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Efficient Data Gathering in Mobile Wireless Sensor Networks

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Abstract: In Mobile Wireless Sensor Networks (MWSNs), nodes are supplemented with implicit or explicit mechanisms that enable these devices to move in space. The packet loss is one of the main challenges that occur due to mobility of such networks and it comes in parallel with energy consumption. Moreover, data collection with the minimum energy consumption is one of the important issues in wireless sensor networks. In the proposed energy-efficient approach, for maximizing the network lifetime, we benefit both cluster and tree structures for data gathering and we select the most reliable and energy-efficient hops for data forwarding. The simulation results show that by using the proposed approach, lifetime, reliability and the throughput of the network will be increased. [Anisi MH, Abdullah AH, Razak SA. **Efficient Data Gathering in Mobile Wireless Sensor Networks.** *Life Sci J* 2012;9(4):2152-2157] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 320

Keywords: Mobile Wireless Sensor Networks; Data aggregation; Residual Energy; Reliability

1. Introduction

Wireless Sensor Networks (WSNs) consists of several sensor enable nodes which are distributed in an environment and use batteries as the energy resource. These tiny sensor nodes, which consist of sensing, data processing, and communicating components, result in the idea of sensor networks based on the collaborative effort of a large number of nodes. Such sensor nodes could be deployed in home, military, science, and industry applications such as transportation, health care, disaster recovery, warfare, security, industrial and building automation, and even space exploration. Among a large variety of applications, phenomena monitoring is one of the key areas in wireless sensor networks and in such networks, you can query the physical quantities of the environment [1], [2] and [3].

In fact, a typical wireless sensor network is composed of a large number of sensor nodes, which are randomly dispersed over the interested area, picking up the signals by all kinds of sensors and the data acquiring unit, processing and transmitting them to a node which is called sink node. The sink node requests sensory information by sending a query throughout the sensor field. This query is received at sensor nodes (or sources). When the node finds data matching the query, the data (or response) is routed back to the sink. For example, if the sensors nodes be in a tree like structure, the base station roles as the root of the tree and each node will have a parent [4], [5]. Therefore, the data items can be transmitted hop by hop from the leaf nodes to the root.

In WSN, In-network data aggregation is one of the effective approaches that can reduce the communication traffic in WSN. Such Schemes can decrease wireless communication among nodes by reducing redundancy in sensor measurements

according to an aggregation function. However, the extracted data in response to a query is only a summary (aggregate) of sensor readings.

In mobile sensor networks, nodes can self-propel via springs, wheels, or they can be attached to transporters, such as vehicles. Sensors have limited energy supply and the sensor network is expected to be functional for a long time, so optimizing the energy consumption to prolong the network lifetime becomes an important issue. Moreover, there is a problem of instability of wireless network and high-fraction of event loss caused by the mobility of network nodes around the mobile Fusion node routes for data collection.

In this paper, we propose an energy-efficient in-Network data aggregation approach in WSN. The proposed approach uses the advantages of both cluster based and tree based approaches. In this approach, the whole network consists of some clusters with the same size. Each node is related to a routing sub tree and each sub tree overwhelms a cluster and the root node of each sub tree is the head node of the related cluster. The energy consumption in wireless transmissions is equal to the square of distance between two nodes in communication. In the proposed approach, all the nodes transmit their data to their neighbor instead of their cluster head. Therefore, the communication distance is reduced and the energy consumption of each node, each cluster and the average energy consumption of the whole networks is reduced and the network lifetime is increased. Furthermore, in the proposed approach, the most appropriate parent according to some benchmarks will be selected for each node which can balance the network load and increase the rate of packet delivery.

2. Related Works

There are several approaches which use tree structure for collecting and aggregating data. The presented approach in [6], with combining Clustering and Directed Diffusion Protocol [7], could process, collect, and aggregate data of sensor nodes without any dependency to the related environment. This paper, with presenting a dynamic clustering structure, could enable the nodes to join to the nearest head cluster while sending data to the gateway node.

Most of data gathering algorithms focus on two key issues. These issues have a network lifetime and saving energy on them [8-11, 4].

In the TAG (Tiny Aggregation) approach [4], each epoch divides to some time slots and these time slots specify to different levels of routing tree in reversal form. In this manner, each node depends on its situation in the tree, and in its related time slot will send its data. The node synchronization of this approach for sending and receiving data could effectively reduce the average energy consumption.

In Directed Diffusion Approach [7], [12] receivers and resources using some attributes for recognizing the produced or required information and the goal of this approach is finding an efficient multi way route between senders and receivers. In this approach, each task is represented as an interest and each interest is a set of attribute-value pairs.

EDDD [13], obtains energy efficiency by using two kinds of gradients, each one uses for different kinds of applications. Whenever the delay is the main issue, real-time filter forwards data through the shortest path between source and sink. In order to perform load balancing between nodes. On the other hand, best effort BE filters will be selected which choose the longer but more energy-efficient paths toward the sink node.

The Link Quality Estimation Based Routing (LQER) is proposed by Chen et al. [14]. LQER forwards data by considering a dynamic window (m, k) that maintain the history of successful transmissions over the link.

In [15] an energy-efficient distributed clustering protocol in the name of Geodesic Sensor Clustering (GESC) is proposed. GESC aims to prolong the network lifetime by estimation of the significance of the sensors relative to the network topology. The significance is calculated in the view of the local network at individual nodes.

The aim of authors in Hierarchical Geographic Multicast Routing (HGMR) for wireless sensor networks [16] is enhancing data forwarding efficiency and increasing the scalability to a large-scale network. HGMR almost incorporates the key design concepts of the Geographic Multicast Routing (GMR) [17] and Hierarchical Rendezvous Point

Multicast (HRPM) protocols [18] and optimizes the two routing protocols in the wireless sensor network environment.

The LEACH (Low-Energy Adaptive Clustering Hierarchy) protocol [19] uses a random approach for distributing energy consumption among the nodes. In this approach, the nodes organize themselves as local clusters and one node roles as a local base station or a cluster head. If the cluster heads can be selected base on a priority permanently and they also can be permanent in the whole life time of system, it is obvious that the bad luck nodes which are selected as the cluster heads will be died soon and the life of all the nodes in their cluster will be finished. Thus, LEACH chooses the cluster head among the nodes which have enough energy randomly. This can prevent the discharging of the battery of a special node. In addition, LEACH uses local data fusion for compressing the data which should be sent from cluster heads to the base station.

FTEP [20] is a dynamic and distributed CH election algorithm based upon two level clustering schemes. If energy level of current CH falls below a threshold value or any CH fails to communicate with cluster members then election process is started which is based on residual energy of sensor nodes.

In EEMC (An Energy Efficient Multi Level Clustering) [21], CHs at each level are elected on the basis of probability function which takes into consideration the residual energy as well as distance factor very efficiently. In this scheme whole information is sent and received by sink node for cluster formation.

Steiner Points Grid Routing was proposed by, Chiu-Kuo Liang, et al.[22] In order to reduce the total energy consumption for data transmission between the source node and the sink node, a different virtual grid structure instead of virtual grid in GGR is constructed. The idea is to construct the virtual grid structure based on the square Steiner trees [23].

In [24] the clustering routing algorithm is used to find out intra cluster and inter cluster link in wireless sensor network clusters are acted as a router, which maintain and distribute of the routing information. After node is selected as cluster head, it will broadcast information that he is the cluster head to the rest of the nodes in the same cluster. The remaining nodes decide to join the cluster according to the size of the received signal.

In [25] three layer mobile node architecture to organize all sensors in MWSN is designed. In this paper, the Shortest Path (SP) routing protocol is used to adapt sensors to update the network topology. SP provides an elegant solution to node movement in multilayer MWSN and reduces energy dissipation.

Ming et al [26] proposed distributed clustering algorithm for data gathering in mobile wireless sensor network. The cluster formation was done using Cluster with Mobility mechanism (CM). Cluster head was elected using two distributed algorithms. It was observed that a better clustering factor and lesser energy consumption were achieved.

3. Proposed Approach

In the proposed approach, it is assumed that the whole network is divided into several clusters; each cluster has a cluster-head (CH). The clustering and the selection of the cluster-head (CH) can be done by using any existing protocol like LEACH, or more efficient approaches such as [26]. The proposed approach is discussed in two main phases including Information Packet Flow and Packet Forwarding.

3.1 Information Packet Flow

In this phase, the cluster head transmits the information packet to its neighbors. The information packets include some information as follow:

Node location: Each node should now its location in prior.

Current Energy: Remaining energy of a node.

Hop count: Number of hops from cluster head.

Speed: The speed of node's movement.

When a node receives the information packet, it considers the sender as one of its possible parents and stores its information. Then, it updates the node location, current energy and data label fields of the packets with its own, increments the hop count and transmit the packet to its neighbors. This process will be done until all the nodes in the cluster receive the information packet.

3.2 Data Forwarding

This phase is studied in two sub phases including Reliable Forward Routing Mechanism and Tree Construction and Data Flow.

3.2.1 Reliable Forward Routing Mechanism

Packet loss is one of the main challenges that occur due to mobility of the sensor nodes in Mobile Wireless Sensor Network (MWSNa) and it comes in parallel with energy consumption. In MWSNs, a node may leave the radio range of its previous hop node which can cause route breakage; therefore, we need a solution for this problem. In the proposed algorithm, data packet will be sent to the node which is the closest node to the destination and does not leave the radio range of its previous hop with the speed of v after time t (Algorithm 1). ' t ' is a constant value that can be assumed different values in different scenarios. For better understanding of the operation of the proposed optimized algorithm, please consider Figure 1.

Algorithm1. Next Hop Selection

When a node receives the request:

1. $J=0$
2. While ($n[j] \neq -1$)
3. {
4. $mindis = 1;$
5. For ($i=1; n[i] \neq -1; i++$)
6. { If ($distance(n[i] \cdot destination) < mindis$)
7. { $mindis = distance(n[i] \cdot destination)$
8. $nexthop = n[i]$ }
9. }
10. if ($j == 0$)
11. $nhop = n[i]$
12. if ($distance(n[i] \cdot node \rightarrow nodeAddr) + vt \leq radio_range$)
13. { $found = True$
14. break
15. }
16. $j++$
17. }
18. if ($found == True$)
19. ForwardRequest($node \cdot request \cdot nexthop$)
20. Else
21. ForwardRequest($noderequest, nhop$)

Considering the distance between neighboring nodes and the destination node it seems that node 27 should be the candidate of the next hop. But, we can observe that this node can move in any direction with the speed of v and time t which is equal to vt . So, there is a probability that after time t , node 27, which was moving with the speed of v , leaves the radio range of the source node. Therefore, in the proposed algorithm, node 27 is not selected as the next hop. So, node 6 will be selected as the next hop because it is the closest node to the destination comparing to all neighboring nodes which do not leave the radio range.

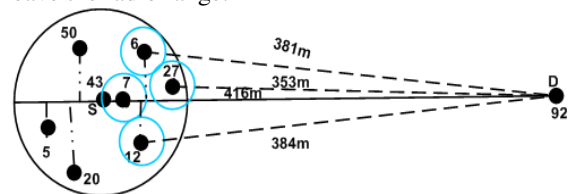


Figure 1. Selecting the next hop in the proposed algorithm

- The distance that a node passes with the speed of v at the time t (vt).
- Radio range of node S

Figure 2 illustrates the mechanism of data forwarding in conventional algorithms and the proposed algorithm.

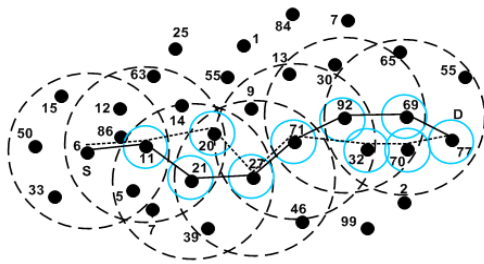


Figure 2. The route discovery in the proposed approach and conventional algorithms

- Radio range of a node
- Selected route in conventional algorithms
- Selected route in the proposed algorithm
- The distance which the node pass with the speed of v at the time t (vt)

In conventional algorithms, the source node will select node 11 as the next hop because it has the minimum distance to the destination comparing to all single hops neighboring nodes of the source node. Also, node 11 will select node 20 as the next hop and following that, node 20 will select node 27 as the next hop. Selecting the next hop will be continuing until reaching the destination node. In the proposed algorithm, the source node will select node 11 as the next hop because it has the minimum distance to the destination and also after the time t , it does not leave the radio range of the source node. So, Node 11 will not select node 20 as the next hop because although it is the closest node to the destination, but there is the probability that it leaves the radio range of node 11 after time t . So, node 21 will be the candidate of the next hop of node 11. Selecting the next hop will be continuing until reaching the destination node.

3.2.2 Tree Construction and Data Flow

When the entire nodes received the information packet, each node selects its parent which should send its data to it. This selection will be done based on the following filters:

1. First, among the possible parent, the one which has the least hop distance from the cluster head (Closest node to cluster head) and does not leave the radio range of its previous hop with the speed of v after time t will be selected.
2. If there is more than one node having condition 1, the node which has the most residual energy will be selected as the parent.

All the above conditions lead to the best parent selection. Filter 1, selects the Reliable shortest path from a node to cluster head and filter 2 increases the network lifetime by participating most durable nodes.

4. Performance Evaluations

The proposed approach is simulated and evaluated with J-Sim (Java-Based simulator) [28]. J-

SIM is simulation software selected to implement the model. It was chosen because it is component-based, a feature that enables users to modify or improve it. J-Sim uses the concept of components instead of the concept of having an object for each individual node. J-Sim uses three top level components: the target node which produces stimuli, the sensor node that reacts to the stimuli, and the sink node which is the ultimate destination. For stimuli reporting, each component is broken into parts and modeled differently within the simulator; this eases the use of different protocols in different simulation runs. In our simulation analysis, sensor nodes are randomly distributed in a $160m \times 160m$ area. The radio range of each node is $30m$ and the default parameters for radio communication model of J-sim are used. Two mobility models are used in evaluation: Random Waypoint without pause time [29], and the Reference Point Group [30] mobility model. We have chosen these models since they are simple and apply to a large number of possible scenarios. The cluster-head is formed by the sink. Source node randomly sends packages with constant bit rate (CBR) to the sink. Packet size is 64 bytes and package rate is 5 pkt/s.

Our energy model is like the energy model in [27]. In this model energy consumption for transmitting k bit is equal to:

$$E_{TX}(K, d) = E_{elec} \times K + \epsilon_{amp} \times K \times d^2$$

And the energy for receiving k bit is equal to:

$$E_{RX}(K) = E_{elec} \times K$$

In these equations, d is a constant value which relates to the distance between two nodes and ϵ_{amp} and E_{elec} are also the constant values which are defined previously and they are equal to:

$$\epsilon_{amp} = 100 \text{ pJ/bit/m}^2 \quad E_{elec} = 50 \text{ nJ/bit}$$

We have compared the proposed approach with LEACH as an innovative Energy-Efficient clustering approach and the approach in [26] which we have called it in our simulations Method 2 as a modern Energy-Efficient clustering approach. As it has mentioned before, our idea is not related to clustering and the selection of the cluster-head (CH) and they can be done by using any existing protocol like LEACH, or more energy efficient approaches. Therefore, For Clustering, we have used the mechanism of Method2 in our simulation which is more energy-efficient in comparison with LEACH.

According to Figure 3, the total residual energy of the nodes will be decreased, gradually. But Comparing to other approaches, the proposed approach, because of using the mentioned technique, can remain more energy.

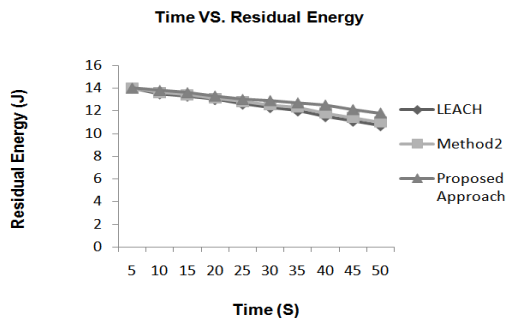


Figure 3. The remaining energy of the nodes after passing time

Figure 4 illustrates the throughputs of the mentioned approaches. Throughput of a node is defined as the average rate of successful message delivery over a communication channel. Thus, we can observe that has the highest throughput among LEACH and Method 2.

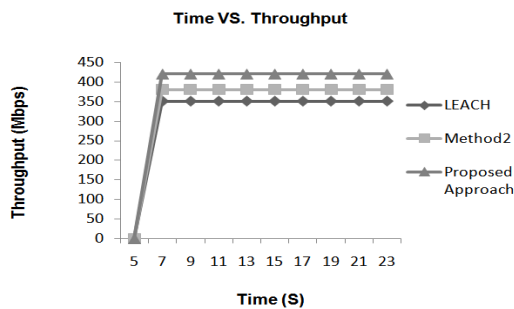


Figure 4. Different Throughput of the approaches

Figure 5 presents the impact of nodes' movement speed on the packet delivery ratio. It illustrates that increasing the nodes' movement speed; reduce the rate of packet delivery. In our proposed approach as the next hop is always the most reliable hop, the rate of packet delivery is better than other approaches.

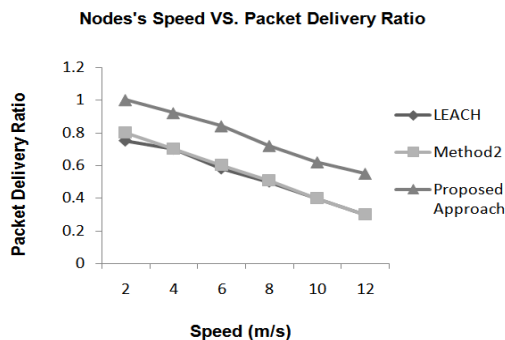


Figure 5. Impact of nodes' movement speed on the packet delivery ratio

5. Conclusions

In mobile sensor networks, nodes can self-propel via springs, wheels, or they can be attached to transporters, such as vehicles. Sensors have limited energy supply and the sensor network is expected to be functional for a long time, so optimizing the energy consumption to prolong the network lifetime becomes an important issue. Moreover, there is a problem of instability of wireless network and high-fraction of event loss caused by the mobility of network nodes around the mobile Fusion node routes for data collection. In this paper, we have proposed an energy-efficient and reliable data aggregation approach in mobile wireless sensor networks which uses an efficient strategy for forwarding data toward the best route. In our algorithm, there are three factors which enable the nodes to choose an appropriate parent in term of energy. These factors are distance, residual energy and chance of leaving the radio range. With the suggested mechanism, the remaining energy of the nodes and the packet delivery ratio will be increased and the life time of the whole network will be increased, too. We have evaluated the proposed approach with some famous and efficient approaches in this area. According to the simulation result, our approach achieves better results in term of maintaining the residual energy of the nodes, throughput and packet delivery ratio.

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Shanghai Cooperation Organization, the Islamic Republic of Iran's security and of United States of America's interests

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Abstract: Shanghai Cooperation Organization which is initiated from China is an organization that seeks a positive and constructive goal to establish regional cooperation. Establishing the organization in the Caspian region with poor level of regional cooperation can create a regional convergence. Regional cooperation issue in Caspian Sea is not on the extent and quantity of the mechanism but the quality of cooperation is speaking. Naturally, in this convergent context, regional nations will be strengthened in order to confront global challenges and threats based on continental and regional criteria. Some analysts know SCO as an instrument for China and Russia to prevent American from accessing to the vast resources of energy in the Caspian Sea. Caspian region is considered as an energy source substitute or successor by many political actors, including United States, China, Russia and EU in the future. This issue is related to its dependency to abundant oil reserves in Saudi Arabia and some other OPEC member states make it possible to speed up the exploitation of these resources to some extent. So, in fact the Caspian can become one of the strategic areas of energy in the world. While, the Caspian can be considered not only as an encountering points of great actors' interests and their regional influence but also as a plateau with high cooperation capacity. Cooperation capacity in the Caspian region is initially relates to coordination among the efforts of all countries, including geopolitical players and the coastal countries. This article investigates the importance of Caspian from the points of SCO member states' interests and United States of America on the other hand.

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1. Introduction

Following the attacks of September 2001, Caspian region in terms of its political importance replaced by Middle East and since then America concentrated its war against terrorism, against the former Iraqi regime, and now against the nationalist and religious insurgents in Iraq in the region. However, Caspian region has maintained its importance as same as before respect to world peace, stability and USA security. Caspian Sea region has been a strategic crossroads for centuries for centuries which linked the empires of Europe, Asia and Africa each other. Control over its important lands and water ways, especially in respect to the spice trade guaranteed the great power and wealth. The vital importance of the area was also a motive for the competition which is called "Great Game". During the Cold War, ideological conflicts increase the geopolitical attractiveness of the region and turned it to a fault sometimes in the East and West campaign, namely capitalism and socialism (Rozman, G., M. Nosov, and K. Watanane, eds. 1999). Nowadays, as the technological transformation of the region decrease the region importance as a commercial way and Cold War is ended, controlling its hydrocarbon resources attracted the attention of political actors and international trading and a central significance has

been given to the region in world geopolitical scope. Although history teaches us new borders are followed by serious risks, but they carry some opportunities for advancement. Current transformations in the contemporary world enhance the importance of nation's cooperation to counter to different threats with international nature. In such circumstances, the role of regional organizations is outstanding. On the other hand, Soviet bloc collapse consolidates the idea that regional organizations make up the twenty-first century blocks. SCO is one of the emerging regional organizations that have significant growth and authors liken it to NAM with scientific function and the twenty-first century definition. Given that Iran was accepted as a supervising member and it is expected to be a member in the future procedures, so recognition of the organization and its functions and positions in regional and international system seems necessary (Bakshi, J.2001). It should be noted that USA as one of the superpowers in international system knows itself as a partner in Asia issues and Asia transformation as a vital factor in its interests.

So it is not indifferent to these transformations as far as plays its role by its military presence in Asia. Thus, United States of America makes a close relationship with the SCO and any

tendency (orientation) in SCO can overshadow USA benefits (Vorobiev, Vitaly. (2001).

1.1. The main question:

The main question is whether Caspian region can be as a confluence of SCO members' interests and USA in future?

2.1. Hypothesis:

- 1- Caspian region can be as a confluence of SCO members 'interests and USA.
- 2- Caspian region can increase the convergence among the SCO members.

