employee participation programs, such as participation of representatives, involvement of the representative and etc, use of organic structures appropriate for units and work groups as well as using both centralized and decentralizeddecision making methods can be taken into consideration.

References

1) Abbaszadegan, Seyyed Mohammad, 2005, The management of troubled organizations, Tehran, Kavir Publications, Fourth edition.
2) Alagheband, A., 2005, Theoretical and principles of educational management, Tehran, Ravan Press, Seventeenth edition.
3) Albrecht, K. and Zemke, R., 2006, Service America in New Economy, New York: McGraw-Hill. Andalleeb, S.S., Siddiqui, N. and Khandakar, S., 2007, Doctors' service orientation in public,private and foreign hospitals, International Journal of Health Care Quality Assurance 20, pp. 253-263.
4) Ali Ahmadi, A. and Fathollah, M. and Tajoddin, I., 2009, A comprehensive approach to strategic management, Tehran, Tolid Danesh publications, Eleventh edition.
5) Armstrong, Michael, 2007, Strategic human resource management: a guide to action, translated by Mohammad Aarabi and Davoud Izadi, Tehran, Cultural Researches Bureau Publications, Third edition.
6) Bakir Arabaci , 2010, Academic and administration personnel's perceptions of organizational climate, Procedia Social and Behavioral Sciences 2, pp. 4445-4450.
7) Bowen, Donald, 1997, Collegues Expreinces in Management and Organizational Behavior, New York: Jhon Wiley and Sons ,inc.
8) Cascio, Wayne F., 1995, Human Resource, Productivity, Quality of work life, prifit, Second Edition, Mcgrow-Hill International Editions.
9) Dessler, Gray, 1994, Fundamentals of Management, Volume II, translated by Davoud Madani, Tehran, Ghomes Publication, Fourth edition.
10) Dickson, M.W. and Resick, C.J. and Hanges, P.J., 2009, When organizational climate is

unambiguous, it is also strong, Journal of Applied Psychology 91, pp. 351-364.
11) Edric L. Spruill, 2010, A Correlational analysis relating organizational climate to employee performance: a case study, a dissertation presented in partial fulfillment of the requirements for the degree doctor of management in organizational leadership, university of phoenix.
12) Etemadi Ahari, Alaodin, 2006, Innovation in educational management: basic principles, Tehran, Dadar Publication, Second edition.
13) F.Noordin and S.Omar, 2010, Organizational Climate and its influence on organizational commitment, international business & economics research journal 2, pp. 1-10.
14) Fiedler, F. and Chemers, M., 1993, Effective Leadership, translated by Sohrab Khalili Shourini, Tehran, Islamic Azad University Press, First edition.
15) French, W. and H. B. Cecil , 2008, Organizational Change Management, translated by Seyyed Mehdi Alwani and Hassan Danaiefard, Tehran, Saffar Publication, Thirteenth edition.
16) Goodarzi, A. and Gaminiyan, V., 2002, Principles, fundamentals and theories of organizational climate, Isfahan, Jahad Daneshgahi Press, First edition.
17) Halpin , R. and P, croft, 1995, Stress and Job Satisfaction:A Study of English Primary School Teachers, Educational Pscholog 4, pp. 437- 489.
18) Hay Groop (2009), Australia: www.haygroup.com.au.
19) Hoy, W. and Miskel, C., 2003, Educational administration: theory, research and practice, translated by of Mir Mohammad Seyyed Abbaszadeh, Tehran, Uromiyeh University Press, Fourth edition.
20) Jamshidian, Mehdi and Khosh Akhlgh, Rahman and Ghiyasian, Morteza, 1996, Application of the hexagonal model of assessment of organizational climate, Journal of Management Knowledge 35-36, pp. 50-55.
21) Johnston, R., 2004, Towards a Better Understanding of Services Excellence, Journal of Managing Service Quality 14, pp. 129-133.
22) Kaplan, R.S and Norton, p.p., 1996, Using the Balanced Scorecard as a Strategic Management System, Harvard Business review 74, pp. 75- 85.
23) Kaplan, Robert S. and Norton, David P., 2009, Strategy-focused organization, translated by Parviz Bakhtiyari, Tehran, Industrial Management Organization Publication, Eighth edition.
24) Karimi, Touraj, 2006, New models of organizational performance assessment, A Monthly Magazine Tadbir on Management 171, pp. 22-29.
25) Khaki, Gholamreza, 2010, Research Method: a thesis-oriented approach, Tehran, Baztab Publications, Sixth edition.
26) Landy, F. J. and Trumbo, D. A., 1980, Psychology of work behavior, Hommewood, ш,: The Dorsey press.
27) Lytle, R. and Timmerman, E.J., 2006, Service Orientation and Performance; an Organizational perspective, Journal of Services Marketing 2, pp. 136-147.
28) Mintzberg, Henry, 1998, Organizing: five effective model, translated by Abolhassan Faghihi and Hossein Vaziri Sabegh, Tehran, Center for Public Management Publications, Seventh edition.
29) Mirkamali, Mohammad, 2001, Human relations in schools, Tehran, Seyasteron Publishing, First edition.
30) Oakland, John S., 2007, Total organizational excellence: achieving world-class performance, translated by Mohsen Alvandi, Tehran, Rasa Press, Second edition.
31) Patterson, M.G and West, M.A and Shackleton, V.J and et.al., 2005, Validation the organizational climate measures: link to managerial practice,productivity and innovation, Journal of Organizational Behavior 5, pp. 379-408.
32) Robbins, Stephen P., 2007, Organizational Behavior Management, Volume I, translated by Ali Parsaian and Mohammad Aarabi, Tehran, Cultural Researches Bureau Publications, Third Edition.
33) Robbins, Stephen P., 2007, Organizational Behavior Management, Volume II, translated by Ali Parsaian and Mohammad Aarabi, Tehran, Cultural Researches Bureau Publications, Third Edition.
34) Sabeti, Zahra, 1999, Examining the relationship between organizational climate and morale of teachers in primary schools in Qom, MS Thesis, State Management Training Center of Qom.
35) Salehi Hosseini, Morteza, 1996, Educational climate and educational advancement, Journal of the Humanities in Zahra University 9-10, pp. 8-75.
36) Schneider, B. and White, S. and Paul, M., 1998, Linking Service Climate and Customer Perceptions of Service Quality: Test of a