3.1. Caspian Sea and the SCO

Caspian Sea region are important for Iran in respect of different strategic aspects, Including: connecting the northern ports to European countries, linking Iran to Russia without intermediaries who can be useful in critical situations, this area can be one of the exchanging ways from the West to East, because it connects Europe to Central Asia and from there to the Far East, Afghanistan and India through Georgia, Azerbaijan, Kazakhstan and Turkmenistan. Therefore, this area could be one of the major ways from West to East, the importance of oil and gas resources and Caspian Sea market for SCO members and Western especially European countries as well as the historical – geographical axis from north Arctic Ocean to the Indian Ocean and from Volga to Lena which is heartland according to Mackinder are the other factors make Caspian Sea as one of the strategic areas in the world (Xinhua News Agency.2001). Doubtlessly, any convergence activity with independence state leads to better situation for Iran. Islamic Republic of Iran is less concerned about the regions that are in the Shanghai Cooperation Organization since Shanghai can play a role in controlling or restricting them. America is interested to Azerbaijan due to its own strategic location and Azerbaijan proximity to Russia, Chechnya and it is trying to establish a joint security force called the "Caspian Protection Guard" or hereby protect the oil and gas resources as well as energy installations in the Caspian basin. The cost for establishing the joint security force is estimated about one hundreds millions dollars and US Defense Department has spoken about sending one hundred and thirty million dollars to realize the project. America's effort to establish a military station in the Caspian Sea basin countries made worry many countries in the region and above all Russia and Iran so that many adjacent countries gathered their warships in the form of a military plan as a " Caspian Sea fleet - Kasfor " together. Russia on the eve of an international conference arranged in which Russia and Iran emphasized on the importance of preventing the conversion of Caspian Sea basin to a military zone for NATO's forces (Goncharov, Pytor). American diplomat, Robert McFarlane says: "Converting the

populous countries like China and India to major petroleum products consumers requires searching for new energy sources that increase the strategic importance of the Caspian Sea. While Islamic Republic of Iran has common interests and benefits with Russia in Central Asia, Caucasus and the Caspian Sea, concerning about the increasing influence of western countries especially the USA in the region is a common point for either Iran or Russia. But Iran does not at all agree that Russia reach to everything it wants in this area, because it may harm Iran's security and national interests. So Kharrazi, Iran former Foreign Minister, in his meeting with Russian authorities was hold in February 2002, pointed to the point that some Caspian Sea adjacent countries want to have a close relationship with Western countries and implicitly expressed his concerns about Russia tendency toward its dominancy on the situation and not allowing the other countries to set their own foreign relations arbitrarily (Wu, H. and C. Chen (2004). The fact is that Caspian region and Central Asia countries are junction scene of all Western governments, Russia, China, as well as Islamic world as a whole, including Iran, Turkey, Afghanistan, Pakistan and even India interest (Zyberk Henry Plater-.2007). Russia, on the other hand, is a country with nuclear weapons that is willing to pretend itself as a victim of Chechen terrorism attack. However, it refuses to involve active American war against terrorism and considers the war in Afghanistan and Iraq mainly for sake of USA's will to be dominant to the region. Other countries in the Caspian region, although not related to terrorism and nuclear weapons, but have challenges at the international level. For example, the Azerbaijani-Armenian dispute over Nagorno-Karabakh has continued to remain, Turkmenistan and Azerbaijan needs to negotiate about their claims over Caspian region (SCO Secretariat (2001). Excluding Russia, other countries in the Caspian Sea are not in better situation than Iran in terms of investment in non-oil sector and added value in industries (Wilson, Jeanne L. 2001). In Azerbaijan, industry section is obviated totally. The reality is that Caspian region countries remain undeveloped and completely separated from international non-oil market. Among them, only Russia can claim that has development and participation in international markets. Caspian region states have been backward technologically states for decades. While in countries such as Iran and Russia, people could create strong competitive economy. Caspian region mainly assume their national defense force and power in the form of military, thus they expense high percentage of their resources on police and army. Practically, Russia as a super power with nuclear weapon and high energy reserves, gradually compete to America, due to Russia empowerment in

the region in where it influences traditionally, the presence of trans-regional force become less in spite of great amount expenditures. Clearing away the America's air base in Uzbekistan and setting a schedule for the U.S. troop's withdrawal of Iraq and Afghanistan can be pointed as an example. Meanwhile, the economic ties between Azerbaijani and Russian neighbors is emerging that indicates this small republic of Caucasus is involved in a kind of isolation, despite of its geopolitical position will lose its function as a strategic ally for the West by increasing Russia and Iran activity as regional actors. Active presence of the Islamic Republic of Iran and Russia in the Azerbaijan economy has led the Azerbaijan to practically pay more attention to its neighbors' interests. Caspian littoral states' heads conference is a very good example in which the military maneuver of trans-regional allies were prevented in Caspian Sea, so the presence of trans-regional countries were lesser than before. Among this, Armenian state with its special security ties with Iran and Russia has become one of a first level ally to Caucasus regional actors and made Azerbaijani authorities worried by observing Russia's policies. In this regard, Azerbaijani state express worry about the recent decision made by Russia on creating facilities for delivering military weapons and equipment to Armenia (SCO site, 2006).

4.1. Russia and Iran:

Russian and Iranian interests are very complex in the Caspian Sea zone, undoubtedly, in the one hand; these two countries cooperate with each other against the growing influence in Iran's nuclear program in military (arms selling and military technology) as well as economic field. Recently a cooperation deed has been signed between Russia and Iran for the next 10 years and accordingly it is predicted that the turnover of commodities will increase and its volume will reach to 10 billion dollars. On the other hand, these two countries have taken different positions on Caspian legal status (Troitskiy, Mikhail.2007). A kind of geopolitical-economic interest is hidden in Russia mild position towards Iran. In geopolitical Caspian area, Iran as the biggest neighbor of Russia possesses an important interest and is considered as one of the regional actors. Russia always desires to establish friendly relations with this country due to its adjacent to Iran. This desire especially is raised from Iranian influence to the South Caucasus and Central Asia. In addition, the alliance with Iran provided Russia with opposition tools against the development of the North Atlantic Treaty Organization and the U.S. influence in South Caucasus and Central Asia to Russia, thus from the strategic points of view, maintaining friendly relations with Iran is most important for Russia. Russia has taken support policy against Iran's

admission as a permanent member of the Shanghai Cooperation Organization rather than opposition. There is a close military and economic cooperation between the two countries and Russia wants to know Iran as its important strategic and economic partner. With regard to nuclear cooperation between two countries, Russia efforts have been exclusively dedicated to economic issues. Warnings and stimulation against Iran may not change the relationship between the two countries. Russia recent approach arose from its aggressive policy toward (Strategic Research Center, 1384), thus Russia diversifies its interests and cooperates with other governments and shows its self-control system and resistance weights towards other states. For the Russian oil pipeline construction and operation is important not only economically but also it is a political issue which allows controlling the region situation effectively (Olcott, Martha Brill.2006). Iran and Russia should be two major converged forces in the region considering the wide strategic geography and their population. But in reality these two countries have marginal influence in the region and it appears to take up a position often alongside the non-convergent forces. Iran's conflict with United States of America and Russia competition to it was a major obstacle before the two countries to play more effective and active role in different regional affairs. For example, Iran and Russia plays a side role in the intercession in regional conflicts and struggles including the Azeri-Armenian conflict, while they themselves have unsolved problems and conflicts with some other countries or ethnic groups their own country or the region. And more importantly, these are countries that still need to address the Caspian Sea issues and find a solution for its legal regime.

5.1. Relations between Iran and China:

China, the other main player seems dark. On the one hand, the growing interests of the country and its presence in Central Asia are clear. But it should be emphasized simultaneously that its presence has not been crystal clear yet. One of the China's important interests in Central Asia is to access to energy resources through the Caspian Sea. These countries possessed a great attractiveness for China and its powerful industries. Supplying energy is considered as one of the major goals for China's foreign policy (Huang, Chin-Hao .2006). The Chinese government is also adjacent to the Middle Asia and is an unquestionable power in the world and confirms its own increasing oil and gas need to energy. Chinese presence in the region is for many different reasons, one its aspect referrers to domestic concerns. China has possessed a significant minority of Muslim population. The term of significant is applied regards to quality and not quantity. There are Muslims in

northwestern of China. This area was formerly part of Eastern Turkestan. Turkish language, Persian handwritings and communication among region people with Muslim is important in terms of quality. The movements are led by Uyghur's which are secessionist based on Chinese government's claims, are mainly located in Turkey and Central Asia. They have adjusted its relations with regional countries to neutralize this threat, for instance, the Chinese Embassy in Yerevan is the largest foreign embassy in Armenia, and while it is not seem Armenia be the most important country for China. China wants to show its opposition toward Ankara's policies by its presence and hereby can pressure Turkey. Because some of the Uyghur leaders are present in Turkey, Uighur leaders attended in Kazakhstan in the past. However, china could control this issue by making border cooperation with Kazakhstan and precede it very carefully. So, china presence in Middle East can be justified by its own worries. Secondly, China views to the Caspian region is as an "energy source" and "labor market", so has invested on Neka - Rey pipeline in the Caspian region to understand the energy market, meanwhile Caspian region is reckoned a very good market for Chinese cheap goods and Beijing will not ignore the market. Development and investment on SCO in 2002 indicated that Chinese firms are very interested in the developing Caspian zone (Fatemi, Sahab). Now use the Caspian Sea, Central Asia and Caucasus opportunities can be considered as a supplement or alternative for Iran traditional channel in the Persian Gulf and through Turkey. This strategy is simultaneous with countries such as China's enthusiasm to use new ways for energy supplying and accessing to new markets for Chinese goods. For many years, China has been concerned about single-trip of crude oil and liquefied gas entering through Indian Ocean which is associated by American force possible supervision and intervenes in Malacca Strait. Using new pipelines from Russia and Kazakhstan to China and beyond the Himalayas and the Tien Shen mountains far from American forces and their oversight, improve energy security in China. The Chinese hope that a pipeline from Iran or the Caspian Sea reach to western parts of China through dry land. Consumer market in Afghanistan, Central Asia and Iran is so attractive that economizes the cost of constructing new ways from Syngyang to Kyrgyzstan, Kazakhstan, Tajikistan, Afghanistan and Pakistan to the West (Moore, M. (2008). In total, China officially emphasized that it does not intend to demonstrate its influence or following its ambitious purposes. But undoubtedly, Caspian is one of the key elements of security or security support for china. In China, security issues are very important and nowadays great attention is paid to it by china and so

the issues of strengthening cooperation within the SCO framework with some of Caspian littoral countries as members are also very important. China has taken the policy of approached position toward Iran. Along this a 25 years energy cooperation program has been signed and it brings two countries relation into new phase. On this basis we can say that at the regional analysis level, China's view to Shanghai organization initially as a tool for institutionalized consolidation in the security environment of the country and secondly know it as an institution to deal with threats against its territory. As well as in Macro-level analysis, it can be said China followed several targets by institutionalized redefining its power in influence via various ways, including the Shanghai Cooperation Organization:

- 1-Creating congruent regional and international environment with its emergence as a major power within the international system;
- 2 – Determining the boundaries for (acceptable) conventional behavior in regional level at first and in the future at international level;
- 3- Reducing and eventually eliminating USA presence and influence as its main rival in Central Asia zone;
- 4- Institutionalizing the presence and influence in environment.

In fact, the Chinese find clearly the fact that the sustainability and future of their economic growth, both in terms of energy consumption and supplying, increasingly tied to the Middle East and Persian Gulf region and so they requires strengthening the presence in and investment on energy industry in the region (Zhong Wu.2007). So that the Fars News Agency quoted from Pulse Asia that China's economy minister reiterated that China's trade volume with SCO member countries has been 7 fold in the past 10 years. Chen Deming at the news conference on the sidelines of the tenth meeting of the Shanghai Cooperation Organization in Astana, Kazakhstan's capital said the Shanghai Cooperation Organization has been operating for 10 years. The organization is not a newly established organization, and now enters to its maturity stage. He also noted the economic and commercial cooperation between the countries of the Shanghai Cooperation organization is being strengthened. Volume of Chinese trade by SCO member countries increased to 7 fold during the 10 years and has reached to 84 billion dollars. China is at the second order of the most important economic partners of Tajikistan and Kyrgyzstan. As well as, China is the main Kazakhstan and Russia's trading partner (John Calabrese.1992). On the other hand, there is concern that America used the war against terrorism to enter to Central Asia and limited China strategic space in there. But SCO should not be a problem in bilateral relations of China - America.

Both countries have the opportunity to work together to change their perception. In fact, China and America have common interests in terms of regional cooperation in Central Asia. They can cooperate in several fronts, such as countering to terrorism, energy, economic development and SCO has potential to be the basis for their cooperation (Energy Business Review (2008)).

6.1. Shanghai Organization and Caspian neighbors Security

Institutions are considered fundamental in any order, international order is not excluded. In this order, the actors attempt to decrease vulnerability by creating the institutions to manage their benefits better. SCO is one of these institutions in which actors have common points in the area of vulnerability and interest due to various issues and above all geography. This "sharing" has made these countries to management their interest better and reduce the vulnerabilities by forming the Shanghai Cooperation Organization. Using this tool, Iran as observers which seeks to gain full membership in this organization, naturally seeks to reduce vulnerability meanwhile manage their interests optimally. Obviously, in this way, finding organization's capabilities and conforming the needs and desires to the organization goals and mission is very important. One of the main features of the Shanghai Cooperation Organization is the apparent imbalance in the role and status of the members. In other words, the SCO is an Organization with newly born countries in Central Asia which are not considered an important actor at the regional level, in the other hand there are major powers like China and Russia with clearly global growth. From this point of view, the will and desires of its main actors should mostly be addressed to know the organization and predicting its future (Cutler, R.M. (2004)), however it should be noted that the energy consumer emphasized on diversification of input energy resource, Islamic Republic of Iran should be considered as a producer with diverse resources in its territory; because Iran is not only a middle east countries and Persian Gulf oil producer, it is also belongs to Eurasia energy region; means that Iran has great and various capacity to play strategic role in energy exchange market in Caspian Sea and central Asia and diversity in supplying from Iran and demands from China and India can be as a point for strengthening energy cooperation inside the organization (Kang, D.C. (2003)). Principles and objectives of the Shanghai Convention institutions are not contradicted with the principles accepted in the field of foreign policy as well as Iran strategic approaches, regardless to political viewpoint, China, Iran and Russia's are moving in dynamic bar of remarkable economic growth and considering the situation of the regional institutions and its good

starting point, it is expected to face with the good fortune in future. Iran membership in the institution accelerates its economic and political objectives basically and participation of countries like Iran in regional contracts will lead to establishing more balance and stability in the security space of Caspian. Caspian is main priorities in Russia's foreign policy. Russia's traditional interest is done in the Caspian through strengthening its position by increasing cooperation in various fields. Exploitation of underground wealth in Russia or other parts of the Caspian Sea to ensure energy security for Russia is very important. Indeed, Russia follows a long-term objectives regarding to its increased military presence in the region and meanwhile by Russia initiative, the Security joint Treaty Organization and the Shanghai signed a joint security cooperation protocol which can be a basis for creating an Eurasian political-military block like NATO in the territory from Belarus to China which has been targeted by Russia, creating the SCO is one of Russia's new strategy consequences. Uzbekistan closed up its American bases in the same period, the work that could not be conducted previously. This is considered as a success for Russia. Among six members of the security treaty, Armenia is a country in which army is equipped by Russia. On the other view, Iran benefits from Russia military presence in the region, while they are competitors in energy area, but they adopted similar policies to Middle East and Caucasia and it is reducing trans-national power attendance. Since the attendance jeopardizes the security of the region and will lead to regional disputes that will reduce the level of trust between countries. Iraq's future, the presence of foreign forces particularly the large number of military forces and Americans sophisticated equipment and communications in the Persian Gulf and all Arabic neighbors of Iran, America's efforts to create a new block consisting of Arabs and Israel against the Iranian influence threat in the Middle East, exacerbating the disputes between Shiite and Sunni people, high pressure oil producers to increase the product and decrease oil prices are altogether homogeny and targeted Iran from other regions that seems Shanghai cannot afford helping Iran. Apparently, Iran in addition to membership in the SCO should use other actors and other mechanisms as well to promote its national security. Iranian presence in the region can reduce the presence of China and the united States, which is coincide with Russia benefits because Iran and Russia follow similar policy in Caucasia. In the other hand, the Russian presence in the region reduce America's military presence that will be in favor of the Islamic Republic of Iran because it reduces threats against Iran meanwhile Iranian presence in the SCO promotes its security relations

with its neighbors and two permanent member of UN Security Council (Russia and China) that will practically lead to regional security elevation. If Caspian Sea is rich of oil and gas, it is not most important mineral resources for the nation because Iran and Russia possess great deal of another resource that makes them free of the need of Caspian oil. Aside from Russia and Iran, there are other three neighbor countries in Caspian Sea as Turkmenistan, Kazakhstan and Azerbaijan and other countries that are located in sidelines farther away. Turkmenistan has clearer situation than other countries. The country possesses gas supplies and uses it to strengthen its relations with Russia. Of course, Turkmen have signed a contract for exporting up to 100 billion cubic meters of gas to Russia but due to limited pipeline capacity, the contract is about annually 8 billion cubic meters gas export to Iran. Also, American missile defense system is considered as a threat not only for Iran but also for all Asian countries and the SCO members. On the other hand, Iran's strategy in dealing with America unilateralism was also considered by members. In fact, all members' perspective toward the world and international policy amplifies Iran strategy. However, regardless of political-economical points of view India, China, Iran and Russia are moving in the direction of economic growth and dynamism. Gathered the poles in one room place the SCO at the high level in economic competitiveness bargaining. However, the Caspian, not only as a place of encountering and confrontation of great actors and the scope of their influence, but also as a plateau with high capacity of cooperation should be considered. Cooperation capacity in the Caspian region is related to coordinating the efforts of all countries, including geopolitical players and the coastal countries. Energy experts believe that the main cause of the West and especially America's tendency toward the Caspian basin is oil and gas resource shortage in the world and searching for new energy sources. Most of powerful countries seek these limited energy resource which in turns requires counted and boring campaign. Thus western countries and American wants to locate in Caspian Sea basin by using various and ludicrous excuses and among them maintaining the establishment and security of Caspian Sea. Beneficiary countries in the region need to act quickly and take the necessary preventive measures in this regard to prevent the occurrence. In discussion on members' opposition toward the American presence and influence in the region, the fact should be noted that the approach and reason for opposition to America influences is not identical. while two powerful countries (Russia and China) knows the presence and influence of America per se as a strategic threat to themselves and believe that this

strategic environment limit their strategic space and scope of influence, although four smaller organizations countries (Uzbekistan, Kazakhstan, Kyrgyzstan and Tajikistan) wants to balance the America and china-Russia axis, they are two opposed of America presence and influence for the two reasons: 1) In most cases, their economic, political, security dependency to Russia they will be cause their following of Moscow's policies. 2- America's involvement in regional regime changing (Weitz, Richard.2008). Although SCO initially aimed to resolve border disputes between China and four neighbor countries, totally the in the Commonwealth countries was created, but it seems that it proceed to become a regional alliance with the military and security objectives (Roland Dannreuther.2003). With USSR collapse, the Central Asian countries faced with serious problems in all areas of security issues that affect the China and Russia. In this regard, the Central Asian states plus Russia and China established the Shanghai Cooperation Organization. Central Asia has a special position in Russia and China's strategic calculations because of various political, economic, and security reasons. Restricting America's role in central Asia region by applying region countries and asking these countries to take up Washington military basis is another aim followed by this organization. It is felt that this trend may shake the political processes that can provide income, social order. Regional arrangements are suitable tool in the hands of national governments to maintain their political independence and as a means to promote national interests and political mobilization and cooperation. Today in our region, energy and its transition energy, transit of goods, economic mutual needs, transmission and sale of narcotics, and cultural identity crisis in the process of globalization as well as communication between traditional and strong values with democratic trends in political structures are as major issues for the Caspian region which provides a list of requirements for regional cooperation in Shanghai organization. One of the security threats in the Caspian region currently is lack of legal regime or unsettling the legal status of the basin. According to experts, there is a security problem in the region and it is the militarization and preventing its militarization by coastal states. The possibility of oil terrorism emergence should not be forgotten (Purnomo Yusgiantoro.2004).

2. Discussions

For a summary of what was said, it can be noted that the Caspian littoral states faced with several political, economic, social, cultural, spatial, institutional and international challenges to be developed. In these countries, issues such as national security, collective sovereignty and human

development should be placed at a high degree of priority. Another key to success in these lands is mobilization and rational use of available resources. Despite the wealth resources as oil and gas reserves, these countries should focus on clarifying and accountability in revenue gained from mentioned resources. Limited natural resources should be spent on sustainable development, namely human and institutional development, and this should be done soon. On the other hand, Iran's security and its interests in the areas of Shanghai and the Caspian region is a sensitive and specific and should be known the importance of these regions is not less than Hormuz Strait. Western countries movement, especially Israel and the United States in these areas should be more carefully considered and political, economic; military and security actions should be taken to providing Iran interest. However, the Caspian should be considered not only as a place for encountering and confrontation of the great actors' interest and the area for their influence but also as a plateau with high capacity of cooperation. Cooperation capacity in the Caspian region is related to coordinating the efforts of all countries, including geopolitical players and the coastal countries. Furthermore, there are areas for economic potential that can provide opportunities for all Caspian region countries. Relying on these two components, the organization can be considered as a tool of stability in security environment and use it in order to stabilize the security environment and paving for achieving the goals in vision plan.

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The survey of effective factors on domestic violence The case study: Neyriz and Estahban cities

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Abstract: Domestic violence is one of the most comprehensive kinds of violence in the world. Study and research on this issue could determine the incidence of these events and its causes. So, the results of such research and studies can be used to find ways to minimize this phenomenon and improve the life of some women tackling it. The main objective of the present study was to evaluate the factors influencing domestic violence against women in Neyriz and Estahban cities. For this purpose, a sample of 600 people was chosen from the studied population. After reviewing other studies and a theory related to violence, some hypotheses were raised and tested. The results showed that the variables financial independence, empathy, and behavior control have a relationship with domestic violence and no relationship was confirmed between the variables stereotypical beliefs and social capital with domestic violence.

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Keywords: Domestic violence; Women; Social capital; Empathy

1. Introduction

Women are half of the members of human community and should have equal rights to another half. Unfortunately, we have observed all forms of discrimination and inequality against women throughout human history, except for a short period. It is centuries that women are considered second-class human beings. Violence against women is not at all restricted to underdeveloped or Muslim communities. Violence against women has broken the boundaries of income, culture, age, and social, economic, and educational class. Women, whether in the Northern Hemisphere or in the Southern Hemisphere, whether in rich and developed countries or in underdeveloped and poor countries, from any race or nationality, are always the victims of violence causing them to be deprived of the basic human rights. This violence have ever been within the families and their footprints are still observable, despite the cultural, social, and even legal growth of modern societies. Home is the first and most important social institution that most people get their first socialization experiences there. In every culture, there are many beliefs and sayings about home as safe and comfortable environment. Home is imagined as a haven of security and prosperity. But for many women, home is a place full of pain, suffering, humiliation, and violence; a violence imposed by men on women at home; a pervasive, prevalent, and widespread violence and a very complex topic for research. It has been stated in the report of World Health Organization in 2006 that 18,000 women of

all ages have been killed due to domestic violence in Europe (Krug *et al.*, 2002). Quoted by Stickley (2008), violence causes decline in women's participation in social institutions, creation of a sense of confidence, economic inequality, etc. It is very embarrassing to the communities and countries that do not do anything to stop it and not only tolerate violence but also neglect and deny it. The main objective of the present study is to evaluate the factors influencing domestic violence against women in Neyriz and Estahban cities. Research on violence against women has been stated since nearly 4 decades that are becoming more comprehensive and deeper day by day. Some of this research (from the past to the present) will be mentioned in next parts. Due to the limited number of paper pages, a summary of previous research and studies has been provided in Table 1. Several factors may affect the formation of social phenomena. Scholars of different sciences and domains look at them from different angles and make theories about them. Phenomenon of violence is no exception. Psychologists, sociologists, criminologists, biologists, and other experts have studied a specific aspect domestic violence. These views and theories will be mentioned in next parts.

1.1. Acquired theories

Social learning theory: This theory emphasizes that people learn to be aggressive through experience or following the patterns. Children who witness violence or are treated with violence in family as the first unit of learning, learn that aggression is an appropriate and effective behavior to get what they

want. They also learn that the use of force is legitimate or not and whether aggression is a way to resolve interpersonal conflicts (Barnett *et al.*, 2004, quoted from Olson *et al.*, 2004; 6).

Table 1: A summary of previous studies on violence against women

Number	Year and author(s)	Title and subject	Variables	Findings
1	Gülçür, L. (1999)	Evaluation of domestic violence and sexual assault in Ankara	Physical, psychological, sexual and economic violence	89%, 39%, 15.7%, and 5.2% of women were treated by psychological violence, physical violence, sexual violence, economic violence, respectively.
2	Tong, A.R.W.C. (2003)	A multivariate model to understand the violent of husbands against their wives	Being exposure to domestic violence in childhood, personality disorder, Alcoholism, Social and economic base of the husband, satisfaction of marriage, Psychological aggression, and positive and conforming trends of spouse abuse	A significant relationship was observed between the studied variables and domestic violence
3	Pelser, E.et.al.(2005)	Violence, the partner of life: The Results from an international study on violence based on gender in Malawi	Physical, emotional, economic, and sexual violence in relation with traditional beliefs of society, educations, alcohol consumption, and family income	There was a significant relationship between different types of violence and traditional beliefs of society, education, alcohol consumption, and family income
54	Marger, Martin N. 2001	The use of social and human capital among Canadian business immigrants	Social capital, parent's negligent behavior patterns, patterns of psychological damage, and domestic violence	Increased rank in social capital scale cause reduction in parent's negligent behavior patterns, patterns of psychological damage, and domestic violence.
5	Stickley, A.et.al2008	Attitudes to violence against women in intimate and marriage relationships in Moscow	Violence, education, economic problems, and alcohol consumption	Violence had an inverse relationship with education and a direct relationship with economic problems and alcohol consumption

Family systems approach: In this theory, family is considered as a dynamic unit in which the behavior of a family member and the incidence of that behavior has an impact on the behavior and responses of other family members (Cunningham, 1998) and the family system is understood based on

processes, patterns, and mutual relationships (Olson *et al.*, 2004). In this approach, violence of confidants has been studied as part of a broader pattern including negative reciprocity, serious pattern, showing the dominance in the family, being rejected, and being ignored. Authority theory: In this theory, the violence caused due to the conflict between man and woman in the family is attributed to the level of authority and domination of man in the family. If authority increases, conflicts also increase. Generally, violent and improper behavior is imposed by those in power on subordinates. This means that those in power want to maintain their surrounding structure by using force and violence. Men apply this tool to dominate women, but degrees and forms of using this tool vary in different societies. Feminist theories: Although there are several feminist perspectives, most theorists of this approach believe that the power imbalance is the cause of violence against women in the family. This imbalance can be seen in patriarchal societies that their structure impedes the equal participation of women in social, economic, and political systems. Social imbalance and inequality between men and women are expanded into the family, where the man imposes his power and control over the woman. Violence is one of the forms of expressing this power. Scientific research show that patriarchal societies which emphasize on the power of men and their domination in political, social, and economic areas, have a large impact on the violent behaviors of men towards women (Cunningham, 1998; 20).

2.1. Ecological model:

Ecological model is almost a new theory about domestic violence. This model indicates that interpersonal violence is the resultant of interaction between various factors at different social levels. This model is depicted as follows on figure 1.



Fig. 1: Ecological model of understanding violence (WHO Multi-country Study on Women's Health and Domestic Violence against Women)

Biological factors and personal history that each person brings to his/her relationships are shown in the innermost circle (Garcia-Moreno *et al.*, 2005; 6). At the individual level, the man has been abused or witnessed violence in the family, the father is not at home or is rejected, or is an alcoholic (Ellsberg & Heinz, 2005; 26). The Second circle shows the first

substrates of violence that are mostly linked to family or other confidants (Garcia-Moreno et al., 2005; 6).

At the level of family and family relationships, the man has the control over all property of the family and decisions which are made within the family and there is a little of marital conflicts (Ellsberg & Heinz, 2005; 26). The third circle represents the structure of social institutions (formal or informal) which include social relationships (neighbors, colleagues, social networks, and friends) (Garcia-Moreno et al., 2005; 6). At the social level, the woman is isolated due to low social mobility and is less socially supported. The community of men condones or ignores violence and pretends it to be lawful (Ellsberg & Heinz, 2005; 26). The fourth circle includes economic issues, social environment, and cultural norms (Garcia-Moreno et al., 2005; 6). At the society level, gender roles have been defined strictly and are imposed on society and the concept of masculinity is misunderstood with violence and rough and the concept of masculine dignity is misinterpreted with domination. The dominant culture of the society has accepted the physical abuse of women and children justifies it with this assumption that man is the owner of woman (Ellsberg & Heinz, 2005; 26).

3.1. Integrative view (theoretical framework of research):

Social phenomena are multidimensional, so they should be studied from different perspectives. Phenomenon of domestic violence is no exception and has cultural, social, legal, psychological, and physical dimensions. Scholars from various fields of science have studied this phenomenon. It is obvious that none of these studies alone seem to be adequate to explain the phenomenon of violence. Hence, we cannot select merely one of the discussed theories as the theoretical framework of the present study. Integrating multiple perspectives in a way that they complement each other seems to be necessary to explain the theoretical framework of domestic violence phenomenon. Multifaceted nature of studied issue makes us to review the models and theories raised in different fields and select those that are closer to the objective and the scope of research and use them as the integrative view. In Iranian society have always been based on patriarchal system throughout the history. This will lead to an imbalance of power within the family and using violent behavior against family members is the result of this imbalance. On the other hand, traditional atmosphere of society, especially about women has not allowed them to participate in economic, social, cultural, etc fields. Undoubtedly, this will be somehow an obstacle to economic independence of women in Iranian society. This issue has been raised in the

theory of feminists and can be used as one of the theoretical bases of research. By reviewing the theories discussed in theoretical framework part, it can be found that feminist theories, theories of Zelto, Strauss, and Giles which have emphasized on sociological and cultural factors have been used as the integrated approach of the study. Research hypotheses have been proposed based on the integrated view and the study of the views of others.

4.1. Research hypotheses:

- 1- Men with different stereotypical beliefs, use violence against their wives in different ways.
- 2- Men with different level of education do not apply the same level of violence against their wives.
- 3- There is a relationship between social capital and domestic violence.
- 4- Men with different levels of behavioral control, impose different levels of domestic violence on their wives.
- 5- There is a significant difference between empathy and violence.

According to above-mentioned views, theoretical model of the present study can be depicted as shown in Figure 2.

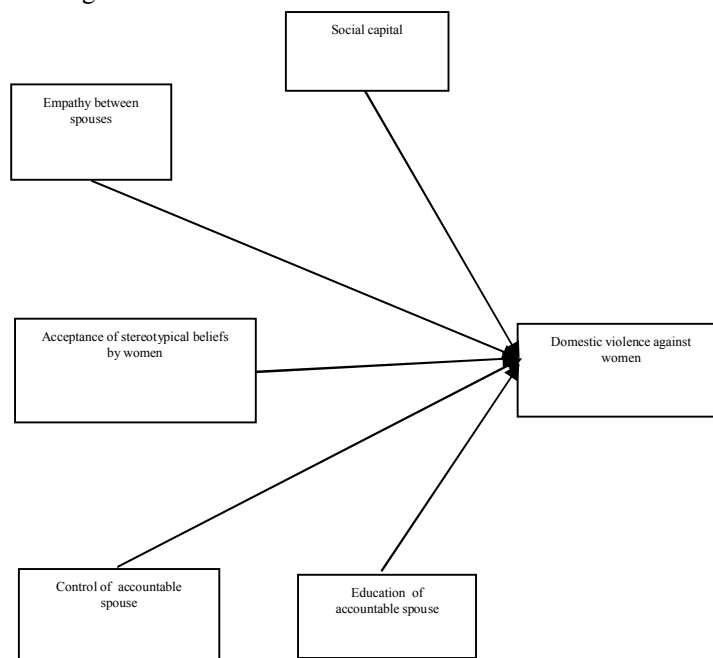


Fig 2: Theoretical model of the present study

5.1. Research Methodology:

This study is based on a survey. Statistical population of this research includes married women of Neyriz and Estahban cities. Cochran formula was used to determine the size of studied sample. Which was obtained 330 for each city? According to the

characteristics of statistical population, multi-stage cluster sampling method was found the best method for sampling. Married women were the unit of sampling those interviewers was sent to their homes to collect the required information. An author-made questionnaire was used to collect data. This questionnaire was developed using the definition of violence and its types and previous studies, especially the research conducted by WHO (World Health Organization) in ten countries for ten years.

The questionnaire consisted of 60 open and closed questions related to the subject of research. In order to make the researchers familiar with the questionnaire and the way of using it, three training sessions were held to help the interviewers to have a better communication with the respondents and ask the questions in an appropriate way. Face validity and construct validity methods were used to determine the validity of the questionnaire.

The correlation was calculated 0.82 in construct validity. Given that some questions of the questionnaire measured the attitude, Cronbach Alpha method was used to determine the reliability of the questionnaire which was obtained 0.78. This figure shows that there is an inner harmony between attitude-measuring statements. Descriptive Statistics tools such as concentration and dispersion indices, one or multivariate tables, and diagram and deductive statistics tools such as Spearman correlation coefficient, Kruskal-Wallis test, and TAU B Kendall test were used to analyze the data. All these tests and analyses were done using SPSS software.

6.1. Definition of research variables:

1.6.1. Domestic violence against women:

Specific indicators to measure the dependent variable (violence against women) are as follows:

- Psychological violence such as mocking and squibbing; lack of attention to recommendations/consultation; threatening to take the children, marry again, get divorced, and kill; inattention, slander, pessimism, disrespecting the responder or the family members of the responder, etc.
- Physical violence such as slapping, pulling hair, biting, hitting, squeezing the throat, etc. Sexual violence such as having sex against the woman's desire, unconventional sexual relationships, etc.
- Economic violence such as not giving spending money to the wife, taking the income of the wife, etc.
- Controlling the behaviors such as preventing the woman from education, prevent the woman from socializing with her family, controlling his social communications, etc.

Social capital: Social capital has been defined as the ability of actors to secure benefits through membership in social networks or other social structures. Social capital emphasizes on characteristics of relationships between people and the norms controlling these relationships. Social capital of family specifically occurs in relationships of family members and implies the relations between parents and children and other family members. Social trust and social networks are indicators of social capital. In the present study, social networks have been specifically taken into account in assessing the relationship between social capital and domestic violence against women. Empathy between spouses: Awareness, knowledge, and understanding of spouse's emotions (Reber, 1985; 238).

- **Controlling the behaviors:** Any behavior from the husband or other family members restricting or controlling the measures and actions of the wife (Reber, 1985; 84, 154).

Stereotypical beliefs: Prejudice and judgment about others without having previous knowledge. Indicators of this variable are shown in Table 4.

Education: Number of years that a person has been engaged in studying in formal educational institutions

2. Data analysis:

Descriptive and deductive indicators were used to analyze the data and then the appropriate and needed statistics were applied to test the research hypotheses. The scale of dependent and independent variables was ordinal. Hence, Kruskal-Wallis and TAU B Kendall's tests were used to test the significant differences between the studied groups and the relationship between them.

1.2. Deductive analysis:

The dependent variable in our study is domestic violence that is divided into two categories of physical and mental. This variable is non-parametric and cannot be quantitatively measured. According to the criteria set for the study of violence and its types, violent behaviors were divided into three categories including low, medium, and high. Altogether, 16 indicators were determined to study the violence (Physical or mental). The violence of men who had imposed 5 or less than 5 of the determined types of violence on their wife was considered "low", the violence of men who had shown 5 to 10 types of violent behaviors was classified as "medium", and the violence of men who had 11 or more violent behaviors was regarded as "high".

Table 2: Frequency distribution of the respondents according to the type of psychological violence

Type of violence	Spouse		Father		Brother		Others		None		No answer		Total	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
mocking and squibing	75	14/2	0	0	10	1.7	16	2/7	316	52/7	173	28/8	600	100
Lack of attention to recommendations/ consultation	82	13/7	6	1	3	0/5	4	0/7	306	51	199	33/2	600	100
not giving spending money	27	4/5	1	0/2	2	0/3	2	0/3	372	62/2	195	32/5	600	100
preventing the woman from education	32	5/3	7	1/2	2	0/3	2	0/3	356	59/3	201	33/5	600	100
slander	13	2/2	0	0	0	0	5	0/8	384	64	198	33	600	100
threatening to take the children	13	2/2	0	0	0	0	2	0/3	377	62/8	208	34/7	600	100
threatening to marry again	16	2/8	0	0	0	0	1	0/2	378	63	204	34	600	100
threatening to get divorced	19	3/2	0	0	0	0	2	0/3	377	62/8	202	33/7	600	100
threatening to kill	8	1/3	0	0	0	0	2	0/3	391	65/2	199	33/2	600	100

Table 3: Frequency distribution of the respondents according to the type of physical violence

Type of violence	Spouse		Father		Brother		Others		None		No answer		Total	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
slapping, pulling hair	40	6/7	0	0	3	0/5	1	0/2	376	62/7	180	30	600	100
punching and kicking, squeezing the throat	16	2/7	0	0	1	0/2	0	0	388	64/7	195	32/5	600	100
Hitting with a belt or hose	10	1/7	0	0	0	0	0	0	393	65/5	197	32/8	600	100
biting, hitting causing injury	11	1/8	0	0	0	0	0	0	390	65	199	33/2	600	100
Twisting the hand causing damage	10	1/7	0	0	0	0	0	0	396	66	194	33/3	600	100
Physical damage or Ruptured eardrum	3	0/5	0	0	0	0	0	0	398	66/3	199	33/2	600	100
Broken bones or ribs	1	0/2	0	0	0	0	0	0	400	6/7	199	33/2	600	100

Table 4: Frequency distribution of the respondents according to their attitude to stereotypical beliefs indices

Variable	Kruskal-Wallis test			TAU B Kendall		
	N	sig	Chi-square	N	sig	R kendall's-b
Stereotypical belief - Violence	584	0/279	2/554	584	0/689	-0/016
Stereotypical belief - physical violence	584	0/236	2/887	584	0/517	-0/027
Stereotypical belief - Mental Violence	584	0/261	2/690	584	0/203	-0/052
Spouse Education - Violence	557	0/001	18/579	557	0/013	-0/096
Spouse Education - Physical Violence	557	0/050	9/450	557	0/058	-0/074
Spouse Education - psychological violence	557	0/001	18/518	557	0/002	-0/120
Social capital - Violence	600	0/012	8/824	600	0/007	-0/105
Social capital - physical violence	600	0/006	10/150	600	0/002	-0/119
Social capital - psychological violence	600	0/065	5/466	600	0/415	-0/32
Behavior control- violence	574	0/001	13/160	574	0/004	0/119
Behavior control- physical violence	574	0/002	12/673	574	0/006	0/113
Behavior control - psychological violence	574	0/001	23/104	574	0/000	0/196
Empathy - Violence	575	0/000	25/038	575	0/000	-0/185
Empathy - physical violence	575	0/000	24/638	575	0/000	-0/185
Empathy - psychological violence	575	0/000	26/494	575	0/000	-0/201

Table 5: The results of Kruskal-Wallis test and TAU B Kendall correlation coefficient

Words and phrases	I agree		I do not agree		I don't know		No answer		Total	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
A good woman should obey her husband even if she does not accept	231	38/5	299	49/8	43	7/2	27	4/5	600	100
Family problems and issues should be only discussed and between the family members	534	89	37	6/2	7	1/2	22	3/7	600	100
It is important for a man to show his wife who is the boss	161	26/8	358	59/7	46	7/7	35	5/8	600	100
A woman should be able to choose her	120	20/8	401	66/8	39	6/5	35	5/8	600	100

own friends, even if her husband doesn't agree										
It is a woman's duty to have sex with her husband, even if the relationship does not feel good	276	46	183	30/5	92	15/3	49	8/2	600	100
A woman comes to her husband's family with a white dress and leaves them with a shroud, even if she is treated with injustice	156	26	388	64/7	29	4/8	27	4/5	600	100
A man has the right to hit his wife if she doesn't do the household chores good	22	3/7	540	90	14	2/3	24	4	600	100
A man has the right to hit his wife if she disobeys him	49	8/2	493	82/2	31	5/2	27	4/5	600	100
A man has the right to beat his wife and take her out of the house if he suspects her loyalty	55	9/2	468	78	49	8/2	28	4/7	600	100

2.2. The first hypothesis: Men with different stereotypical beliefs, use violence against their wives in different ways:

As shown in Table 5, this hypothesis deals with the difference between different levels of stereotypical beliefs and the imposed violence. In order to examine the significant difference between these two variables, Kruskal-Wallis test was used. The results indicate that there is no significant statistical difference between different levels of stereotypical beliefs and violence. This means that faith in stereotypical beliefs has no impact on the level of violence. On the other hand, the relationship between these two variables was also examining using TAU B Kendall test. The results shown in Table 5 indicate that this relationship is insignificant (Sig. = 0.689). This was also observed in different types of violence (Physical and psychological).

3.2. The second hypothesis: Men with different level of education do not apply the same level of violence against their wives:

Undoubtedly, education level of a person can be effective in formation of his/her attitudes and their practice. The impact of education on family relations and in particular the relationship between spouses is a topic that needs to be studied. The effect and relationship of this variable with violence were also studied and tested. For this purpose, the education level of the spouses of the respondents (husbands) were divided into 6 categories including illiterate, elementary or guidance school, high school, associate's degree or a bachelor degree, a master degree or higher, and seminary education. The question is that whether the education levels affect the rate of men's violence against women or not? The results show that education level has an impact on the rate of violence. This means that the higher the education level of men is, the lower the rate of violence will be and vice versa. This inverse relationship was also observed in TAU B Kendall test. It should be noted that this relationship also holds true for the indicators of physical and psychological violence.

4.2. The third hypothesis: There is a relationship between social capital and domestic violence:

Table 5 shows that there is a significant relationship between these two variables (Sig. = 0.007 for domestic violence and Sig. = 0.002 for physical violence), except in cases of psychological violence (Sig. = 0.415). The difference between the average levels of social capital and levels of violence were also tested. The results of Kruskal-Wallis test shows that violence has a significant relationship with different levels of social capital. This means that women who have less social capital tolerate more violence and vice versa.

Table 6: Mean and standard deviation of domestic violence by spouse's education level

Education level	Frequency	Mean	Standard deviation
illiterate	33	1/032	0/049
elementary or guidance school	146	1/014	0/033
high school	197	1/012	0/027
associate's degree or a bachelor degree	173	1/008	0/022
a master degree or higher	11	1/004	0/010
Total	557	1/012	0/029

Table 7: Mean and standard deviation of violence in terms of social capital

Levels of attitudes	Frequency	Mean	Standard deviation
Low	79	1/012	0/033
Medium	412	1/011	0/027
High	109	1/017	0/032
Total	600	1/012	0/03

5.2. The fourth hypothesis: Men with different levels of behavioral control, impose different levels of domestic violence on their wives:

The findings related to this hypothesis, shown in Table 5, indicate that there is a significant

relationship between the rate of exercising the domestic violence in general and its indicators (physical and mental) and different levels of behavior control. On the other hand, the relationship between different levels of behavior control and violence was also examined. This means that the less the controlling behaviors of men is, the less violent behaviors will be imposed on women and vice versa.

6.2. The fifth hypothesis: There is a significant difference between empathy and violence:

The findings related to this hypothesis, shown in Table 5, indicate that there is a significant relationship between mean levels of empathy and violence. Also, a significant inverse correlation was found between all levels of empathy with domestic violence and its indicators. This means that the more the empathy between spouses is, the less the violence would be.

3. Discussions

"Faith in stereotypical beliefs" was one of the variables supposed to be effective imposing violence against women. In a nutshell, we can say that stereotypical beliefs are prejudices and judgments about others without having previous knowledge. Undoubtedly, prejudices about the beliefs within the society can practically affect the actions of actors. So, we tried to see that whether these beliefs can be effective in imposing domestic violence or not. Hence, this hypothesis was raised and tested. Our default assumption in this hypothesis is that those who believe in stereotypical beliefs are more likely to show violent behaviors and vice versa. This hypothesis was tested and the results showed that this variable has no significant relationship with domestic violence. To ensure more, the concept of domestic violence was divided into two parts including physical violence and psychological violence. It was observed that faith in stereotypical beliefs has a significant statistical relationship with none of these two indicators. In a study conducted by Tang (2003; 95) in Canada, the significant relationship of this variable with domestic violence was confirmed. Also, in a study conducted in Malawi in 2005, 57% of women believed that traditional beliefs of the society are the cause of domestic violence. In another research conducted by Akin and Soubasi in Turkey and published in 2004, a significant relationship was found between physical violence and traditional beliefs, while the present study rejects such a relationship. This may be due to the differences between communities in terms of culture, society, religion, etc. Studies have shown that in countries where these stereotypical beliefs are less common, less violence and patriarchy are seen. The study conducted by Nayak *et al* confirms this argument.

The results of testing the hypothesis of significance of difference between different levels of education and domestic violence showed that educated the more the men are, the less likely they are to use violence against their wife. However, it should not be forgotten that this factor alone will not guarantee the non-violent behaviors. The relationship between men's education and domestic violence was confirmed in the studies conducted by Polser *et al* and also Stickely *et al*.

Pierre Bourdieu has divided the types of capital into three parts including economic capital, symbolic capital, and cultural capital. Having or not having any of these types of capital can determine a person's destiny in personal and social life. Social capital is defined as the ability of actors to secure benefits through membership in social networks or other social structures. Social capital emphasizes on characteristics of relationships between people and the norms controlling these relationships. Social capital of family specifically occurs in relationships of family members and implies the relations between parents and children and other family members. Social trust and social networks are indicators of social capital. In the present study, social networks have been specifically taken into account in assessing the relationship between social capital and domestic violence against women. One of the factors that can affect violent or non-violent against women is the social capital of women. The relationship between social capital and violence against women was not confirmed in the present study. Even after dividing the domestic violence against women into physical and psychological violence, no relationship was found between these variables. However, a relationship between these two variables was found in a study by Zoltor *et al* (2006). This means that women who had a rich social capital were less exposed to domestic violence. One of the questions in the questionnaire dealt with this issue that whether the women had talked about the violence imposed on them or not. The data indicate that more than half the respondents who were abused by violence did not talk about it with anyone and rest of them only consulted their parents, sisters, and brothers. As the level of education of most respondents and their parents was low, they had lower levels of social capital. Those who had higher social capital didn't manage to use it because it was a taboo for them to talk about the inner issues of family with others outside the home and family. So, non-confirmation of the inverse relationship between these variables can be due to above-mentioned reasons. However, the role of other unknown factors should not be ignored in this regard.

When a family is formed by the marriage of two persons, according to the society's cultural system, certain normative patterns that are already defined will rule the family. These patterns vary in different communities. Patriarchal and authoritarian patterns are common in some societies, while democratic models are preferred in other cultures. These patterns naturally affect the family norms. Evidence indicates that patriarchal model has been dominant in the family system around the world and this it shows that men mainly want to consciously or unconsciously control their partner's behavior or thoughts. Traditional and patriarchal patterns have been also common in Iranian culture throughout the history, although we have witnessed some changes and developments in the family system in recent decades influenced by the global cultural patterns. As we move from large cities to smaller cities, we see that these cultural patterns are more highlighted. This mainly to traditionalism and the high cost of breaking the traditions in such communities. It is obvious that the communities studied in the present research are not no exception. Behavior control in this study intends some cases such as preventing from socializing with the family, relatives, and friends, indifference, sensitivity of man about the normal relations of his wife with other men (colleagues, neighbors, etc), and so on. The relationship between this variable with domestic violence was examined and the research hypothesis was confirmed. This means that the more the controlling behaviors of the man is, the more severe reactions the wife would show followed by the exercise of various types of violence (Psychological, physical, financial, etc) by the man against his wife. The research data and evidence show that the men who have more control over the behaviors of their wives will resort to violent behaviors more than other men. Findings about above-mentioned hypothesis can confirm the theory of domination and authority raised by new Marxists and Feminists. They believe that similarly to normative system ruling the society which tries to control the behaviors of actors; men try to do so within the family.

Usually, several factors are involved in a successful marriage. These factors include cultural identity, having the same religious beliefs, deep interest in each other, empathy between spouses, etc. Empathy between spouses can be defined as awareness, knowledge, and understanding of another person's emotions. This variable can be measured through various indicators. Chalabi says that if you want to reduce violence in families, family members should agree and cooperate with each other, have empathy with each other, consult with each other, and have common interests in dealing with problems.

As discussed in previous part, there is a significant negative relationship between empathy and imposing or not imposing the violence on women by their husbands. This means that the likelihood of imposing violence on women is less in families where there is more empathy and sympathy between spouses. This hypothesis was also confirmed in the present study. Chalabi and Rasoulzadeh also confirmed the inverse relationship between empathy and violence against children in their study.

1.3. Recommendations and Guidelines:

Based on the findings of the present study, the following guidelines are recommended in order to reduce domestic violence against women:

Instructional strategies:

- 1- Education of children (girls and boys) from the first years of school in order to learn the skills of communication, problem solving, and dealing with aggression.
- 2- Public education through the mass media to change attitudes towards women as the second sex.
- 3- Making women familiar with their rights.
- 4- Increasing the level of education of women and men.

2.3. Application of preventive measures:

- 1- Trying to reach equality in terms of women's and men's rights through the activities of human rights organizations.
- 2- Proposing and implementing plans to prevent violence against women, especially domestic violence.
- 3- Increasing social awareness and trying to change attitudes, beliefs, and values which consider violence against women a common behavior and overlook it.
- 4- Developing women's NGOs to train them.
- 5- Establishing a permanent organization to gather information and statistics on violence against women.
- 6- Supporting research on violence against women and ways to prevent it and also practical application of the presented solutions.

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Effectiveness of educational programs based on Pender's theory on the health and symptoms in patients with obsessive - compulsive disorder

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Abstract: Introduction: obsessive – compulsive disorder is a chronic disease with prevalence 2% to 3% general community and estimates 40% of society in Iran. Now, research has shown that the cause of many chronic diseases is lifestyle and human behavior and health promoting behavior is one of the best ways by which people can maintain their health and control. The aim of this study is promoting of health lifestyle patients with obsessive - compulsive disorder based on the teachings Pender health promotion theory and its subsequent effects on symptoms disease. **Methods:** The sample included 8 patients who were eligible under the program of volunteer training Pender health promotion model and were followed for 3 months. Tools used in this research were Health Promoting Lifestyle Profile II and Madsly Inventory to identify symptom obsessive - compulsive disorder. **Results:** The results showed a significant difference between mean scores of health promoting lifestyle before and after the intervention ($p = 0/01$) such that educational programs promoting healthy lifestyles increases significantly in the six dimension excluding the responsibility and spirituality. Although the mean scores for symptoms of obsessive - compulsive decreased after the intervention but these differences were not significant ($P = 0.054$) however, this difference in the scales of doubt -task and revision ($P = 0/04$) was significant. **Discussion:** Despite the limitations of existing in this research to generalize the results including small numbers of samples and the lack of control group, however, in conclusion, this study can be primary study the effect of educational program provided by nurses for promoting patients' health with chronic disease, obsessive – compulsive and even reduced some their symptoms.