Causal Model, Journal of Applied Psychology 2, pp. 150-163.
37) Shirazi, Ali, 1994, Educational Management, Mashhad, Jahad Daneshgahi Press, First edition.
38) Tabarsa, Gholamreza, 1999, Reviewing and elaborating the role of strategic requirements in the assessment model of performance of public organizations, Proceedings of Conference on Performance Evaluation of Executive Agencies, Performance Evaluation Commission, Tehran, Iran.
39) Talebpour, Mehdi, 2001, Analysis of occupational attitudes of managers, staff and faculty members of physical education and its relationship with organizational climate, PhD thesis, Tehran University.
40) Wongrassamee, S. and Simmons, J.E.L and Diner. P.D., 2003, Performance Measurement tools: The balanced scorecard and the edition excellence model, Measuring Business Excellence 1, pp. 14-29.
41) Yarmohammadian, M. and Bahrami, S. and Karimian, K., 2005, Review of four models of performance management, Journal of Management and Development 63, pp. 19-26.

11/10/2012

Life Science Journal

(Acta Zhengzhou University Overseas Edition)

Call for Papers

The academic journal "***Life Science Journal***" (ISSN: 1097-8135) is inviting you to publish your papers.

Life Science Journal, the Acta Zhengzhou University Oversea Version registered in the United States, is an international journal with the purpose to enhance our natural and scientific knowledge dissemination in the world under the free publication principle. The journal is calling for papers from all who are associated with Zhengzhou University-home and abroad. Any valuable papers or reports that are related to life science-in their broadest sense-are welcome. Other academic articles that are less relevant but are of high quality will also be considered and published. Papers submitted could be reviews, objective descriptions, research reports, opinions/debates, news, letters, and other types of writings. Let's work together to disseminate our research results and our opinions.

Please send your manuscript to editor@sciencepub.net.

Address:
Life Science Journal - Acta Zhengzhou University Overseas Edition
Marsland Press
PO Box 180432, Richmond Hill, New York 11418, USA
Telephone: (347) 321-7172
Emails: editor@sciencepub.net; sciencepub@gmail.com; lifesciencej@gmail.com;
Website: http://www.sciencepub.net; http://www.lifesciencesite.com

Volume 9, Number 4, (Cumulative No.31) Part 19 December 25, 2012 ISSN:1097-8135

Life Science Journal

Marsland Press

PO Box 180432, Richmond Hill, New York 11418, USA

Website:
http://www.sciencepub.net

Emails:
editor@sciencepub.net
sciencepub@gmail.com

Phone: (347) 321-7172

ISSN 1097-8135