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1. Introduction

Obsessive-compulsive disorder (OCD) is one of the most common psychiatric disorders noticed by western psychiatrists since 19th century (1, 2). The main symptoms of this complicated syndrome are unwanted, frequent and intrusive thoughts (*Obsessive thoughts*) followed by some frequent and intrusive behaviors (*Compulsive behaviors*). Indeed, the patient performs such behavior to escape from his/her paralyzing and endless anxiety or neutralize the obsessive thoughts (3, 4, and 5). The obsessive-compulsive patients have insights about their disease. It means that these patients know that their thoughts and behaviors are abnormal and inappropriate for their personality. According to psychological classifications, the obsession is one of severe neuroses diminishing the patient's mental and behavioral balance and accommodation with environment (6). In 2002, the World Health Organization (WHO) reported that Obsessive-compulsive disorder is responsible for the 5 cases of each 10 cases of disability in the world and the prevalence of this disorder are increasing

dramatically in rich developed countries(7). 2 to 3 percent of general population can be suffered by obsessive-compulsive disorder in their life. It has been estimated that 10 percent of outpatient visits of psychiatric clinics and offices are related to this disorder (2). The prevalence of the obsessive-compulsive disorder is 2-fold higher than schizophrenia and bipolar disorders (8). The website of Iranian scientific database has published that the prevalence of obsessive-compulsive personality disorder is about 40 percent in Iran (9). The adolescence and early adulthood are the common ages of involvement by the disorder. No different rates of the involvement can be found among males, females and children of different ethnicity, cultural background, and social and educational level (4). The theories about the disorder and its related etiology proposed by various psychiatrists up to now have no confirmed experimental basis and no effective therapeutic measures have been provided through these theories (1). The studies demonstrated that the disorder is resistant to treatments. The treatments last averagely about 14 to 17 years since the onset of the

disease (4). Some of experts called the disorder as “latent epidemic” (8). Similar to other chronic diseases, some risk factors have been proposed for the obsessive-compulsive disorder. Consequently, the correction of such risk factors should not be omitted and replaced by the medications. According to the today’s researches, many of the chronic disease are originated from inappropriate human lifestyle and behaviors. Hence, the health-promoting behaviors are one of the best approaches to keep public health (10). Improving the public health through lifestyle modification and control and omitting of the risk factors can result in minimized cost and side effects, decreased hospitalization and lower interfering with daily activities. In addition, such measures can increase the effectiveness of medical and non-medical treatments and improve the quality of life. The lifestyle is a collection of the behaviors that an individual choose them as a pattern for life. Lifestyle modification should be considered as an essential factor to improve the symptoms and minimize the side effects along with other therapeutic options (12).

One of new health-promoting patterns is Pender’s health promotion theory developed in 2005. Pender, who is a theorist of nursing, based his theory on theory of social learning and emphasized on importance of motivating factors and health behaviors (13). This theory constitutes the theoretical framework of present study. (13). Pender’s power in defining health is that he doesn’t confine nurses and other health care teams to intervening in order to reduce the risk of disease and he gives more chances to nurses to examine individuals, families, and communities so that they try to improve health, and promote functional abilities and better life styles. This model which is one of the central theories in nursing, directs nurses so that they would systematically examine clients in terms of perceived self- efficacy, perceived barriers and benefits of action, and interpersonal and situational influences and would be able to set the arrangements for promoting health-enhancing behavior in individuals based on their own individual interventions (14). Many studies have indicated that the rate of depression related to obsessive-compulsive disorder and the intensity of obsessive-compulsive symptoms highly affect life quality and some reported that getting better scores in physical aspect of life quality was resulted by employment (15). In this research, the researchers have tried in addition to study different aspects of such patients’ lives, which have a special position in prioritizing to be offered various non-drug treatments, also consider doing behaviors which will promote the health of such patients. In their studies Bystritsky and et al (1999) emphasized that written treatment procedures of patients with

obsessive-compulsive disorder will affect their perception and subjective scale of their lives quality more than objective parameters such as family support, disability, and employment and specialists are needed to – while treating patients with chronic diseases such as obsessive-compulsive disorder – care about improving the quality of their lives in addition to practicing usual treatments (15). Many studies have reported the effect of educational programs based on Pander’s model on enhancing health-promoting lifestyle of healthy people and patients with chronic diseases (16, 17, and 18). The findings of Safabakhsh and et al(2004) studies showed that educational programs based on Pander’s theory after 3 sessions of teaching the method of having healthy life and 3 months pursuing, caused a meaningful increase of patients’ health-promoting lifestyle scores after coronary bypass surgery in experimental group (11).

1.1. Research materials and methodology:

This research is a quasi-experimental study with before and after intervention control. The research population includes all patients with obsessive-compulsive disorder who have been admitted to two psychiatric clinics in Dezful. Purposeful sampling initially consisted of 9 volunteer patients introduced by psychiatrists who had inclusion criteria to participate in the study such as not having another chronic mental disorder like schizophrenia and bipolar disorders, being adult, and being accompanied by one family member in all stages of training programs. In the end, the samples reduced to 8 people because one of them was not present in training sessions. The tools used in this research were Health Promoting Lifestyle Profile II₁ (HPLPII) and Maudsley Obsessive Compulsive Inventory (MOCI) 2. Health Promoting Lifestyle Profile II which is planned based on Pander’s model, was first prepared by Walker and Hill Polerecky₃ and then some changes were made in it in 2002. This profile includes a multi-dimensional assessment of health promoting behavior and it measures the frequency of applying health promoting behavior in six dimensions of taking health responsibility, physical activity, nutrition, spiritual growth, stress management and interpersonal behavior. The profile contains 52 questions and is scored by using 4-point Likert Scale as Never (1), Sometimes (2), Usually (3), and Always (4). The range of total score of health promoting behavior is 50-208 and for each dimension a separate score is calculated. Higher scores represent doing healthier behavior and lifestyle. Profile makers suggest that the scores must be studied and interpreted in 1-4 scales. Cronbach's alpha and test-retest reliability of this profile in many domestic and foreign studies is reported to be 0.8 -

0.93. Cronbach's alpha in each dimension is reported as 0.7 – 0.94. (17, 21, 22, 23). The profile used in this research was the copy that had been translated and confirmed by 10 professors teaching English at Shiraz Medical School in 2004 (11). Maudsley obsessive compulsive inventory is one of the most popular tools based on patients' report with rumination and sensitive to treatment changes. This tool was made in Maudsley Hospital by Harrison and Rachman in 1977. This inventory contains 30 questions with True or False options for each question. In this inventory there is a general score for obsession and separate scores for each disorder including checking, washing / cleaning, slowness / repetition, doubting / conscientiousness. Test score is between 1 to 30 and high score indicates more signs of mental-practical obsession. This inventory is used as a norm in many countries and at present it has been translated to persian as well and has high reliability and validity. Norman₁ and et al (1999) have reported its. Cronbach's alpha as 0.85. In Iran Ghasemzade (2001) studied the content validity of this tool and Aliloo calculated the test –retest reliability of this tool in students of Tehran Teachers Training University (Tarbiat Moalem-E Tehran) which was 0.82 (25, 5). One of the shortcomings of this inventory is that there are just two questions in relation to mental rumination which could not be a proper criterion for judgment on this kind of obsession. In this research the content validity of the tools was approved of by 7 members of university board of science with master degree in nursing and psychiatry and 3 patients with obsessive-compulsive disorder. Due to large number of questions and little number of samples, reliability was measured on 16 completed scales in the end, and Cronbach's alpha for health promoting lifestyle profile II and Maudsley obsessive-compulsive inventory was 0.94 and 0.88 respectively.

2. Material and Methods

Ethical approval was granted by the research ethics committees of the research board Islamic azad university Dezful. All subjects who signed informed consent form attended training programs which were held in two 60-minute sessions in four-person groups in one-week interval with one certain member of their family in training and treatment center of Dezful great hospital. Participants in these classes were trained based on Pender's teachings in relation to six dimensions including health responsibility, physical activity, nutrition, interpersonal relations, stress management, and spiritual growth. In these sessions educational clips were played, pamphlet and CDs were distributed and some books were introduced and handed out to the participants to be studied. During three months the subjects and their single family

member were separately guided through telephone conversations to perform health promoting behavior and their problems and barriers were considered and examined and health promoting lifestyle profile and Maudsley inventory were completed before the sessions and after three months of treatment and studying in presence of researchers. All data was analyzed by SPSS 16 software and descriptive statistics including (frequencies, means, Skew Index, data distribution curves) and also inferential statistics (T-Test and Wilcoxon Test) were used.

3. Results

All patients in this research were female. Most of them hadn't got diploma, and were married, housewives, and in their 20th (20 -29). They had developed this disease since 1-5 years ago when most of them were 20-39 years old. The entire experimental group was treated by Clomipramine for 7 months to 10 years. 4 patients had been hospitalized due to this disorder and were treated by medications. Health promoting lifestyle average score was 111.37 out of 208 before intervention and 139.75 after intervention. This difference was in favor of after invention score in increasing health promoting lifestyle scores of the subjects. The majority of subjects' answers to health promoting behavior before intervention were so that half of them had chosen "Never", "Sometimes" options and the other half had chosen "Usually" in four-point Likert scale of this profile. After intervention most of them had answered "sometimes" and "Usually". The highest scores of participants' health promoting lifestyle before intervention were related to spiritual growth, interpersonal relations, nutrition, health responsibility, stress management, and physical activity respectively. (Table1).

Table 1: health promoting lifestyle scores and their micro scales before and after intervention

Group	Tool's Total Score	Subjects Score Before Intervention	Subjects scores After Intervention
		Average	Average
Lifestyle	208	111/37	139/75
Responsibility	36	19/62	24/87
Physical activity	32	11/00	18/37
Nutrition	36	20/62	25/50
Spirituality	36	22/37	24/50
INTERPERSONAL RELATIONS	36	21/12	25/25
Stress Management	32	16/62	21/25

Total average score of obsessive-compulsive symptoms was 18.87 out of 30 before intervention which reduced to 13.5 after intervention. The maximum scores of obsessive-compulsive symptoms before intervention were related to doubting - conscientiousness, rechecking, slowness - repetition, and washing (Table 2).

Table 2: obsessive-compulsive disorder scores and subscales before and after intervention

Group	Tool's Total score	Subjects Score Before Intervention	Subjects scores After Intervention
		Average	Average
Obsession	*30	18/87	13/50
Rechecking	9	6/25	3/87
Washing	11	5/62	5/00
Slowness- Repetition	7	4/00	2/75
Doubting Conscientiousness	7	5/37	3/87

* Subscale scores are common in several questions

With drawing distribution curve of lifestyle scores and obsessive-compulsive symptoms before and after intervention and also calculating Pearson's skew index and Skew Coefficient it was known that these scores had normal distribution, therefore it was possible to administer parametric paired t-test in order to compare and modify changes although nonparametric Wilcoxon test was also used in these cases which generally had similar results with t-test except in total obsessive-compulsive scores. Findings indicated that there was a significant difference between average scores of lifestyle before and after intervention ($P=0.01$). In other words, educational programs improved health promoting lifestyle of patients with obsessive-compulsive disorder. Also the results in subscales of this tool indicated a significant difference between the scores of physical activities, nutrition, interpersonal relations and stress management but this difference was not significant in subscales of responsibility and spirituality.

Research findings also indicated that the difference between total average scores of obsessive-compulsive symptoms before and after intervention was not significant ($P=0.053$) but there was a significant difference in subscales of this tool that is rechecking and doubting – conscientiousness ($P=0.04$). In other words, health promoting educational programs decreased obsessive-compulsive signs in all kinds of rechecking and doubting – conscientiousness.

Pearson's correlation coefficient didn't show any meaningful relations between scores of obsessive-compulsive signs of Maudsley inventory and scores of health promoting lifestyle profile in this research.

4. Discussions

Total average score of the subjects' health promoting lifestyle profile was 111.37 before intervention with the highest score related to spirituality and interpersonal relations and lowest one related to physical activity and stress management. The findings of a research conducted by Motlagh and et al(2011) on 440 students at medical school of Yazd university indicated that the average score of the subjects' health promoting lifestyle profile was 130.3 with the highest score related to the subscale of

spirituality and the lowest score related to physical activity (10).also In Jalili's and et al(2008) research, total score of students' lifestyle is reported as 134.6 (25). Comparison of findings in these two researches and present research shows that the score of health promoting lifestyle profile in patients with obsessive-compulsive disorder in this research is less healthy. Also, the results of the highest and the lowest score in different dimensions of this profile matched each other except in stress management. Spirituality high score in these findings might be related to the culture and religious system of Iranian society. Every time people feel they are growing, believe that their lives are purposeful, are waiting for future, and are trying to achieve their long term goals in their lives and feel that there are connected to a superpower above them, indicate the signs of health in this dimension (10). Getting the lowest score in physical activities seems to be a general health problem in developing societies and in our society (21). Low scores in stress management, with regard to possible causes of developing obsession and the individual's inability in dealing with problems and stress, is not far fetched (1) to be related to paying more attention to controlling and preventing the side effects of not performing these kinds of behavior among healthy people and the patients. In a research conducted by kheirgo and et al(2012), in comparing health promoting lifestyle profile of healthy people and patients with chronic rheumatoid arthritis, the results indicated a significant statistical difference and lower score of patients in all dimensions of the profile except stress management (26). In Shu-Ving Hou's study (2010), the results showed that the scores of life quality of patients with obsessive-compulsive disorder – by applying QQL (Quality of Life) scale in general dimensions, psychology and social support were lower than control group (healthy individuals) (27). Subjects participating in this research showed a significant increase of scores in health promoting lifestyle profile ($P=0.01$). Moreover, a significant increase in subscales of physical activities, nutrition, interpersonal relations and stress management was observed. However, these educational programs didn't show any significant increase in responsibility and spirituality ($P=0.054$). In Bystritsky's study (1999), the results indicated significant improvement of life quality of the patients after suitable nondrug treatments of obsessive-compulsive disorder (15). The findings of present research match with the results of Carreno and et al (2006) after implementing similar educational programs in a group of ordinary people. Carreno reported a significant increase of total average scores of health promoting lifestyle profile in two different groups of women ($P=0.0001$) based on Pander's model. This

increase was in all six dimensions of lifestyle profile (20). Therefore implemented educational programs in this research in two dimensions of responsibility and spirituality couldn't make significant changes in increasing this form of healthy behavior and modification in implementing these programs in these two dimensions seems to be needed. Total average score of obsessive compulsive disorder signs of the subjects in this research was 18.87 out of 30 before intervention. The lowest score of obsessive-compulsive signs before intervention was related to washing and the highest score was related to the subscales of doubting – conscientiousness. In a research done by Imani and et al, the total average score of obsessive-compulsive signs is reported to be 21 / 43 for 43 patients (2). In a research done by Sajadian and et al, the total average score of obsessive-compulsive signs (18 patients) was 16 and the highest score in experimental group was related to doubting – conscientiousness subscales and the lowest score was related to washing scale which match with the results of present research (23). Considering the results, it seems that the scores of the patients' obsessive-compulsive signs in these researches were average or above average. In Kaplan and Saduk textbook of psychiatry, pollution is mentioned as the most common pattern of obsessive-compulsive signs which is followed by washing and the patterns of doubting, obtrusive thoughts (rechecking) and slowness are respectively ranked in next stages in terms of being common (27). However, it seems that in this research and study of Sajadian and et al(2008), patients got higher score in patterns of doubting and conscientiousness and this difference requires more examination of these obsessive-compulsive patterns in our society(23). Of course, one of the causes of this difference might be related to the complaint of patients who have developed washing pattern and their going to clinics for treatment and also related to the side effects and problems of this unhealthy behavior in comparison to doubting –conscientiousness pattern. Moreover, this kind of disorder is faster and more clearly recognized by family members. Observing insignificant relationship between the scores of health promoting lifestyle profile and common obsessive-compulsive disorder signs in this research matches with Bystritsky's study (1999) in the usage of life quality scale (15). Although the average score of obsessive-compulsive signs reduced to 13.5 after intervention, this difference was not statistically significant ($P=0.053$) even though it might be considered significant by some experts. Moreover, in this research the average score of obsessive-compulsive signs reduced in for dimensions of inventory but it

was statistically significant only in two dimensions that is rechecking and doubting – conscientiousness.

In his studies, the researcher didn't find any research in relation to health promotion of patients with obsessive-compulsive disorder through intervention and its effect on reducing obsessive-compulsive signs ; however, numerous researches have been done on effective nondrug methods of reducing obsessive-compulsive signs which have often been done among small groups of patients with obsessive-compulsive disorder with 1- 12 subjects in experimental group and with or without control group and the results have been reported to be significant and positive in all cases. some examples of these interventions were mind awareness, cognitive behavioral treatment, separate mind awareness, and exposure which were to some extent and in some cases indirectly related to the teachings of Pender's health promotion model (2, 29, 31, 23, 32, 28). Since all the subjects in this research were treated by medications for 7 months to 10 years, it seems that medication effects together with educational programs could significantly reduce the signs of obsession in some dimensions during these three months. Non-drug treatments especially when the patient is in regular, constant touch with an interested, compassionate and encouraging specialist might help the patient to continue to their usual performance by relying on him and without such help, the patients would be completely overwhelmed by their own symptoms (28). In this research, the subjects remarked that educational programs of healthy behavior and recommendations to do them by one member of treatment team which is held with interest and time investment, would be more acceptable for them than being educated through sources and other people and the constant contact of the researchers with subjects specially the patients with mental disorders during three months would impress the patients to care about doing healthy behavior. Family psychotherapy would also help the patients and would reduce family discrepancy in relation to the patient and making a therapeutic alliance with healthy family members would definitely help the patient (28). According to the subjects of the research, in implementing educational programs of this research, the presence of the patients' companions and their attention to teachings of Bender's model seems to be very significant in different aspects such as active participation of the subjects in classes, pursuing and doing activities.

In treating the patients with obsessive-compulsive disorder, the following non-medication treatments are always discussed: reducing stress, changing life conditions, employment and amusement, communication and living in a

community, moral and spiritual methods and proving their pride and self- efficacy so that they can manage their own affairs and save themselves (33). All these matters have been somehow considered in teachings of Pender's model based on his theoretical structure and can be offered quite well by the nurses.

1.4. Conclusion:

Nowadays, caring about the quality of life is one of the concerns of international societies and researchers; and World Health Organization (WHO) as a pioneering organization, has recently paid special attention to developing assessment and evaluation of health such as birth and death beyond traditional health criteria (34). Obsessive-compulsive disorder is a common chronic mental disorder all around the world and well-controlled studies have concluded that main treatments associated with other affective programs would be very effective and efficient in achieving treatment goals very quickly (32). The results of this research showed that implementing health promotion programs very simply and in a short time by nurses can promote healthier lifestyle nearly in all its dimensions in patients with obsessive-compulsive disorder. Moreover, observing the significant decrease of some signs of obsessive-compulsive disorder after implementing educational programs which was not much predictable marks the importance of paying attention to these programs together with other treatment methods. Few number of volunteer participants and impossibility of attending more participants, and not having a control group are some limitations of this research in generalizing the findings; however, this study by its own can be considered as an initial research on paying attention to the implementation of such educational programs by nurses, and can be accompanied by novel ideas and thoughts to increase life quality and to treat such patients more effectively

2.4. Suggestions:

Considering the limitations of this research, it is suggested that the effect of these educational programs based on Pender's model be studied in certain larger groups if possible in terms of attending criteria and having a control group in order to be able to generalize the results more. But based on their experience in this research, the researchers suggest that these educational programs be offered to the patients quite individually by nurses

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The effect of tow modes of educational intervention on attitude toward cesarean section and vaginal delivery in pregnant women

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Abstract: The request for cesarean section has increased. According to importance of educational and behavioral intervention, this study performed to determine the effect of tow modes of educational intervention on pregnant women's attitudes toward vaginal delivery and cesarean section. This is quasi experimental and prospective study. Women who were in 3rd trimester of pregnancy selected. Sampling was multistage and purposeful. Case group received planned educational intervention and control group receive routine educational intervention. Questionnaires were filled before and one month after intervention. Data was analyzed by SPSS software using descriptive, analytical statistics. Mean age in control group and case group were 24.20(4.73), 23.44(4.9) respectively. There was significant difference between mean score of total attitude between case and control group, after educational intervention. ($p < 0.05$). More studies about attitude and behavioral intervention suggested.

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1. Introduction

Today, caesarean section is one of the most preferred surgeries throughout the world, but its increase due to non-medical reasons is also observed across the globe. This increase in the caesarean section illustrates that neither health system employees nor their clients regard this surgery to entail any serious dangers (World Health Organization, 2010).

Statistics reveal that 25.7% of all deliveries are caesarean section, ranging from 2.3% in Angola to 46.2% in China. The caesarean section due to non-medical reasons ranges from 0.01% to 2.1% in 23 countries (World Health Organization, 2010). According to the published statistics of the World Health Organization, the rate of caesarean section in Iran is 41.9%, 6% of which is unnecessary (Gibbons L et al., 2010)

The factors affecting caesarean section are complex and considering them in efficacy of interventions to reduce caesarean section is extremely challenging. The decision to perform caesarean section is made by the mother and the physician, and can be influenced by a wide range of external factors.

This decision can be made during pregnancy or even before delivery with medical reasons (for mother and the baby), or due to psychological or social reasons (Khunpradit S et al., 2011).

Although there are behavioral and interventional factors at different levels of programming that affect the behavior related to caesarean surgery, one of the factors related to mothers is the mothers' attitude and their request for caesarean section (Yazdizadeh et al., 2011). The maternal request for caesarean section is a controversial factor in caesarean and occurs in presence of lack of medical and midwifery indices (Cunningham, 2010). In fact, attitude is an emotional response based on knowledge and the approach of an acceptable attitude is sourced from the Allport concept and that evaluation of an individual is from acceptability or non-acceptability of his purpose or action (Zanna & Rempel, 2008).

Mother's complications are twice as much in caesarean section in contrast vaginal delivery. The principle causes include postpartum infection, bleeding, and thromboembolism. It has been mentioned that not all complications appear

immediately after delivery. Declea et al. found that re-admission to the hospital 30 days after delivery in caesarean section is twice as much as in vaginal delivery (Cunningham, 2010).

Belief in quick recovery in vaginal delivery (Aali & Motamedi, 2005; Manthata, Hall, Steyn, & Grove, 2006; Stoll, 2009), better mother-baby bonding are the trends related to vaginal delivery (Aali & Motamedi, 2005; Manthata et al., 2006; mostafavizade, mashughi, & rostamnejad, 2006; Stoll, 2009), fear of vaginal delivery and contractions related to vaginal delivery (mostafavizade et al., 2006; Stoll, 2009) are the primary reasons for preferring caesarean section over vaginal delivery. Also, the right to choose delivery method is among reasons given for maternal tendencies (Hogberg, Lynoe, & Wulff, 2008).

Although some studies reject the belief in mothers' attitude and request for caesarean section and blame healthcare system for the increase in caesarean section in the recent two decades (Lee, Khang, & Lee, 2004), all levels are important in education and interventions.

There have been some studies on attitude in Iran as well as studies on the effect of education on attitude (Aali & Motamedi, 2005; Amidi & Akbarzadeh 2006; mostafavizade et al., 2006; Sharifirad, Rezaeian, Soltani, Javaheri, & Amidi Mazaheri, 2010; Tofighi Niaki, Behmanesh, Mashmuli, & Azimi 2010), but in respect of assessment of the attitudes of those who have almost definitely decided to have caesarean section, there have not been any studies other than a few minor cases (Sharifirad et al., 2010). In a study by Moeini (Moeini, Besharati, Hazavehei, & Moghimbeigi, 2011), the mean score of attitude in elective caesarean group was lower than that in the case groups, the same study recommends solutions such as education of pregnant women and young girls according to theory and behavioral patterns and family counseling at the health centers. Given the importance of proper health education and behavior change strategies (Moeini et al., 2011; WorldHealthOrganization, 2010; Yazdizadeh et al., 2011), the present study examines pregnant women's attitudes who highly intended to have caesarean section in health care centers in Sabzevar, in two methods of routine educational intervention and a planned education program.

2. Material and Method

The present study is a prospective quasi-experimental study. The study population consists of primiparous women highly intent on having caesarean section delivery in health centers in Sabzevar.

The sample size was determined 45 women in the control group and 45 in the study group according to the relevant formula. The sampling method was multi-stage, in that, first health centers in the city of Sabzevar were classified in terms of socio-economic status into 3 classes. Then in each class of high, middle, and low, two health centers were randomly selected and divided into control and case centers. In each center, 15 eligible women who were willing to participate in the intervention and cooperation were chosen with the easy sampling method.

Primiparous women in their third trimester who were willing to have caesarean section and were eligible for vaginal delivery were enrolled. If a participant was not willing to participate or was eligible for caesarean section for any medical reason, she was excluded.

The intervention method was such that the control group received routine education related to the third trimester of pregnancy and had the choice of delivery, and the case group underwent scheduled intervention program, also an education session which ran for maximum of 60 hours, using group discussion techniques, films, and use of models. Within one to two weeks, printed materials about choice of delivery and after care was handed to women. At this stage, face to face education about choice of delivery method was given. The pre-test using questionnaires before educational intervention, and post-test, almost 2 months after intervention which was 2 to 3 weeks to estimated delivery time were completed in an interview. Delivery method was assessed by checking family records after delivery.

The data collection tool was a questionnaire including the following: 9 demographic questions, 16 awareness questions, 17 attitude questions on a five point Likert scale, and 2 intentional behavior questions. The attitude questions on a five point Likert scale ranged from totally agree to totally disagree, and for the ease of comparison and analysis of data, scores were based on 100. Thus, the range of the score of each attitude question and mean of total scores were from 0 to 100, and was classified as score of 0 to 25 poor, 25 to 50 moderate, 50 to 75 good, and 75 to 100 very good. The validity of The questionnaire was made through content validity. Thus, the questions related to attitude were extracted after reviewing scientific

literature and were approved by 3 experts in the field. The reliability of the attitude questionnaire was determined through Cranbach's alpha ($\alpha=0.70$).

The data were analyzed using the statistical software SPSS, descriptive and analytical statistics, including central and dispersion indices and the Fisher exact tests, chi-squared test, Mann-Whitney,

Wilcoxon test, and independent t-test. Levels lower than 0.05 were considered significant.

3. Results

The mean age of the control group was 20.24 (4.73) and of the case group 23.44 (4.9) years, and the mean gestational age in the control and case groups was 6.46 (0.98) and 6.26 (0.78) months, respectively.

In this study, in the case group, 2 women (4.4%) had elementary education, 6 (13.3%) had middle school education, 18 (40%) had high school diplomas, and 19 (42.2) had higher education. In the control group, 4 (8.9%) had elementary education, 9 (20%) had middle school education, 16 (35.6%) had high school diploma, and 16 (35.6%) had higher education. The chi-square test did not reveal any significant differences between the two groups in respect of their education.

In the case group, 42 women (93.3%) had expected pregnancies, and in the control group, 44 (97%) had expected pregnancies. The chi-square test did not show any significant differences between the two groups in this respect.

Before intervention, Fisher’s exact test did not show any significant differences between the two groups in respect of women’s intentions to choose caesarean section delivery (see table 1).

Table 2 compares the overall attitude score between the control and case groups before and after the educational intervention.

Table 3 compares the mean scores of the attitude in the control and case groups, also between the two groups.

Intention group	Case group	Control group
I would never select cesarean section	0(0%)	1(2.2%)
I would probably select cesarean section	22(48.9%)	27(60%)
I would definitely select cesarean section	23(51.1)	17(37.8%)
Fisher test result	P=0.28	

Mean score of attitude	case Mea n	SD	Control mea n	SD	Independent-t test result
Before intervention	50.0	10.3	48.3	8.5	P=0.38
After intervention	49.8	9.05	40.7	10.2	P<0.001

table3: comparison of attitude mean scores of case and control groups, before and after intervention

Attitude toward type of delivery groups		Case		Control		Result
		Mean	SD	Mean	SD	
Mother right to select type of delivery	Before intervention	21.11	21.94	12.77	16.53	*P=0.04
	After intervention	17.22	1.83	15.00	1.79	*P=0.50
	Result	**P=0.17		**P=0.30		
vaginal delivery is not Agonizing	Before intervention	59.44	29.33	56.66	26.32	*p=0.53
	After intervention	58.33	2.38	46.11	2.76	*p=0.03
	Result	**p=0.83		**p=0.14		
delivery selection and financial status	Before intervention	49.44	23.53	50.55	26.90	*p=0.83
	After intervention	65.55	2.15	51.66	2.68	*p=0.006
	Result	**p=0.003		**p=0.83		
level of mother education and delivery selection	Before intervention	42.77	21.73	52.22	24.89	*p=0.07
	After intervention	68.33	1.79	47.22	2.33	*p<0.001
	Result	**p<0.001		**p=59		
vaginal delivery as sign of mother success	Before intervention	41.66	22.61	37.22	2.73	*p=0.37
	After intervention	30.55	1.98	47.22	2.33	*p=0.11
	Result	**p=0.007		**p=0.36		
mother knowledge in delivery selection	Before intervention	18.88	19.33	15.00	17.99	*p=0.31
	After intervention	16.11	2.00	16.11	2.07	*p=0.91
	Result	**p=0.34		**p=0.76		

vaginal delivery is not scaring	Before intervention	63.33	29.48	47.22	2.39	*p=0.61
	After intervention	67.22	24.88	33.88	2.45	*p=0.008
	Result	**p=0.01		**p<0.001		
vaginal delivery and sexual relationship problems	Before intervention	56.11	25.68	61.11	2.10	*p=0.93
	After intervention	61.11	2.10	48.33	2.15	*p=0.008
	Result	**p=0.33		**p=0.16		
Lack of fatigue in vaginal delivery	Before intervention	63.33	2.41	52.77	2.14	*p=0.053
	After intervention	52.77	2.14	40.55	2.15	*p=0.006
	Result	**p=0.08		**p=0.02		
Caesarean section delivery and lack of enjoyment of immediately seeing the baby	Before intervention	52.22	2.54	55.55	2.43	*p=0.60
	After intervention	54.22	2.54	38.33	2.29	*p=0.001
	Result	**p=0.67		**p=0.01		
Caesarean section and the intelligence of babies born in this way	Before intervention	51.11	2.33	51.66	1.87	*p=0.89
	After intervention	64.44	2.35	49.44	2.74	*p=0.001
	Result	**p=0.71		**p=0.02		
Seeing birth of the baby by mother	Before intervention	48.33	2.22	62.77	1.89	*p=0.66
	After intervention	51.11	2.71	49.44	2.74	*p=0.007
	Result	**p=0.81		**p=0.009		
Caesarean section delivery and quality of care in hospital and at home	Before intervention	50.00	2.44	52.22	2.60	*p=0.71
	After intervention	62.77	1.89	42.66	2.64	*p=0.002
	Result	**p=0.02		**p=0.58		
The role of delivery pressure in baby's health	Before intervention	47.77	1.49	46.11	2.49	*p=0.78
	After intervention	47.22	2.33	51.11	1.99	*p=0.45
	Result	**p=0.58		**p=0.13		
Unbearable pain of caesarean	Before intervention	62.22	2.17	52.22	2.12	*p=0.02
	After intervention	60.55	2.09	43.33	2.09	*p<0.001
	Result	**p=.57		**p=0.05		
Mother producing more milk in natural birth	Before intervention	51.66	1.79	43.33	1.71	*p=0.01
	After intervention	36.11	1.55	42.22	2.76	*p=0.14
	Result	**p<0.001		**p=0.63		
Caesarean section is not a suitable method of avoiding pain.	Before intervention	71.66	2.03	65.00	2.40	*p=0.11
	After intervention	42.77	2.23	37.77	2.53	*p=0.30
	Result	**p<0.001		**p<0.001		

*Mann-Whitney test result, **Wilcoxon test result. Note

4. Discussions

The present study examines the attitudes of primiparous women highly intent on having caesarean section delivery in two methods of routine education and planned educational intervention.

With respect to the joy of seeing the baby after vaginal delivery, the educational intervention was able to maintain and enhance the desired attitude in pregnant women, whilst in the control group, it was not so. About the impact of education on the attitude, this study was consistent with the study by Tofighinia et al (Tofighi Niaki et al., 2010). In Kerman (Aali & Motamedi, 2005), where 44.1% completely agreed on better quality of mother-baby bonding in vaginal delivery and only 3.4% disagreed. Also in some

studies, 20% believed in the mother-baby relationship (Manthata et al., 2006), and in another study, only 2% expressed improved bonding (Stoll, 2009).

In a study by Ahmadiania et al (Ahmad-Nia et al., 2009), women with higher educational status had chosen caesarean section. The present study was able to significantly improve the attitude of women about education and caesarean section and in this respect this study is in concurrence with other studies (Tofighi Niaki et al., 2010).

In the current study, the case group had a more favorable attitude toward wealth and caesarean section, which was the same as similar studies conducted in Iran (Tofighi Niaki et al., 2010).

Stoll study indicated that high percentage (53%) mentioned the natural process of the phenomena of birth as the reason for preferring vaginal delivery (Stoll, 2009), also studies conducted in Australia (Grivell & Dodd, 2010) have indicated that mother's anxiety was the most important influencing factor in choosing delivery method and fear of pain was identified as the primary reason for choosing caesarean section. In the present study, the case group gained a more favorable attitude toward vaginal delivery not being fearsome and this attitude remained stable until after intervention, which in terms of the effect of education on the attitudes was consistent with the results of the study by Tofighinia et al (Tofighi Niaki et al., 2010).

With respect to the type of delivery and intelligence of the baby, this study was able to find a significant difference between the control and case groups concurring with the study by Tofighinia et al (Tofighi Niaki et al., 2010).

In the study conducted, in most areas of attitude, difference was observed between the two groups, which could indicate the influence of techniques employed including: films, group discussion, brain storming, and printed materials, and their impact on attitude change (Gilbert, Sawyer, & McNeill, 2011).

According to results obtained, in comparison between the case and the control groups in the entire case group, a more desirable attitude toward vaginal delivery was maintained until after intervention. In the present study, the attitudes of participants in the case group did not change, but in the control group it was considerably reduced.

There have been some studies reporting the effect of education on attitude (Amidi & Akbarzadeh 2006; Sharifirad et al., 2010; Tofighi Niaki et al., 2010). However, in a study by Toghiani et al., education did not show any effect on attitude, and no difference was observed between control and case groups in terms of attitude. The present investigation is somewhat similar to both studies, as it managed to stabilize attitudes while showing a difference between the two groups.

Although the difference in attitudes between control and case groups was seen at the end of intervention, the general attitude in the case group was moderate to favorable. It is important to pay attention to this point in employing change of attitude methods. When people lack attitude and somehow they cannot use their accessible attitude from memory, it is more likely for them to be influenced by other subjects that may not be a true reflection of their own attitudes (Wilson & Schooler, J.W, 2008).

In fact every action can be predicted through attitude toward expected behavior, Therefore, results of studies indicate that the relationship between

attitude and behavior can range from nothing to excellence (Fazio H.R, 2008). It seems there are a multitude of complex factors that are highly important both about attitude and other behavioral factors in those women who have made definite decisions to choose caesarean section. Thus, it is recommended that behavioral techniques and models of health education and enhancement of health be used alongside qualitative studies.

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Intein as a Novel Strategy for Protein Purification

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Abstract: Inteins are parts of proteins that cut themselves out of the whole protein entirely on their own. An important development in the area of recombinant protein purification has been the incorporation of self-cleaving protein elements into a variety of fusion-based purification systems. Inteins appear most frequently in Archaea, but they are found in organisms belonging to all three domains of life and in viral and phage proteins. Most inteins consist of two domains: One is involved in autocatalytic splicing, and the other is an endonuclease that is important in the spread of inteins. This review focuses on the evolution and technical application of inteins and only briefly summarizes recent advances in the study of the catalytic activities and structures of inteins. We further investigated the recent expanded applications of the Express Protein Ligation (EPL) technology in the fields of proteomics and bioimaging. This work is expected to provide a rough outline for the evaluation of these methods for large-scale bioprocessing of a variety of products.

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Introduction

Inteins (internal proteins) are genetic elements similar to self-splicing introns; however, inteins are transcribed and translated together with their host protein. Only at the protein level do the inteins excise themselves from the host protein. The two portions of the host protein separated by the intein are called exteins (external proteins) (1,2,3). During the splicing process the intein is excised, the two exteins are joined by a peptide bond, and the host protein assumes its normal folding and function. The first intein was discovered in 1987 when the carrot and *Neurospora crassa* vacuolar ATPases were compared with a putative Ca²⁺ pumping ATPase. The latter had been isolated as a gene whose mutation made yeast resistant against the calmodulin antagonist trifluoperazine (4). The beginning and end of the encoded protein was very similar to the vacuolar ATPase subunits whose sequences had been submitted to the databanks at the same time. However, the central region of the putative calcium pump had no similarity to any known ATPase. Rather, this portion showed weak similarity to endonucleases. Anraku's lab (5) isolated the cDNA for the yeast vacuolar ATPase A-subunit and found the same sequence, including the central region, that had been earlier described as the trifluoperazine resistance gene (4). Surprisingly, denaturing

polyacrylamide gel electrophoresis of the isolated protein demonstrated that the catalytic subunit of the functioning yeast V-ATPase had a molecular weight of only 70 kDa, as expected for a subunit without the insertion. Subsequently Kane et al. (6) showed that the insertion was still present in the mRNA, that the whole protein including the insertion was translated, and that the insertion spliced itself out of the protein during posttranslational processing. The concept that one gene determines one enzyme has long been a common principle for genetic information transfer (18, 19). In 1990, evidence that one gene produces two enzymes via protein splicing emerged from the structural study of the *Saccharomyces cerevisiae* VMA1 gene (20) followed by its expression analyses (20,21). The nascent 120-kDa translational product of VMA1 excises out the 50-kDa VDE site-specific endonuclease (VMA1-derived endonuclease (22) or VMA1 intein) and splices the N- and C-terminal exteins to form the mature 70-kDa catalytic subunit of the vacuolar ATPase. Since the first discovery of the VMA1 intein, more than 100 putative inteins have been identified in eubacteria, archaea, and eukaea species (23). Though only few have been proven to undergo protein splicing, their N- and C-terminal junctions are highly conserved (see the VMA1 sequence shown in Fig.1).

	N-Extein		Intein		C-Extein		Splicing
	1	284	362	738	1071		
VMA1	M	NYSNSDAIIYVGCFAKG	THE	VVVHNCGERGNEMAEVL	D		Splicing
XC-VDE-His		MTIYVGCFAKG	THE	VVVHNCGHHHHHGR			++
MIIYVG-VDE-CGER-C ₁		MIIYVGCFAKG	THE	VVVHNCGERGNEMAEVL	D		++
N ₁ -MIIYVG-VDE-CGER	M	NYSNSDAIIYVGCFAKG	THE	VVVHNCGERG			++
XA-VDE		MIIYVGAFAKG	THE	VVVHNAGERG			-
X10SAS		<u>MSNSDAIIYVGS</u> FAKG	<u>TNE</u>	VVVH <u>AS</u> GERGNEMAE			-
X10SSS		<u>MSNSDAIIYVGS</u> FAKG	<u>TNE</u>	VVVH <u>SS</u> GERGNEMAE			-
X10SNS		<u>MSNSDAIIYVGS</u> FAKG	<u>TNE</u>	VVVH <u>NS</u> GERGNEMAE			+
X10SNC		<u>MSNSDAIIYVGS</u> FAKG	<u>TNE</u>	VVVH <u>NC</u> GERGNEMAE			++
X10CNS		<u>MSNSDAIIYVGC</u> FAKG	<u>TNE</u>	VVVH <u>NS</u> GERGNEMAE			++
X10CNC		<u>MSNSDAIIYVGC</u> FAKG	<u>TNE</u>	VVVH <u>NC</u> GERGNEMAE			++

Figure 1. Sequences of the VMA1 protein and recombinants. The N- and C-terminal sequences of the recombinants are aligned with the VMA1 sequence of which the residues from Cys284 to Asn737 correspond to the VDE intein. Residues subjected to the mutation studies are indicated with bold characters. The N- and C-terminal side polypeptides are indicated with N₁ and C₁, respectively. The replacements in the X10-series VDE recombinants are underlined. Splicing activity for each recombinant discussed in the manuscript is represented with a corresponding sign in the 'Splicing' column.

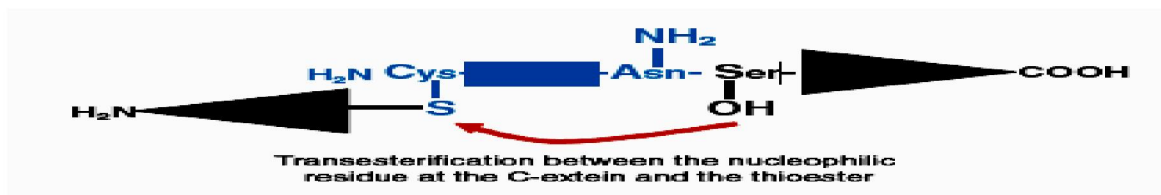
Mechanism of Protein Splicing

Substantial information about the chemical reactions involved in protein splicing is available (7, 8, 9, 10, 11, 12, 13, 14, 15) and was recently reviewed in (16). Briefly, protein splicing involves the following four steps.

Step 1 The amino-terminal splice junction of the intein is activated by an N-O or N-S shift that leads to an ester or thioester intermediate. As a result of this rearrangement, the N-extein binds to the oxygen of a serine or to the sulfur of a cysteine residue at the amino-terminal splice junction.



Step 2 Cleavage of the ester at the amino-terminal splice junction occurs through attack of a nucleophilic residue located at the carboxy-terminal splice junction. This transesterification results in a branched protein intermediate.



Step 3 The cleavage proceeds through asparagine cyclization, which causes intein excision and splicing of the two exteins by an ester bond. Several inteins have glutamine rather than asparagine residues at their C-terminal end, suggesting that cleavage in these inteins might occur via an aminoglutarimide rather than an aminosuccinimide intermediate (16, 17).



Step 4 A spontaneous rearrangement results in formation of a peptide bond between the two exteins.

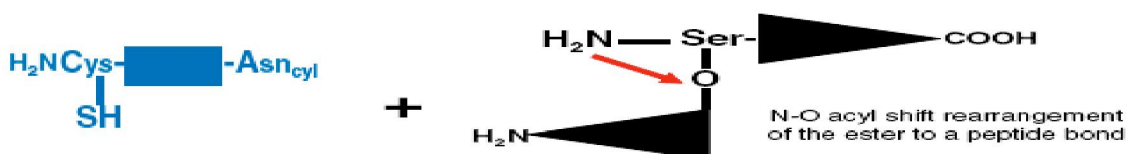


Figure 2. Structure of mini-inteins and large inteins

Inteins are classified into two groups, large and minimal (mini) (24). Large inteins contain a homing endonuclease domain that is absent in mini-inteins. Homing endonucleases are site-specific, double-strand DNA endonucleases that promote the lateral transfer between genomes of their own coding region with flanking sequences, in a recombination-dependent process known as “homing.” Usually, homing endonucleases are licing domain, and a central endonuclease domain. Splicing-efficient mini-inteins have been engineered from large inteins by deleting the central endonuclease domain, demonstrating that the endonuclease domain is not involved in protein splicing (27,28,29). The splicing domain is split by the endonuclease domain into N- and C-terminal subdomains, encoded by an open reading frame within an intron or intein (25,26). Large inteins are bifunctional proteins, with a protein splicing which contain conserved blocks of amino acids, with blocks A, N2, B, and N4 in the N-terminal subdomain, and blocks G and F in the C-terminal subdomain (30, 31) These domains can also be identified in mini-inteins (Fig. 3). The three-dimensional structures of naturally occurring mini-inteins and engineered mini-inteins reveal that the N- and C-terminal splicing domains form a common horseshoe-like 12- β -strand scaffold termed the Hedgehog. Intein (HINT) module (32,33,34,35,36,37). All known inteins share a low degree of sequence similarity, with conserved residues only at the N- and C-termini. Most inteins begin with Ser or Cys and end in His-Asn, or in His-Gln. The first amino acid of the C-extein is an invariant Ser, Thr, or Cys, but the residue preceding the intein at the N-extein is not conserved (38). However, residues proximal to the intein-splicing junction at both the N- and C-terminal exteins were recently found to accelerate or attenuate protein splicing (39).

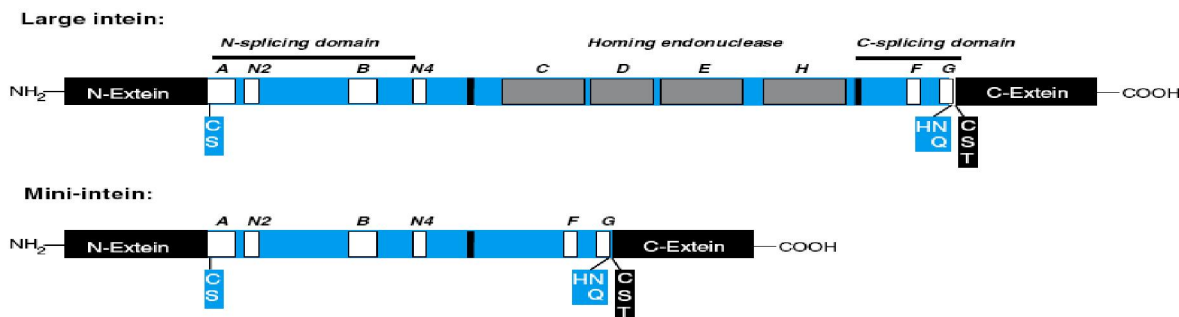


Figure 3: Structure of large and mini-inteins. Conserved elements in a large intein and mini-intein are indicated. The white and grey areas A, N2, B, N4, C, D, E, H, F, and G are conserved intein motifs identified by Pietrokovski (40) and Perler et al. (41). The exteins are illustrated in black and the intein sequence in blue.

Application of intein in biotechnology

1) Self-circularization by inteins

Cyclic antibiotics display an increased activity and stability in comparison to their linear analogs. Inteins play a growing role in the production of cyclic peptides through the aforementioned IPL technique (42). The protein of interest is fused through its C-terminus, to the N-terminus of an intein, in which the C-terminal Asn has been mutated to be incapable of cleaving the C-terminal binding tag. The N-terminus of the target protein is altered so the second residue after the Met is a Cys. After purification of the target protein, the N-terminal Met is removed using methionyl-aminopeptidase from *E. coli*, resulting in an N-terminal Cys residue (43,44). After purification, including elution from the column by thiol induced N-terminal cleavage of the intein, the linear peptide contains a C-terminal thioester and a Cys at its N-terminus that can react to form a new peptide bond. The introduction of a non-native linker sequence improves cleavage efficiency, but also has the potential to interfere with the biological activity of the cyclic protein. Another problem is the possibility of polymerization instead of cyclization by activated peptides. Split inteins have also been applied in the generation of cyclic proteins and peptides. The very timely and elegant Split Intein-mediated Circular Ligation Of Peptides a ProteinS (SICLOPPS) system uses the naturally split *Synechocystis* sp. *Ssp DnaE* intein, which is fused in a rearranged order (IC–target protein–IN), allowing the efficient cyclization of the target protein by reconstitution of the *Ssp DnaE* intein. Using this method, it was possible to generate cyclic peptides that are short as eight amino acid residues. SICLOPPS has been used in inhibitor studies for the rapid synthesis of very large cyclic peptide libraries that are superior to the traditional chemically generated libraries, and which can be screened *in vivo* for new potent therapeutic drugs (45, 44). In recent years, SICLOPPS has been impressively used, for instance, to identify several inhibitors for the dimerization of ribonucleotide reductase and 5- aminoimidazole-4-carboxyamide-ribotide transformylase (46).

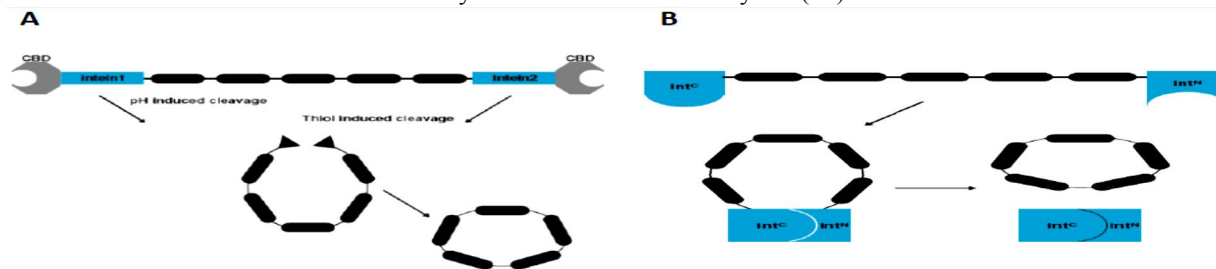


Figure 4. (A) Self-circularization of peptides. A Self-circularization of proteins using the TWIN system. A target protein is embedded between two intein sequences, which are modified for N- or C-terminal cleavage, respectively. The inducible splicing reaction of the inteins leads to the generation of an activated thioester residue and an N-terminal Cys for the spontaneous circularization of the linear peptide. (B) Utilization of the Split Intein-mediated Circular Ligation of Peptides a Protein S (SICLOPPS) also enables the circularization of peptides. In this system, the order of the naturally split *Synechocystis* sp. *Ssp DnaE* intein is inverted (IC–target protein–IN), and the reconstitution of the *Ssp DnaE* intein allows the efficient cyclization of the target protein.

2) Intein-Mediated, *In Vitro* and *In Vivo* Protein Modifications with Small Molecules

Native chemical ligation was developed for the synthesis of peptides by condensation of their unprotected segments (47). This technique requires a synthetic peptide with a C-terminal thioester and another with an N-terminal cysteine residue to yield a native peptide bond at the site of ligation. Though useful, this approach was limited to the synthesis of small proteins of 100-200 residues in size, as multiple ligations have proven to be technically demanding. By combining the intein-mediated protein splicing with the chemistry of native chemical ligation, it is now possible to engineer unnatural proteins of, in principle at least, unlimited sizes. This new approach is known as the Expressed Protein Ligation or intein-mediated protein ligation (EPL or IPL) (48). Briefly, it refers to the use of an Intein-based Protein Ligation system to generate a protein thioester from the corresponding protein-intein fusion. Unique functionalities can then be incorporated into the proteins using the chemistry of native chemical ligation. Over the years, intein mediated protein ligation has become an extremely powerful platform for the chemical semi-synthesis and engineering of proteins. For instance, the technique has been used for the incorporation of non coded amino acids into protein sequences (49), the isolation of cytotoxic proteins (49), and the synthesis of the 600-amino acid N-terminal segment of the 70 subunit of *Escherichia. coli* RNA polymerase(49), just to name a few. Trans-splicing inteins (50), in which functionally mature intein was split into two fragments and only regained their activity upon reconstitution of the two fragments, have been employed in protein semi-synthesis(50), and for the study of protein structure/function relationship by segmental isotopic labeling of proteins for NMR analysis (50). At least two independent groups had reported the use of split inteins for the synthesis of cyclized proteins and peptides (51). Recently, the use of split inteins has been applied to the study of protein-protein interactions and the translocation of proteins in living cells (51). For a more in-depth coverage of the Express Protein Ligation and its applications, readers are directed to the most recent review by Muir (48). Biotin-avidin system is an interesting and highly exploited system for a plethora of diverse applications in modern biology. The success of this system would depend on the various approaches available for the incorporation of the biotin moiety into a protein of interest. Traditionally, protein biotinylation has been achieved using simple bioconjugate techniques with biotin-containing reactive chemicals (53). This typically results in the non specific biotinylation and, in many cases, the inevitable inactivation of the target protein. Alternative techniques for the site-specific biotinylation of proteins have been developed (54, 55). Cronan *et al.* identified a set of peptide sequences, which upon fusion to a target protein could be biotinylated by the enzyme biotin ligase. The biotin ligase works by covalently attaching the biotin moiety to a specific lysine residue in the peptide sequence (54). This thus provides a site-specific approach for protein biotinylation, both *in vitro* and *in vivo*, although the process was often inefficient and toxic to the host cell when performed *in vivo* (55). To overcome some of the limitations faced in current protein biotinylation techniques, the use of intein-mediated protein ligation for the site-specific biotinylation of proteins were investigated (56). The protein of interest was fused through its C-terminus to an intein, which had its other terminus fused to a chitin-binding domain (56,56). Upon expression in the host cell, the cell lysate containing the fusion protein was first loaded onto a column packed with chitin beads followed by the addition of a thiol-cleaving reagent (e.g. cysteine-biotin; inset in Figure 5).

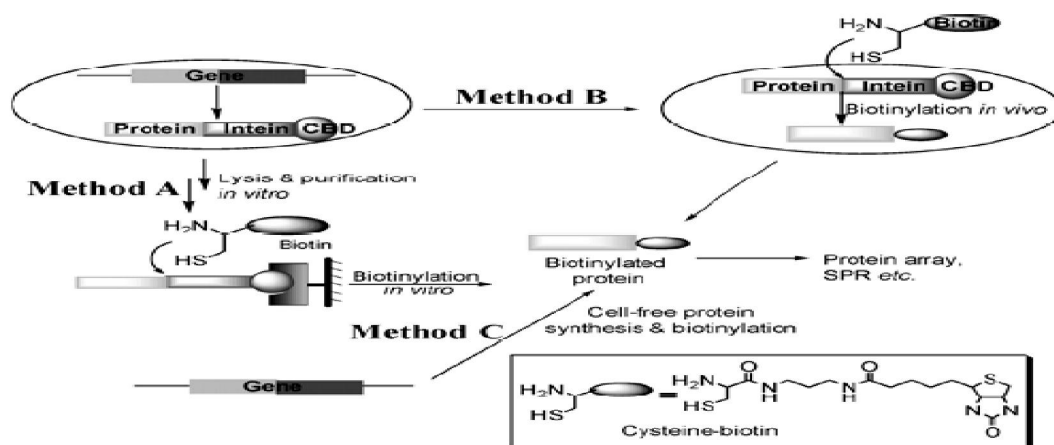


Figure 5. Three intein-mediated protein biotinylation strategies. (Method A) *In vitro* biotinylation of column-bound proteins; (Method B) *In vivo* biotinylation in live cells; (Method C) Cell-free biotinylation of proteins.

The fusion protein underwent self-cleavage, catalyzed by the fused intein, and resulted in the protein having a reactive thioester group at the C-terminal. At this stage, the thiol side chain from the addition of cysteine-biotin attacked the thioester functionality and the resulting thioester-linked intermediate underwent spontaneous rearrangement, affording a native peptide bond to generate proteins that were site-specifically biotinylated at their C-termini (Figure 5; Method A). This strategy is simple yet efficient and capable of biotinylating various proteins from different biological sources. In addition, this strategy could be readily adopted in a 96-well format, enabling highthroughput generation of a large number of biotinylated proteins. Next, this strategy extended to *in vivo* biotinylation of proteins in both bacterial and mammalian systems (Figure 5; Method B). The simple addition of the cell-permeable cysteine-biotin probe to the growth media followed by further incubation of the cells resulted in substantial biotinylation of the proteins inside the cells. Further optimizations of the cell growth and *in vivo* biotinylation conditions led to an increase in the level of protein biotinylation in the cells. For the bacterial system, the only other band observed on the western blot was acetyl-CoA carboxylase, an endogenous biotinylated protein found in bacterial cells. Similarly for the mammalian system, the three other biotinylated proteins observed on the western blots, besides the target protein, were the endogenous biotinylated proteins. The efficiency of intein-mediated protein biotinylation, both *in vitro* and *in vivo*, depends greatly on the intein fused to target protein (56). A cell free system has many potential advantages over traditional *in vivo* recombinant protein expression in cells (57). Cellular toxicities due to overexpression of certain proteins, possible degradation by endogenous proteases and formation of inclusion bodies of proteins could potentially be avoided all together in a cell free system. It should be noted however, although the cell free biotinylation approach seems the most simple out of the three strategies presented in Figure 5, the efficiency of protein expression and subsequent biotinylation depended on a few other factors including the DNA quality and concentration, the nature of the target protein and etc. The utility of the above-described site-specific biotinylation of proteins is in the field of protein arrays. Array-based technologies are one of the most promising technologies developed in the post-genomic era to study proteins in a high-throughput fashion (58). One of the key aspects in generating a uniform functional protein array is the ability to immobilize proteins onto glass slides and at the same time ensuring that their native activity is not lost. This is because proteins are “delicate” they may unfold and lose their activity if

not properly attached to a suitable surface. While a variety of approaches have been developed which allow site-specific immobilization of small molecules and peptides in a microarray (59), relatively few methods are available for protein immobilization (58, 60-62). In most cases, these approaches are non-specific, resulting in randomly orientated protein immobilization (58,60). Uniform site-specific immobilizations of functional proteins was first reported by Zhu *et al.*, who successfully created a functional “yeast proteome array” by attaching thousands of (His) 6-tagged proteins onto Ni-NTA-coated glass slides (60). However, the noncovalent (His) 6-Ni-NTA interaction is not very strong, often susceptible to interference by commonly used chemicals and salts, making this strategy useful to only a handful of down-stream protein array applications (56, 61, 62,63). Mrksich and co-workers captured cultinase-fused proteins onto glass surfaces coated with a phosphonate ligand, achieving site-specific and covalent immobilization of the proteins (61). Scientists successfully developed a site specific method to covalently immobilize hAGT-fused proteins onto modified glass surfaces (61). Also they used Sfp phosphopantetheinyl transferase to mediate site-specific covalent immobilization of target proteins fused to the peptide carrier protein (PCP) excised from a nonribosomal peptide synthetase (NRPS) (61). Recently, scientists described the use of EPL to express functionally active proteins which possess a C-terminal thioester handle, and subsequently immobilized them to a cysteine-modified glass slide, generating the corresponding protein array (61).

Summary and Future Outlook

The site-specific modification of proteins represents a powerful approach by which one can manipulate/ control the protein activities and distribution, thereby studying and understanding the biological function of proteins in the cell. Intein-mediated protein ligation is one such tool that allows the specific incorporation of novel functionalities into proteins. Both strategies were applied to the creation of protein arrays using biotin-avidin system and the chemistry of native chemical ligation, respectively. Scientists also extended the EPL to the field of bioimaging by synthesizing different cell-permeable small molecules probes that are able to site-specifically label N-terminal cysteine containing proteins expressed inside a living cell. Current efforts are looking at other forms of proteins that undergo auto-proteolysis. The family of hedgehog proteins found in animals is one example (64). These proteins are responsible for the patterning of a variety of structure in animal embryogenesis. Hedgehog proteins were found to undergo a self-cleavage reaction, which

was mediated by its carboxyl-terminal end to generate reactive intermediates required for protein ligation. Hence the study of hedgehog proteins might open up another possibility for mammalian-based protein modifications/engineering.

Currently, there are very few enzyme-based approaches for protein ligation (65, 66). One is subtiligase, an engineered subtilisin that have been shown to catalyze the ligation between peptide fragments through a process known as reverse proteolysis (65). Another is a transpeptidase found in the cell envelope of many Gram-positive bacteria Sortase (66). Sortase recognizes an LPXTG motif and cleaves between the threonine and glycine residue pentaglycine located on the peptidoglycan of the cell wall (66).

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Patients Perception and Satisfaction of the Ambulance Service (115) at Shahrekord, IranMehrdad sharifi¹, Shahram Baraz², Falaheddin Mohammadi³, Monir Ramezani⁴, Safar Ali Esmaeili Vardanjani⁵¹Ms, Manager of Health Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran²Doctoral Candidate, School of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran³Ms, Department of Angiography, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran⁴Doctoral Candidate, Faculty Member of School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran⁵Ms in Nursing Education, Shahrekord University of Medical Science, Shahrekord, Iran
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Abstract: The services provided to the patients of pre-hospital emergency center and their satisfactions indicate the quality of pre-hospital emergency services. The goal of this study is to investigate the satisfaction of patients with Ambulance Service services (115) in Shahrekord in the first half of (2012). In this descriptive and analytic study, 450 patients transferred to the hospital by pre-hospital emergency center were chosen using simple random sampling method and data was collected by using satisfaction evaluation questionnaire. The information obtained under SPSS software version 16 was analyzed by statistical descriptive test, independent t test, variance analysis test and Pierson Correlation test. The findings showed that satisfaction level with pre-hospital emergency services in men, low-educated people, married people, those with the record of using emergency services and those with emergency problems was significantly higher than others. Satisfaction level in all fields was above 50% and was totally 71.12. The highest level of satisfaction was for the efficiency of emergency center (58, 78) and the lowest level of satisfaction in the questions was for the performance of technicians (58, 73). Patients' satisfaction with emergency services and their quality is considered as one of the main concepts in pre-hospital emergency procedures, in the manner that the results of this study showed that patients' satisfaction in different fields were high and satisfactory and the technicians should allocate much more time for interaction with patients in order to improve their satisfaction.

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1. Introduction

Self-treatment at home is the first line of treatment all over the world. Most of the patients and their relatives seek for other treatment ways when they fail to treat themselves at home. Today, one of the most important and most available alternatives is to use pre-hospital emergency services (Press, 2006). In health care system, the first contact of critical and emergency patients is generally made with pre-hospital emergency center (Esmaeili Vardanjani et al., 2011). This first contact has an important effect on the patients' view about other sections of the treatment system. Therefore, patients' satisfaction with this system will affect on satisfaction with other sections as well.

In the past, treatment was the only criterion used for evaluating the quality of cares and level of patients' satisfaction (Vuori, 1991). But gradually, other aspects of caring such as softness, availability, quality of interpersonal communications between the patients and care providers were added as different aspects of satisfaction to the previous criterion, i.e.,

patient's improvement (Haddad et al., 1998). Gradually, factors such as economic aspects and reputation seeking by hospitals and their managers led to the satisfaction of patients to be more considered by the managers (Margolis et al., 2003).

Patients' satisfaction includes a series of their experiences of health care system (Press, 2006) arising from their evaluation of how the care provider has mentally and physically communicated with them and how their physical and mental needs have been met by the care provider (Oluwadiya et al., 2010). Patients' satisfaction has a basic role in health preservation and disease prevention, in the manner that increase of patients' satisfaction will result in their physical and mental recovery (Rodbari et al., 2009).

Considering the importance of patients' satisfaction with the services provided by pre-hospital emergency center and also considering the fact that at the present time an exact and accurate attention to the satisfaction aspects of emergency patients and their special caring needs is felt at this

stage between the domestic and foreign studies, the present study was conducted with the goal of evaluating the satisfaction level of patients with the services provided by the pre-hospital emergency center (115) in Shahr-e-Kord city, Chahar Mahal va Bakhtiari Center.

2. Material and Methods

The present study is a descriptive and analytic study conducted in Shahrekord city in the first half of 1391 (2012). Since no estimation of patients' satisfaction was available, sample volume was estimated at 384 people by considering $p=0.05$, a confidence interval of 95% and an accuracy of 5% and finally 450 samples were studied by considering the possible loss. Samples were selected from among the patients and injured people who had been transferred by the ambulances of pre-hospital emergency center of Shahrekord city to Hajar and Kashani Hospitals of that city. To obtain the number of samples in any of the pre-hospital emergency stations, the quota of each station was determined considering the statistics of patients transferred from any of the stations to the hospital and by using classification sampling. Then, the samples were selected by using simple sampling method and the days of the week. The criteria for inclusion of samples in the study included transfer to hospital by ambulance and subsequent hospitalization in the hospital. The criteria for exclusion from the study included the patients with a consciousness level less than 15 GCS, children less than 12 years old, the patients with much pain or high stress and dissatisfaction of patients for participation in the study. In case of any companion, patients who were not conscious or could not answer and/or children less than 12 years old, their companions were used for answering and participating in the study and in case of no companion, the patients were excluded from the study.

Since satisfaction is a complete and multidimensional issue, one of the most important and principal accepted ways to study the patients' satisfaction is the use of multidimensional questionnaires that evaluate different areas of patients' experiences (Oluwadiya et al., 2010). Therefore, questionnaires were used in this study to investigate the patients' satisfaction. To prepare a questionnaire, two questionnaires were merged including Emergency Care Satisfaction Scale questionnaire (CECSS¹) (Anders et al., 2010) and the questionnaire used for investigation of patients' satisfaction with the pre-hospital emergency services in Malaysia (Anisah et al., 2008). After translation and fulfillment of the comments of a few professors

of Shahrekord University of Medical Science for the purpose of reliability and validity, the contents of the questionnaire in view of validity was confirmed and its reliability was proved through dividing into two halves using Cronbach's alpha ($\alpha = 0.81$) considering the concept of satisfaction which is subject to time. The final questionnaire consisted of 33 questions, 9 questions were used to study demographic information and 24 were used in Likert Scale from 1 to 10 to study the satisfaction of patients with pre-hospital emergency services. The 9 questions related to demographic characteristics included age, gender, education, marital status, records of enjoying emergency services, patient's problem, period of using pre-hospital emergency services, time of mission (day or night) and job (dependence on the healthcare system, i.e., 1st or 2nd grade family members of healthcare system personnel). The 24 satisfaction questions included 5 questions about ambulance, 5 questions about the behavior of technicians with the patient and companions, 5 questions about the professionalism of technicians, 5 about their performances, 4 questions about pre-hospital emergency efficiency and one question about general viewpoint of patients concerning pre-hospital emergency. Data was analyzed by using SPSS software, version 16, statistical descriptive test, independent t test, variance analysis and Pierson Correlation test.

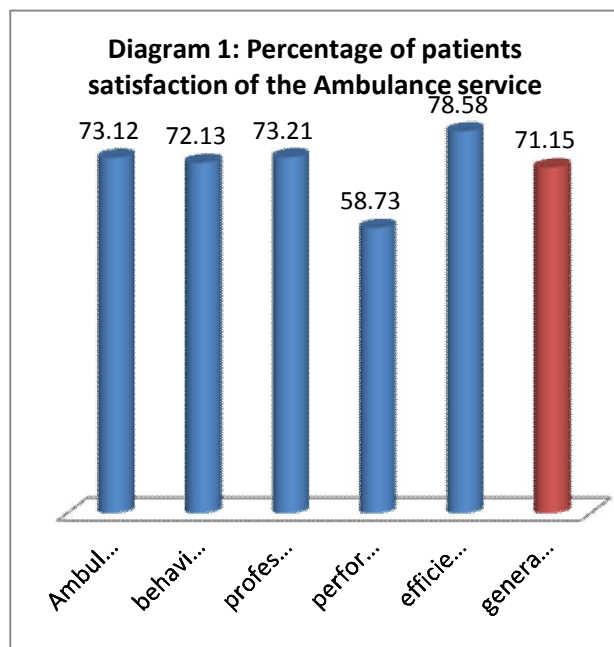
3. Results

Based on the obtained results, the group who had used pre-hospital emergency services the most were in the age range of 15 to 30 (37.3%) and 30 to 45 (26.8%) and the group who had used pre-hospital emergency services the least include those above 75 years old (4.6%). 53.6% of the samples included women and 46.4% were men. Most of them had academic degrees (34%). 60.8% of them were married and 39.2 were single. Most of them (74.5%) had already enjoyed emergency services.

Based on the results of independent t test and variance analysis, satisfaction with pre-hospital emergency services in men, low educated people, married people, those who had already enjoyed emergency service and those who had emergency problems was significantly higher than in other patients (table 1). Satisfaction level in all areas was above 50% and was generally 71.12% (graph 1). The highest satisfaction level observed in the answered questions was for general appearance of ambulance, relaxation and safety feeling upon seeing the ambulance and technicians and availability of technicians. Moreover, the least level of satisfaction was for technicians' answering to all patients' questions and the comfort during transfer with ambulance (table 1).

¹ - Consumer Emergency Care Satisfaction Scale

	Variables	Ambulance	Behavior of technicians	Technicians' professionalism	Technicians' performances	Efficiency of emergency center (115)	Total score of satisfaction
		Mean (standard deviation)	Mean (standard deviation)	Mean (standard deviation)	Mean (standard deviation)	Mean (standard deviation)	Mean (standard deviation)
Gender	Male	39/88(7/14)	40/19(8/95)	32/23(7/69)	30/19(1/19)	25/80(5/02)	1/68(3/36)
	Female	33/68(7/78)	32/48(8/68)	26/73(7/44)	28/68(9/65)	21/64(5/39)	1/43(3/57)
	p-value	0/000	0/000	0/000	0/377	0/000	0/000
Education	Elementary school	38/76(6/97)	37/89(7/84)	30/97(6/96)	33/04(8/46)	23/80(4/35)	1/64(3/05)
	Junior school	40/57(3/64)	42/85(6/59)	32/42(6/65)	25/85(1/1)	25/14(4/48)	1/66(2/18)
	High school diploma	37/36(7/25)	37/89(8/51)	30/08(7/67)	28/50(1/03)	24/52(5/60)	1/58(3/21)
	Academic degree	32/84(8/71)	31/3(10/41)	26/25(8/58)	26/59(1/16)	22/11(6/50)	1/39(4/16)
	p-value	0/000	0/000	0/005	0/002	0/118	0/000
Marital status	Single	34/91(9/35)	34/83(11/1)	28/48(9/67)	26/53(1/44)	23/1(6/56)	1/47(4/25)
	Married	37/62(7/01)	36/86(8/37)	29/80(6/76)	31/19(9/98)	23/90(4/90)	1/59(3/21)
	p-value	0/043	0/203	0/321	0/009	0/369	0/050
Previous use of emergency services	+	38/82(5/08)	39/10(6/75)	31/28(6/27)	33/30(9/53)	25/10(3/68)	1/67(2/60)
	-	35/78(8/77)	35/02(10/2)	28/60(8/45)	28/01(1/08)	23/05(6/05)	1/50(3/90)
	p-value	0/043	0/021	0/072	0/008	0/048	0/012
Patient's problem	Emergency	39/28(5/75)	39/52(7/18)	32/02(6/12)	32/21(9/92)	25/64(3/70)	1/68(2/50)
	Non-emergency	29/35(8/96)	26/92(9/19)	22/04(8)	21/83(9/32)	18/09(6/11)	1/18(3/83)
	p-value	0/000	0/000	0/000	0/000	0/000	0/000
Period of enjoying emergency services	Less than 30 min.	36/77(7/34)	36/04(9/69)	28/48(8/04)	27/80(1/06)	23/51(5/92)	1/52(3/54)
	30-60 min.	36/08(8/49)	35/75(9/43)	29/65(7/94)	30/11(1/05)	23/49(5/39)	1/55(3/72)
	More than 60 min.	50(0/0)	50(0/0)	40(0/0)	49(1/41)	29(1/41)	2/18(2/82)
	p-value	0/50	0/116	0/110	0/014	0/390	0/046



Independent t test showed that there was no significant difference between satisfaction and its areas and dependence on the health system (1st and 2nd grades patients are of the personnel of healthcare system) and time of mission (day and night) ($p>0.05$).

Pearson correlation test showed a direct and significant relation between satisfaction areas (ambulance, behavior of technicians, their

professionalism, their performance and the efficiency of emergency center (115) ($p=0.000$). Moreover, a positive and significant correlation was observed between satisfaction and general satisfaction ($p<0.000$).

4. Discussions

The obtained results showed that generally most of the participants gave high scores to all questions of the questionnaire designed for investigating people's satisfaction with pre-hospital emergency services. The highest items of satisfaction were for efficiency of emergency center (115) in the areas including the time it takes for the ambulance to reach the incident place, the time it takes for the ambulance to reach hospital from the incident place, and the speed of reception at the hospital. It seems that the reason for the high score given by people to the question about their satisfaction with the period of ambulance response in this study was related to the small area of Shahrekord city, lack of any traffic in that city, existence of 4 stations in that city that had been located in suitable distances from each other and could cover different parts of the city quite well. One of the reasons of low response time in this study can be related to the high importance attached by the technicians to the time it takes for the ambulance to reach the incident place and to the transfer of patient with maximum speed to the hospital. Therefore, in most cases they drive with a high speed and continuous audible alarms, they pass red lights and move in the opposite sides. It seems better to

consider this issue a bit more. May be it is better to provide a better response time, to spend more time beside the patient while considering the critical time for transferring the patient to the hospital, to consider a safe speed for the ambulance and to control and manage to some extent the ambulances that use continuous audible alarms, pass red lights and move in the opposite directions.

Prompt response of the pre-hospital emergency personnel in the critical missions is one of the high expectations of people and authorities and the emergency service system is strictly seeking to achieve that. Therefore, most of the pre-hospital emergency service systems have set the evaluation of their performance based on the level of achievement to such prompt response and its reduced time (AL-Shaqsi, 2010). Although response time is one of the criteria for the quality of emergency services, it should be noted that the lives of patients and technicians as well as caring quality must not be sacrificed for ambulance speed or reducing the response time (Pricel, 2006). Response time is called Pitfall and it has been specified that making efforts for reducing the response time will result in losing the tie for collecting information, evaluation of patient's condition and situation of the incident place, necessary time for communicating with the patient, etc. These cases will have a negative effect on the quality of caring the patient (AL-Shaqsi, 2010). The pressures of time and the environment surrounding the patient of injured person will force the pre-hospital emergency nurses to make decisions without having sufficient information. In emergency and complex situations, the decisions made by the nurses are not always correct and justifiable (Esmaeili Vardanjani et al., 2011). Although response time is a very important factor in reducing the mortality of diseases and emergency incidents, the existing shortcomings in manpower and ambulance equipment may reduce the effectiveness of the performed missions (Bahrami et al., 2011). Pricel believes that the technicians should emphasize on the quality criteria for caring the patients much more than response time which disturbs the caring procedure and will have negative and inappropriate effects on health, safety, welfare and good feeling of the patients (Pricel, 2006).

Another item that got the highest score in this study was the patients' satisfaction with reception period in the hospital. The reason is that the pre-hospital emergency personnel are obliged to deliver their patient to the hospital and that the physicians working in the emergency ward prioritize the reception of the patients transferred by the ambulance. Moreover, technicians must deliver their patients to the emergency ward of the hospital in the

least minimum time and must then return to their stations to be prepared for the next possible missions. These all have reduced the time for patients to be received in the hospital as well as their increased satisfaction.

Another reason for high satisfaction of people with pre-hospital emergency services in this study includes sending ambulances almost for all phone calls to the emergency center (115). Emergency services which are provided for free have increased people's satisfaction. Studies have shown that high costs of hospitals reduce patient's satisfaction. Furthermore, a significant relation between the paid price and patients' satisfaction has stated in other studies as well (Rezaei, 2003; Jafari et al., 2007; Khashjan et al., 2006; Malek-Malekan et al., 2010).

The present study which was conducted convergent to other studies (Rodbari et al., 2009; Jafari et al., 2007; Mosaddeghzadeh, 2006) showed that satisfaction in low educated individuals was more than educated individuals. The results of the study made by Roudbari et al. confirmed the results obtained from the present study and showed that low educated people have lower expectations due to their low education (Rodbari et al., 2009).

In this study, satisfaction among male patients was higher than that of women due to lack of female technicians and nurses in the ambulance. In the study conducted by Akbari et al. (Stewart, 2001) and Jafari et al. (Jafari et al., 2007), satisfaction between the two genders had no significant difference, but Mesdagh Zadeh showed that patients' gender is effective in their satisfaction (Mosaddeghzadeh, 2006). However, patient's gender is one of the important and effective factors in the decisions made by nurses in pre-hospital emergency missions (Vuori, 1991).

In the present study, age-related findings on the patients showed that those between 15-30 years old had the highest level of satisfaction. Roudbari et al. showed that high satisfaction of patients with 15-30 years old was due to their pain tolerance threshold (Rodbari et al., 2009). Furthermore, it has been indicated that there is a significant relation between age and level of satisfaction and emergency services (Khashjan et al., 2006).

No significant relation was observed between the use pre-hospital emergency services and patients' satisfaction level. It seems that patients with acute and emergency problems were more satisfied as compared to non-emergency cases. In this relation, the study conducted by Akbari et al. showed that those patients suffering acute pain had declared to be more satisfied (Stewart, 2001).

The areas with the least score in this study were related to the performance of technicians for the items "The technician provided sufficient explanations for his measures" and "The technician ensured that he has answered all my questions". The reasons of this dissatisfaction include lack of sufficient time in emergency missions to provide the patient and his/her companions with necessary explanations. Esmaeili et al. explained that irritation of patient and his/her companions and actions to the contrary of their desires are common issues in emergency cases. This is because that there is no sufficient time for talking and explaining to the patient. They also explained that most of the pre-hospital emergency nurses are upset that due to the time pressure they cannot explain the patient's condition for his/her relatives (Esmaeili Vardanjani et al., 2011). Another reason for low scores given to this area is the high importance the technicians attach to the efficiency of emergency center (115), i.e., time indexes of emergency because as the conduction speed of missions increases, the time necessary for explaining the taken measures to the patient and answering to his questions as well as giving sufficient time to the patient for asking questions will reduce. It has been shown in this study that the highest score for the efficiency of emergency center (115) was given to time criteria and the least score was related to performance area. Pricel explains that the technicians should emphasize on caring quality criteria instead of highly emphasizing on the response time that disturbs the caring procedure and has inappropriate and negative effects on health, safety and well being of the patients (Pricel, 2006).

Another item that affects the satisfaction of patients with pre-hospital emergency services is the appearance of ambulance and technicians. These two are the first cases that patients observe and judge about them. Therefore, cleanliness and good looking appearance of ambulance and emergency personnel is one of the effective cases on the patients' satisfaction. Anish believes that the cloths and uniforms of technicians reflect their adornment, cleanliness and professionalism of personnel and treatment team (Anisah et al., 2008). The available equipment and facilities inside the ambulance is another item that had a significant relation with the satisfaction of patients in our study. Esmaeili et al. explained that availability of necessary equipment and facilities inside the ambulance proportional to the mission as well as having knowledge and capability and being experienced in using the equipment and facilities are effective factors in the decisions made by pre-hospital emergency nurses (Esmaeili Vardanjani et al., 2011). In this relation, Vaitkaitis explained that exhaustion of ambulances in the pre-hospital

emergency center is the most important acute problem of pre-hospital emergency services (Vaitkaitis, 2008).

Professionalism of technicians and their self confidence and qualification were the issues that were questioned in the present study to investigate the patients' satisfaction. It was specified that there was a significant relation between professionalism, self confidence and qualification of personnel and the patients' satisfaction. Abedi et al. considered theoretic knowledge, clinical skill and the capability to make correct decision in facing critical situations by caring staff as qualification (Abedi et al., 2004). Ramezani Badr et al. explained that a nurse is capable and efficient that has sufficient knowledge and skill and can use the information correctly (Ramezani-Badr et al., 2009). Self confidence during the missions is one of the key items in decision making capability of pre-hospital emergency nurses and as a result in the patients' satisfaction. Self confidence increases decision making and correct performance. Necessary and sufficient knowledge and experience are the most important factors for providing self confidence in the pre-hospital emergency nurses (Esmaeili Vardanjani et al., 2011).

Conclusion

The results of this study show that patients' satisfaction with pre-hospital emergency services in Shahr-e-Kord is in a good and satisfaction level. Although pre-hospital emergency personnel are under pressure in view of time and especially during emergency mission, it is recommended that they provide the patients and his/her companions with necessary and sufficient explanations about the measures they make and provide them with more time for asking questions or answering their questions. It is also recommended that while considering the critical factor of time, they have a safe communication and interaction with patients in order to remove their information demands.

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Epidemiologic of Winter Sports Injuries in the Tube Riding Track of Kohrang City, Shahrekord, Iran

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Abstract: Winter sports are fun and exciting and at the same time may be quite risky. Injuries and damages increase if environment, tools and equipments are not standard or athletes are not sufficiently skilled. Tube riding is one of winter sports. Because of a tube rider does not have any control over tube speed, route guidance and does not brake and stop, As a result of injuries in tube riding is very high. This study aims that the epidemiologic investigation of injuries caused by tube riding in the track of Kohrang city in 2009. In this retrospective census study data collected by using the mission records and available documents in the emergency station (115) of Kohrang city, in winter 2009. Total performed missions of the station from June 22, 2009 (no earlier statistics were available in that station) to March 20, 2010 included 216 missions, 183 missions were nonrelated to the tube riding track and 33 cases included those who had been injured in the tube riding track. The injuries caused by tube riding had occurred on Thursdays and Fridays of November, December and January months (on non-vacations days the track is closed). The injuries had all been injured at the tube riding track and the skiing track had no injured person during that year. Of the total 33 people who had been injured at the tube riding track, 15 were women and 18 were men within the age range of 8 to 52 years old. 6 head traumas, one femoral fracture, one facial trauma and nose fracture, 1 chest and sternum trauma, 8 hand traumas, 5 multiple traumas, and 3 lower organs traumas had been recorded. Considering the large number of injured people and the fact that 15% of the missions of that station had been performed only within 24 days of the year (Thursdays and Fridays of November, December and January months), it seems necessary to make managements to reduce the injuries caused by tube riding. Moreover, it is recommended that the information of injured people and those who refer to the clinic is recorded completely and exactly.

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Keywords: Epidemiology, Tube Riding, Kohrang City, Winter Sports

1. Introduction

Tube Riding: One of the most popular winter sports in our country Iran is a tube riding. Tube riding is a winter sports or better winter recreation that people using inflated car tubes as a device like a sledge for sliding down on gradient snow.

Abedi et al (2009) named tube riding winter sport as a non-standard sport, and stated that the amount and severity of injuries resulting from this non standard winter sport is a very high. As well as have expressed that the non standard tubes as a sport tool is the main causes of injuries in tubes riding winter sports. Since the athlete does not have any control over the tube (in terms of speed control and guidance of the tube in the along the track), the extent and severity of injuries is very high than any other winter sports (skiing, snowboarding, sleigh rides,

etc). In addition to the nonstandard tube as an sports vehicle, the other factors causing injuries in nonstandard tube riding sports can be included: the lack of standard and special track for tube riding, Encounter tube riders with natural obstacles (trees, shrubs, rocks, ups and downs the surface of track and...), artificial barriers (lights, fences, tables, etc), the overturning tube rider on the ramp of track, encounter tube rider with other tube riders on the surface of track because a lot of tube riders at the same time crowded on the track, encounter tube rider with the viewers that standing around the track, encounter tube riding with people who are climbing from track, On the other hand, because the players ride the tube as groups and collectively, if the event of accident injured several people at the same time (Abedi et al; 2009).

Sport and recreational activities are one of the important parts of a healthy lifestyle (Marshall and Guskiewicz 2003; Shephard, 2003). Sport activities have changed into one of the most important parts of modern life. Most people want much more times to spend for fun and entertainment and an increasing trend can be seen in the number of people who join the clubs and stadiums (Majewski et al., 2006). However, physical and mental benefits and advantages of that may be reduced as the result of the injuries caused by such activities (Marshall and Guskiewicz, 2003; Shephard, 2003). Skiing is the desirable sport of about 200 million people throughout the world (Hunter, 1999) and snowboard is a winter sport whose popularity has been significantly increased within the recent two decades (Muller et al., 2000). Based on the report of National Sports Institute, each year nearly 10 million people do Alpine skiing and more than two and half million people do snowboarding (Rash, 2002). Skiing, snowboarding, sleigh riding and other winter sports are very interesting while at the same time being dangerous (Rash 2002). Physical and mental advantages of a sport may be reduced as the result of injuries caused by that (Marshall and Guskiewicz, 2003; Shephard, 2003). Fortunately, most of the injuries caused as the result of winter sports are small and light though participation in such sports may result in important effects (Ganter et al., 2003). Sports are mostly accompanied with a high proportion of injuries, e.g., snowboarding, skating and climbing which are increasingly becoming popular and common (Majewski et al., 2006). Since sports are mostly accompanied with a high proportion of injuries and are increasingly becoming popular and common (Steinbrück, 1999) and since the level of injuries increases simultaneous to the increase of popularity of sports (Majewski et al., 2006) and since the treatment of sport injuries are most often deathlike, irremediable and cost and time consuming, preventive strategies are therefore highly important. Successful prevention and control of injuries requires accurate information of problem extensiveness for pre and post interventions. Identification of causes, risk factors and identification of accurate mechanism of injury should be performed before beginning any program to prevent sport injuries. Moreover, measurement of injury should include an accurate and standard definition of injury and its severity, a systematic method to collect information as well as identification of the population exposed at risk and the relevant time (Parkari, 2001). Considering the mentioned subjects, high level of injuries caused by winter sports in Kohrang Zone and lack of any investigation and research in this field, the researcher

decided to investigate the experiences of those who had been injured in winter sports in the said zone.

2. Material and Methods

In this retrospective census study data collected by using the available documents in the emergency station (115) of Kohrang city, in the manner that by referring to the said station, all the missions performed following the accidents relevant to tube riding in winter 2009 that had been recorded in the mission forms were investigated. The people who had been injured in the track were either transferred by the emergency station ambulance or personally referred to the clinic of Kohrang city or were transferred by personal vehicles. There is no statistics of those who were injured in the tube riding track and referred to the clinic (due to non-separation of injured people based on the causes of accidents) or those who were transferred by personal vehicles.

3. Results

Total performed missions of the station from June 22, 2009 (no earlier statistics were available in that station) to March 20, 2010 included 216 missions out of which 64 cases included accidents, 78 were related to cases such as cardiac, respiratory, etc., 41 cases were related to the missions between the stations (transfers from Kohrang clinic to the Farsan city hospital) and 33 cases included those who had been injured in the tube riding track. The injuries caused by tube riding had occurred on Thursdays and Fridays of November, December and January months, just 3 months of year (on non-vacation days the track is closed). Of the total 33 people who had been injured at the tube riding track, 15 were women and 18 were men within the age range of 8 to 52 years old. 6 head traumas (18%), 6 waistline traumas (18%), one femoral fracture (3%), one facial trauma and nose fracture (3%), one chest and sternum trauma (3%), 4 hand cut offs (12%), 4 hand traumas (12%), 5 multiple traumas (15%), and 3 lower organs traumas (9%) have been recorded. Of the total above statistics, two injured people did not accept to be transferred by ambulance and were instead transferred by personal vehicles. 22 injured people were transferred to the clinic of Kohrang city and 8 were transferred to the hospital.

4. Discussions

Paul et al. (2009) has stated that chest trauma is the second cause of injury in skiing and snowboarding after head trauma and includes ribs, pneumothorax and hemothorax fractures. Unfortunately, no protective equipment has so far recommended for prevention from chest trauma. In a past-view study entitled "Investigating the Risk of

Factors, Model and Level of Injuries Caused by Skiing and Snowboarding in the Alps" conducted within 1996-2006, Paul et al. showed that a total number 196 people had been injured within the said 10 years (56.6% skiers and 43.5% snowboarders) out of which 43 people needed to be hospitalized in ICU and 5 people died (4 cerebral strokes and 1 cardiac arrest). Most of the injuries were caused by falling on the ground and hitting against natural objects. The most common injuries included head trauma followed by chest trauma, spinal cord trauma and lower organs trauma as the result of which 79 injured people needed surgical operations. Langran (2002) in a retrospective study entitled "Model of Injuries in Ski boarding in 2002" conducted within 1999-2002 in the Caringorm zone of Scotland, Langran showed that a daily number of 21,140 people came to that zone for ski boarding within 252 days of the year and that 84 types of injuries in 80 people had been recorded within 2 years. The primary reasons of injuries of these people included 65 cases of falling on the ground, 3 cases of deviation to the left, 8 cases of clash and accident and 4 cases of injury due to jumping. Factors of injuries included personal errors (68 cases), equipment deficiency (one case), clashing with other ski boards (one case), clashing with manmade obstacles (one case), clashing with natural obstacles (two cases) and unknown reasons (4 cases). Type of injuries included fractures (30 cases), wound and laceration (7 cases), ligament stretch (39 cases), bruising and soreness (5 cases), cerebral contusion and consciousness loss (two cases) and dislocation (one case). Of the total 80 injured people, 2 of them had used helmets but 78 had not. Preventive strategies therefore, are of great importance (Parkari, 2001). Considering that sports are mostly followed by a high ratio of injuries and that they are increasingly becoming popular among people (Steinbrück, 1999., Pazargadi et al., 2012; Khachian et al., 2012) and that injuries also increase simultaneous to the increased popularity of sports (Langran et al., 2006) and considering that treatment of sports injuries are mostly deathlike, irremediable, costly and time consuming, preventive strategies are therefore are highly important. One of these preventive strategies is the use of protective equipment such as helmet and back protectors. However, no protective equipment is used in tube riding and the level of injuries caused to head and waistline include 18%. In a retrospective study entitled "Investigating the Risk of Factors, Model and Level of Injuries Caused by Skiing and Snowboarding in the Alps" conducted within 1996-2006, Paul et al. showed that despite the fact that head trauma was the most common injury; only a limited number of people (13%) had used helmets.

Several studies have indicated the advantages of using helmets in preventing the injuries caused by head trauma (Levy et al., 2007). Another study conducted by Sulheim et al. has shown that use of a helmet reduces the risk of cerebral injury in both skiing and snowboarding groups up to 60% (Sulheim et al., 2006). In a study entitled investigating the advantages of back protectors in winter sports in relation to equipment safety conducted in 2010, Michael et al. showed that using and wearing back protectors prevent from spinal canal injuries. Most injuries have occurred in relation to falling on the ground and clashing with natural objects (Paul et al., 2009). Moreover, one of the causes of injury in this study included clashing of tube riders with natural objects (shrubs, large and small stones, etc.), other tube riders and other people. Giti et al. (2001) noted beginner tube riders and use of non-standard equipment as other causes of injury. This is while tube itself is a dangerous and non-standard equipment and tube riders do not have any control on it.

Conclusion

Considering high number of injured people and the fact that 15% of the missions of that station had been performed only within 24 days of the year (Thursdays and Fridays of November, December and January months), making arrangements to reduce the level of injuries caused by tube riding seems to be necessary. Moreover, it is recommended that the information of injured people and those who refer to the clinic and emergency station is recorded completely and exactly.

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The Relation between Self-Citation and Impact Factor in Medical Science Open Access Journals in ISI & DOAJ Databases

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Abstract: Citation is one of the important elements in scientific literature which has a significant role in information production and generation. Self-citation is a part of citation behavior. Relying on their articles, journals can change the number of citations and consequently the level of journal impact factor. This research aims at investigating the relation between self-citation and impact factor in the open access journals indexed in ISI and DOAJ in medical science in 2007-08. In this research, indexes such as the relation between self-citation of journal and impact factor and the effect of self-citation rate of the journal in open access performance are investigated. Research method is an analytical method conducted by using citation analysis technique. SPSS statistical software was used to examine and analyze the data and its inferential analysis methods such as Pierson Factor were used as well. Statistical society includes 168 journals. The results showed a self-citation rate of 28% for the journal. The findings indicate that there is a significant relation between self-citation and impact factor. After omitting self-citation, the level of self-citation in the performance of journals showed that 60% of the titles in the medical science experienced ranking increase, 27% experienced ranking decrease and 13% remained unchanged.

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Keywords: Citation, Institute for Scientific Information (ISI), Directory of Open Access Journals (DOAJ), Journal Self-citation, Impact Factor, Medical Science

1. Introduction

Information reliability is one of the most important quality criteria in scientific works. A scientific work is based on the past resources and cannot rely on itself. Beni (2002) believes that if a scientific work has annually 5 to 10 references several years after its publication, it is likely that its contents will be integrated in the knowledge body of the relevant scientific field, in the manner that the article will contribute in increasing the scientific knowledge of that field. Citations have a special position in the scientific works. In fact, a scientific article is authentic when it cites the previous works of the relevant field. Citation is used as an index to evaluate the effect of scientific works. The more a scientific work is available, the more it will be cited and consequently, the more it will have impact. Sometimes we see self-citation in citation behaviors. For the first time, Garfield and Sher (1964) studied the quantitative approach to self-citation. According to Glanzel (2006), Mc Roberts was the first who critically studied self-citation in 1989. Self-citation includes citations in which the author of a document cites his previous work or the journal in which the document has been published. In other words, self-

citation is usually defined as a citation in which the citing and cited article has at least one common author. Self-citation may sometimes make a work difficult to impact. Although authors may have good reasons to cite their own works, these citations are not always good indications for the importance of scientific works. Citation of previous works may distort the number of citations and may reduce citation reliability as a criterion to evaluate the quality of scientific works. Editors sometimes adapt publication strategy by maximizing impact factor in the manner that in some cases they try to calculate the impact factor such that they can change it in favor of their publication. Aksnes (2006) has reported that the articles accepted by editors are returned to the authors and the authors are then asked to refer to the articles of the same journal through they are not relevant to the subject of article and this increases self-citation of the journal. For this reason, we should understand the correct ways for self-citation and the impact method of other citations by these self-citations. Modifications should be made to avoid distortion of citations so that the competence and reliability of the authors and journals remain perfect. Since self-citation in the journals is inevitable, it is

necessary to study the relation between self-citation and impact method. Therefore, the present research studies this relation in the open access journals of medical science indexed in ISI and DOAJ.

Research Questions

Efforts are made in this research to answer the following questions:

How much is a journal's self-citation in the open access journals of medical science?

Is there any correlation between the journal's self-citation and impact factor in the open access journals of medical science?

What is the impact of self-citation on the performance of medical science journals?

According to Garfield and Sher (1964), self-citation does not show anything inauspicious if it is not in a high level. In the studies they made, they came to the conclusion that an author's self-citation is averagely 20%. In a research, Bonzi (1991) studied citation motivations and compared self-citation and citation of others. He concluded that authors' motivations in self-citation and citation of others were not highly different. In his research, Pichappan (1994) studied self-citation in astrophysics and astronomy publications and concluded that self-citer and self-cited levels were 173% and 391%, respectively. Self-citation increases in those magazines with more articles. In other words, there is a direct relation between the number of articles and the rate of self-citation. Lawrence was the first one who made researches in relation to citation in open access journals. He investigated the relation of possible free access to the complete text of the article and the number of citations received in the articles of computer science conferences in 1989-1999 in three websites, namely Scopus, ISI Thomson and Siteseer. His researches showed that the number of citations of free access articles was 336% higher than the number of citations of the published articles. In this analysis, Lawrence assumed the quality of all studied articles to be the same. In his research, Hyland (2003) studied author's self-citation in sociological, business, philosophical, biological, psychological, mechanical and electronic journals and showed the methods used by authors for self-citation. He believes that self-citation emphasizes on thematic expertise of a person and stabilizes the author's interpretations and ideas in new findings based on previous researches. In his research, Frandsen (2007) studied the role of self-citation in analyzing the mechanism of impact factor of social science journals. He concluded that there was a positive relation between a journal's impact factor and the increase of self-citations. Variables such as geographical place and language impact on this relation as well. As indicated in that research,

self-citation factor of non-American journals is 0.00339 less than that of North American journals. Furthermore, self-citation in non-English journals is 0.0094 less than English magazines. In a research on self-citation, Krauss (2007) studied 6 ecological journals. Based on his results, 16% of the citations of those journals included self-citation. Those magazines with high impact factors had high self-citation as well. Other findings of that research showed that the authors' researches made within the recent seven years had been cited more in their works. In their research, Craig et al. (2007) studied the relation of open access journals and their self-citation. They concluded that there was a direct relation between free access and visibility of a journal and the increase of self-citations (Khachian et al., 2012; Shokati et al., 2012).

2. Material and Methods

Using citation analysis method, this research was made in 2007-08 on 168 journals of medical science with impact factor. For this purpose, two databases of ISI and DOAJ were referred and journals were extracted for study and the number of journal's self-citation was specified. The data was then analyzed statistically using SPSS software and correlation factor statistical test.

3. Results

The findings of this research for the following questions are as follows:

How much is a journal's self-citation in the open access journals of medical science?

Journal's self-citation percentage in this research was calculated as follows and the results are shown in table 1.

$$\text{Journal's self-citation rate} = 100 \times \frac{\text{No. of Journal's self-citations}}{\text{Total citations}}$$

Table 1. Journal's self-citation percentage

No. Journals	54
No. of Citations	198397
No. of Self-citations	55714
Self-citation Percentage	28%

Table 1 shows that journal's self-citation percentage in medical science is 28%.

Is there any correlation between the journal's self-citation and impact factor in the open access journals of medical science?

To answer this question, impact factor of each journal was compared to the non-self-citation impact factor of the journal which was obtained according to the following formula.

Non-self-citation impact factor of journal in 2008 = (Journal's self-citation in 2007 and 2008) – (total citations received in 2007 and 2008)/total articles of the journal in 2007 and 2008

Pierson correlation test was used to evaluate the significant relation of journal's self-citation and impact factor. The results are shown in table 3 and diagram 1.

Table 3. Correlation between the journal's self-citation and impact factor

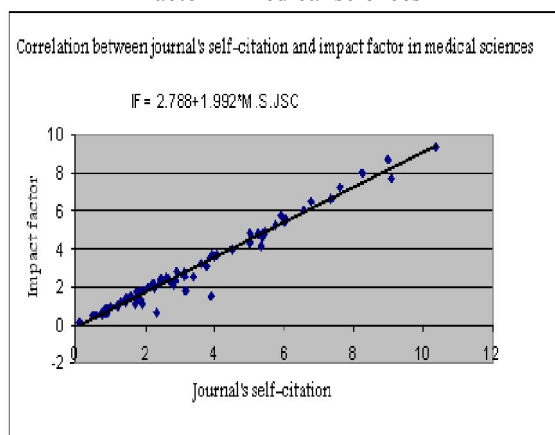
Journal's self-citation	Impact factor		
0/73/4**	1	Pierson correlation	Impact factor
0/000		P value	
161	167	Qty.	
1	0/73/4**	Pierson correlation	Journal's self-citation
	0/000	P value	
161	161	Qty.	

Correlation between journal's self-citation and impact factor in medical science is 73/4. P value is smaller than 0.01. Therefore, there is a significant correlation between self-citation and impact factor. The linear equation of this correlation is as follows:

Impact factor = 2/788 + 1/992 × journal's self-citation in medical science (R2=53.8, P < 0.01)

The linear equation shows that any change in the journal's self-citation will cause 1/992% change in the impact factor. Equivalent specification factor is 0.53.

Correlation between journal's self-citation and impact factor in medical sciences



The findings of this question show that based on the coefficient test, the obtained amounts of linear regression between the two variables in this field are significant and the diagram coefficient and its constant are also valid based on the tests. The results indicate that there is a high significant correlation between journal's self-citation and impact factor in medical science, in the manner that as self-citation increases, impact factor of the journal increases as well. The research made by Frandsen (2007) has confirmed this fact. In his research, he showed that there is a positive relation between journals' impact factor and self-citation, i.e., those journals with high impact factors has higher self-citation. The results indicate that the journals with high impact factors possibly tend to increase impact factor through self-citation. Increase of self-citation will be a negative effort if made without any reason and only to increase the journal's rank since in this way the works of an author are wrongly shown to be highly cited. When evaluation is made based on the number of citations and when citations show rewards, self-citation falsely increases the importance of an article in the scientific community and will potentially confuse the impact of the research. Maybe it can be said that those authors who publish their articles in highly cited open access journals tend both to increase the number of citations made by others through open access and increased visibility of the article and to stabilize their own scientific reputation and also to make prominent their previous works. On the other hand, maybe these authors highly cite their previous works due to their arrogance. Authors may tend to cite their own works to increase the number of citations or to make prominent their previous works. Anyway, self-citation motivations are issues which should be considered.

Impact of Journal's Self-Citation on the Performance of Journals

To answer this question, the impact factor of open access journals in 2004-2005 separated based on the fields of basic sciences and their ranks were compared to non-self-citation impact factor and the relevant rank. In the following table, rank changes of journals versus non-self-citation impact factor of journal in the field studied in this research are shown.

Table No. 7. Impact of journal's self-citation on the performance of journals

Change Percentage	No change		Negative		Positive		otal Number of Journals
	umber of Journals	hange Percentage	umber of Journals	hange Percentage	umber of Journals		
%3	2	%7	5	%0	01	68	

According to the data of the above table, 60% of total journals enjoyed rank improvement against the impact factor of non-self-citation, 27% experienced rank decrease and 13% remained unchanged. Each journal has a rank in the citation reports database of journals based on its impact factor. Since the level of calculated impact factor is specified by inclusion of self-citation and since self-citations are sometimes a way to alter the impact factor of each journal, it can be said that self-citation should be considered in selecting any journal. In this question, the journal's rank in this scientific field was specified without considering self-citation and was then compared to the scientific level of the same journal in ISI to determine the difference between the ranks of journals with and without consideration of self-citation.

4. Discussions

Citation is one of the criteria to evaluate the scientific reliability of a work. Increased self-citation of a journal or an author can have an impact on the increased rank of the journal or relevant author. But self-citation is one of the types of reference and it cannot be ignored. Each journal or author has usually a few references to its previous works. In the journals' citation reports of ISI, maximum self-citation is 20% and in other researches it is 3 to 36%. The results of the present research showed that self-citation is usual for the journals and is one of the citations but it should be made to a common extent. Self-citation of the journal and author in the studied field is 28% and 36%, respectively. According to Pierson statistical test, the relation between self-citations and impact factor in this field in open access journals was significant. Considering the findings of the research, there is a positive relation between self-citation and impact factor in medical science in open access journals. Based on the obtained results and by comparing the performances of journals before and after omission of self-citation, it was observed that 87% of the studied subjects experienced a change in their ranks and only 13% of them remained unchanged. Maybe it can be said that the number of articles and authors as well as the tendency of journal editors to increase or decrease self-citation lead to these changes in the ranks of the journals.

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Solid-State Fermentation for The Production of Dextran from *Saccharomyces cerevisiae* and Its Cytotoxic Effects

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Abstract: Maximum yield of dextran was obtained when using ground date seeds. Different concentrations of date seeds were applied and the highest dextran production was achieved at 6 g/flask. Extraction of dextran was carried out using ethanol. The molecular weight of the purified dextran was 67 kDa by GPC. Spectral analysis showed that dextran contains D-glucose units in a linear chain with consecutive α -(1,6) linkages. The melting temperature (T_m) was 70.56°C, and the value of ΔH was -290.57 mJ, as determined by DSC analysis. The TGA clearly showed the thermal stability of purified dextran. The analysis showed three stages of degradation process. An initial loss of about 0.577 mg (2.17%) weight occurred at 30-75°C, second loss of about 0.822 mg (3.1%) weight occurred at 75-125°C and the third loss of about 0.427 mg (1.61%) weight occurred at 125-175°C. Surface morphology of dextran using scanning electron microscopy showed dextran has a crystalline form which is attributed to the presence of hydroxyl groups which increase crystallinity of dextran, also, dextran showed a compact structure characterized by transversal arrangement which reflects brittleness of dextran and seems to have a porous structure. The cytotoxicity assays on human normal melanocytes (HFB 4) revealed no toxic effect. However, a clear decrease in cell survival was observed in case of human liver carcinoma (HEPG 2) and cervical carcinoma (HELA) tumor cell lines.

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Key words: solid state fermentation; agricultural wastes; *Saccharomyces cerevisiae*; dextran; FT-IR; antitumor.

1. Introduction

In a time where prices are increasing in wide steps, search for cheap industrial raw materials has evolved. The use of industrial or agricultural wastes could save disposal efforts and pollution hazards. Solid-state fermentation (SSF) is a means for the microbial conversion of lignocellulosic biomass. SSF is defined as the growth of microorganisms in the absence or near absence of free water with inert or natural substrates as solid support (Pandey *et al.*, 1999). SSF is an advantageous method for degrading lignin and improving the digestibility of agricultural straw. Compared with submerged fermentation, SSF possesses many advantages such as low effluent generation, requirement for simpler fermentation equipment, and the direct applicability of the fermented product for feeding (Yang *et al.*, 2001). During SSF, microorganisms produce lignocellulolytic enzymes, degrade components of the cell wall, and synthesize microbial proteins. A number of microorganisms, mainly white rot fungi, have been used for producing microbial proteins and lignocellulolytic enzymes by SSF from different agricultural residues (Bisaria *et al.*, 1997; Niladevi *et al.*, 2007; Arora and Sharma, 2009; Li *et al.*, 2011).

Dextrans are synthesized by dextransucrase, an extracellular enzyme secreted by lactic acid bacteria *viz.*, *Leuconostoc*, *Lactobacillus* and

Streptococcus (Katina *et al.*, 2009), *Pediococcus* (Patel *et al.*, 2010). Dextrans are glucose polymers (Thoren, 1981), which structurally and predominantly consist of linear α -1,6-glucosidic linkage with some degree of branching *via* α -1,3 linkage (Larsen, 1989). In addition to high water solubility, dextran polymers are stable under mild acidic and basic conditions (Schacht, 1987) and contain large number of hydroxyl groups for conjugation. These suitable physicochemical characteristics along with the low cost and a history of clinical use make dextran attractive for use in pharmaceutical, food, agricultural and fine chemical industries (Naessens *et al.*, 2005; Purama and Goyal, 2005) and most of all as potential macromolecular drug or protein carriers (Mehvar, 2001).

A macromolecular drug carrier is typically composed of a macromolecule covalently linked to a therapeutic agent, and it targets solid tumors either passively (*via* its molecular weight and charge) or actively (*via* a specific affinity [e.g., an antibody] or stimulus) (Ringsdorf, 1975; Tomlinson, 1985; Duncan, 2003). In addition to the enhanced permeability and retention effect, macromolecular drug carriers have a longer plasma half-life, reduced toxicity in normal tissue, and higher activity against multiple drug-resistant cell lines than typical chemotherapeutic agents, and they have the ability to

increase solubility of poorly soluble drugs in plasma (Kopecek *et al.*, 2000; Duncan, 2003). Because of these characteristics, macromolecular drug carriers coupled to a low molecular drug often have higher anticancer efficacy than the low molecular weight drug alone (Kopecek *et al.*, 2000; Duncan, 2003).

The objective of this work was firstly, to use of date seeds waste, thus saving efforts in its disposal, secondly, production of dextran, a polysaccharide with wide and important industrial and pharmaceutical applications, and finally, studying the cytotoxic effect of the produced dextran against human normal and tumor cell lines.

2. Materials and Methods

Microorganism and culture conditions

S. cerevisiae NRRL Y-1534 (CBS 1429) was kindly provided from National Regional Research Laboratory, United States Department of Agriculture, Agricultural Research Services, USA to Prof. Tarek A. A. Moussa and maintained on YM medium which contains (g/l): yeast extract 3 g, malt extract 3 g, peptone 5 g and dextrose 10 g.

Preparation of agricultural wastes

The date seeds were washed and left to air dry. The air dried seeds were ground to fine particles using blender. The rice and wheat straws were collected and left to air dry then ground. The wheat bran was bought from the market.

Production of dextran from agricultural wastes using *S. cerevisiae*

S. cerevisiae was cultured on solid medium composed of: agricultural wastes, 4 g; yeast extract, 0.3 g; K₂HPO₄, 0.5g, all components were mixed in 500 ml flasks. The culture was incubated at 25°C for 48 hrs. The produced dextran was purified and weighed.

Production of dextran from different weights of date seeds wastes using *S. cerevisiae*

S. cerevisiae was cultured on solid medium composed of: yeast extract, 0.3 g; K₂HPO₄, 0.5 g, all components were mixed in 500 ml flasks. Date seeds waste was added to the flasks in different weights (2, 4, 6, 8 or 10 g). After incubation at 25°C for 48 hrs, dextran was purified and weighed.

Extraction and purification of dextran

100 ml of dist. water was added to the whole flask which was shaken well and then the contents were filtered. These steps were repeated twice and the filtrates were collected and combined. Extraction of dextran was carried out according to Behravan *et al.* (2003); equal volume of ethanol was added, kept at 4°C for 24 hrs. The solution was centrifuged at 5000 rpm. The supernatant was discarded and the precipitate was dissolved in minimal volume of water. Twenty mg of activated charcoal were added

to the dissolved precipitate and boiled, then filter. The protein was precipitated by adding amyl alcohol/chloroform, then centrifuge at 5000 rpm and the precipitated protein was removed. Equal volume of cold ethanol (1:1 v/v) was added to the supernatant to precipitate dextran. The obtained dextran was dried in desiccators on anhydrous calcium chloride and weighed.

Gel Permeation Chromatography (GPC)

Average molecular weight of the dextran was determined with gel permeation chromatography coupled with refractive index detection using a TSK G4000 PW_{XL} column. The sample with concentration 60 mg/ml was injected. The mobile phase was 0.02% (w/v) sodium azide in HPLC grade water at a flow rate of 0.5 ml min⁻¹. Fractions (250 µl, each) were collected at room temperature. The column was calibrated with respect to fraction volume using five standard polymers with molecular weights from 25 to 2000 kDa.

Structural Spectroscopy

Purified sample was analyzed by transmittance IR spectroscopy in the form of KBr pellet using a Fourier Transform Infrared spectrometer (FTIR 6100). The ¹HNMR spectrum of the sample was recorded on a Varian Mercury VX-300 spectrometer. The purified dextran was dissolved in D₂O (10 mg /ml). ¹HNMR was run at a base frequency of 300 MHz.

Differential Scanning Calorimetry (DSC) and Thermogravimetric Analyzer (TGA)

Differential scanning calorimetry analysis was conducted using a DSC-50 Shimadzu Differential Scanning Calorimeter. The sample was tightly sealed in aluminum pans and heated at a constant rate 10°C min⁻¹ over a temperature 30-150°C and under nitrogen purge. Thermogravimetric studies were carried out using a TGA-50 Shimadzu.

Scanning Electron Microscopy (SEM)

Morphology of the obtained dextran was examined by an SEM. The dried sample was mounted on the SEM stub with double-sided tape then sputter coated with gold using SPI-ModuleTM sputter coater (SPI Supplies Division of Structure Probe, Inc.). The sample surface was imaged using a Jeol JSM-5200 scanning microscope operated at 10 kV.

Cytotoxicity Assays

Cytotoxicity of the obtained dextran was tested against the normal human cell line: human normal melanocytes (HFB 4), and the human tumor cell lines: breast carcinoma (MCF 7), liver carcinoma (HEPG 2) and cervical carcinoma (HELA). The method of Skehan *et al.* (1990) was adopted. Cells were plated in 96-multiwell plate (10⁴ cells/well) for 24 hrs before treatment with dextran to allow attachment of cell to the wall of the plate. Different

concentrations (1000, 2000, 3000 and 4000 µg/ml) were added to the cell monolayer triplicate wells prepared for each individual dose. Monolayer cells were incubated with dextran for 48 hrs at 37°C and in an atmosphere of 5 % CO₂. After incubation, cells were fixed, washed and stained with Sulfo-Rhodamine-B stain. Excess stain was washed with acetic acid and attached stain was recovered with Tris-EDTA buffer. Color intensity was measured by an ELISA reader (Meter tech. Σ 960, USA). The relation between cell survival (as percentage of control) and dextran concentration was plotted to get the survival curve of each normal or tumor cell line after subjecting to dextran. Cell survival (%) was calculated as follows:

$$\text{Survival (\%)} = (I_t/I_c) \times 100$$

Where, I_t is the color intensity of treated cells and I_c is the color intensity of untreated cells.

3. Results and Discussion

Dextran is a very important polysaccharide commonly used in routine medical, microsurgical and laboratory procedures (de Carvalho *et al.*, 2001; Rotureau *et al.*, 2004; Khalikova *et al.*, 2005; Dhaneshwar *et al.*, 2006). Dextran derivatives are used for reducing platelet adhesiveness (Siddika *et al.*, 1997; Huynh *et al.*, 2001), wound healing (Logeart-Avramoglou *et al.*, 2002), tumor targeting of gene expression (Hosseinkhani *et al.*, 2003) and osmotic pressure control in biological molecules (Rotureau *et al.*, 2006) and human enzyme regulation (Ledoux *et al.*, 2003). Dextran derivatives have well reported antiproliferative and anti-tumor properties (Bittoun *et al.*, 1999). Dextran is receiving attention in the formulation of macromolecular prodrugs of acid sensitive drugs to target them to the colon and in this way, highly sensitive anticancer drugs, such as mitomycin C, can be safely targeted to its site of action (Cheung *et al.*, 2005). Dextran is being used for sustained release studies of several sensitive drug molecules after their covalent attachment (mostly esters) onto polymer backbone (Miyazaki *et al.*, 2003).

In this study, different agricultural wastes were used as carbon sources in the fermentation medium of *S. cerevisiae* for the production of dextran. Highest dextran production was obtained from medium with ground date seeds waste compared with other tested agricultural wastes (Table 1). Date seeds wastes were chosen for the production of dextran in the next experiments.

Different weights of ground date seeds were tried. The data presented in Table 2 showed that increasing date seeds weight caused a corresponding increase in dextran production. Maximum dextran yield was achieved when using 6 g of ground date

seeds/500 ml flask; however, there was a decrease in the amount of obtained dextran following this concentration.

Probably higher concentrations of date seeds in the fermentation medium showed a substrate inhibitory effect causing decrease in dextran production (Martinez-Espindola and Lopez-Munguia, 1985). Similar results were obtained with sucrose as a substrate for dextran production (Kim *et al.*, 2003; Sarwat *et al.*, 2008).

There are numerous literature reports on use of gel permeation chromatography (GPC) for the assessment of molecular weights (Nilsson and Nilsson, 1974; Richter *et al.*, 1983; Meredith, 1984; Komatsu *et al.*, 1993; Van and Daenens, 1993; Mulloy *et al.*, 1997; Karmarkar *et al.*, 2006). The purity and molecular weight of the produced dextran from *S. cerevisiae* was investigated by GPC analysis. A single and unimodal peak was observed (Fig. 1), which identified the obtained dextran not being contaminated. The peak of dextran was from fractions 22-42 and of the tip of peak was at fraction no. 38 which appears after 9.5 ml (each fraction is 250 µl), so from calibration curve, the molecular weight was about 67 kDa (Fig. 1).

The FT-IR spectra were used to investigate the functional groups of commercial dextrans and pullulans and their nature in terms of their monomeric units and their linkages (Shingel, 2002). Several other reports also supported the use of FT-IR spectral data for the characterization of glucans showing anti-cancer properties (Cao *et al.*, 2006; Liu *et al.*, 2007). FT-IR spectrum data of the purified dextran is presented in Table 3. The band in the region of 3400 cm⁻¹ was due to the hydroxyl stretching vibration of the polysaccharide (Liu *et al.*, 2007; Purama *et al.*, 2009; Patel *et al.*, 2010). The band in the region of 2930 cm⁻¹ was due to C-H stretching vibration and the band in the region of 1639 cm⁻¹ was due to carboxyl group (Cao *et al.*, 2006; Liu *et al.*, 2007). The absorption peaks at 616 and 906 cm⁻¹ indicate the existence of α-glycosidic bond. The main characteristic bands found in the spectra of dextran at 1152, 1095 and 1024 cm⁻¹ are due to valent vibrations of C-O and C-C bonds and deformational vibrations of the CCH, COH and HCO bonds, this was in context with the results reported by many researchers (Shingel, 2002; Purama *et al.*, 2009). The band at 1152 cm⁻¹ is assigned to valent vibrations of C-O-C bond and glycosidic bridge. The peak at 1103 cm⁻¹ is due to the vibration of the C-O bond at the C-4 position of glucose residue (Shingel, 2002; Purama *et al.*, 2009). The presence of peak at 1020 cm⁻¹ is due to the great chain flexibility present in dextran around the α-(1,6) glycosidic bonds as shown earlier (Shingel, 2002). FTIR spectra of our samples also

show a band in the region of 750-1300 cm^{-1} that corresponds to the carbohydrates region (Table 3). These wave numbers are within the so-called fingerprint region, where the bands are specific for each polysaccharide, allowing its possible detection (Sen and Erboz, 2010). The FTIR spectra of dextran have been investigated in the range between 4000 and 400 cm^{-1} (Shingel, 2002). FTIR spectral analysis of *S. cerevisiae* NRRL Y-1534 dextran showed that it contains α -(1,6) linkages. This was further confirmed by ^1H NMR analysis.

In this study, the ^1H NMR spectrum for the purified dextran was carried out. It was reported that the distribution of ^1H NMR spectral resonances range between 3 and 6 ppm for different dextrans (Seymour, 1979). The ^1H NMR spectral resonances (H-2–H-6) lie in the 3-4 ppm region while the hemiacetal H-1 resonance is in the 4–6 ppm region (Sidebotham, 1974; Majumder and Goyal, 2009). Seymour (1974) assigned a 4.9 ppm resonance for the H-1 of the α -(1,6) linked glucosyl residues of dextran. Likely, in this work a 4.8 ppm resonance could be assigned for the H-1 of the α -(1,6) linked main chain of dextran from *S. cerevisiae*. Purama et al. (2009) found that the ^1H NMR spectrum of *Leuconostoc mesenteroides* NRRL B-640 have an H-1 at 4.9 ppm deducing production of highly linear, α -(1,6) linked, water soluble dextran. The dextran produced by *Pediococcus pentosaceus* (Patel et al., 2010) showed similar results.

Differential scanning calorimetry (DSC) is a technique that measures the energy difference between a sample and the reference cell as a function of time when they are submitted to a heating program. The technique is useful for polymers, especially hydrogels, because the structural changes accompanied by energetic effects can be followed in DSC curves. As the temperature increases the sample eventually reaches its melting temperature (T_m), which was 70.56°C. The melting process resulted in an endothermic peak in the DSC curve. The enthalpy (ΔH) value was -290.57 mJ (Fig. 2).

The thermogravimetric analysis clearly showed the thermal stability of purified dextran. The analysis showed a three stage of degradation process. An initial loss of about 0.577 mg (2.17%) weight occurred at 30-75°C, second loss of about 0.822 mg (3.1%) weight occurred at 75-125°C and the third loss of about 0.427 mg (1.61%) weight occurred at 125-175°C. Thermal parameters as the melting point and decomposition temperature are useful to engineers who must select polymers to withstand a given thermal environment.

The surface morphology of the purified dextran produced by *S. cerevisiae* was studied. In Fig. 4a, dextran appears in a crystalline form which is

attributed to the presence of hydroxyl groups which increase crystallinity of the polymer (Purama et al., 2009). Dextran shows a compact structure (Fig. 3b) characterized by transversal arrangement which reflects brittleness of dextran [52]. Meanwhile, dextran seems to have a porous structure (Fig. 3c). The small pore distribution can cause dextran to hold water and thus be used as a texturing agent in food industry. These small pores may also be responsible for the compactness of the polymer and the stability of the gel structure when subjected to external forces and the maintenance of the texture properties during storage (Khan et al., 2007; Purama et al., 2009).

Table 1. Effect of different agricultural wastes on the production of dextran by *Saccharomyces cerevisiae* on solid-state fermentation

Substrate	Dextran (g/100 ml)
Date seeds	1.092
Rice straw	0.813
Wheat bran	0.880
Wheat straw	0.961

Table 2. Effect of different weights of date seeds wastes on the production of dextran by *Saccharomyces cerevisiae* on solid-state fermentation

Date seeds wt.	Dextran (g/100 ml)
2	1.056
4	1.092
6	1.560
8	1.242
10	1.068

Results of dextran cytotoxicity assay revealed that it has no obvious harmful effect on human normal melanocytes (HFB 4) even after the concentration was raised up to 4000 $\mu\text{g}/\text{ml}$ (Fig. 4). It can be deduced that dextran produced by *S. cerevisiae* is a non-toxic compound which can be safely used in biomedical applications including drug delivery. The results are in agreement with the previous findings of De Groot et al. (2001). When dextran was tested against the human tumor cell lines: breast carcinoma (MCF 7), it had almost no effect. However, a clear decrease in cell survival was observed in case of liver carcinoma (HEPG 2) and cervical carcinoma (HELA). On the other hand, a dextran from another source (Patel et al., 2010) showed no effect on HELA cells at a concentration of 1000 $\mu\text{g}/\text{ml}$. Results in the current study suggest that dextran produced by *S. cerevisiae* could have a potential for investigation for tumor therapy as a polymer-drug conjugate. Dreher et al. (2006) studied penetration of macromolecular drug carriers to tumors. Increasing the molecular weight of dextran statistically significantly reduced

its vascular permeability but increased its plasma half-life. Tumor accumulation was maximal for dextrans with molecular weights between 40 and 70 kDa, which lie in the range of clinically available and successful macromolecular drug carriers (Duncan,

2003). Dextran in the present work exhibited a molecular weight of about 67 kDa. It could thus show a potential in the use as a macromolecular drug carrier.

Table 3. FTIR spectrum for the purified dextran produced by *Saccharomyces cerevisiae* on solid-state fermentation

No.	Position	Intensity	Group	Comments
1	3434.6	81.6	$\nu(\text{OH})$	Stretching
2	2926.45	88.37	C-H	-CH stretching of CH_2 and CH_3 groups
3	2859.9	90.05		
4	1740.44	90.46	CHO	
5	1630.52	88.12	$\delta(\text{HOH}), \delta(\text{OH}), -\text{COO}-$	asymmetrical stretching of carboxylic groups
6	1433.82	90.21	$\delta(\text{OH}), -\text{COO}-$	symmetrical stretching of carboxylic groups
7	1331.61	92.22	$\delta(\text{OH})$	
8	1263.15	92.12		
9	1152.26	91.16	C-O-C	glycosidic bridge
10	1095.37	89.88	C-O, C-C	At C4 position of glucose residue
11	1024.98	88.24	α -(1,6) glycosidic bonds	chain flexibility present in dextran around the glycosidic bonds
12	760.78	95.71	$\gamma(\text{OH})$	
13	616.07	93.43		Glycosidic bond
14	418.47	93.86		

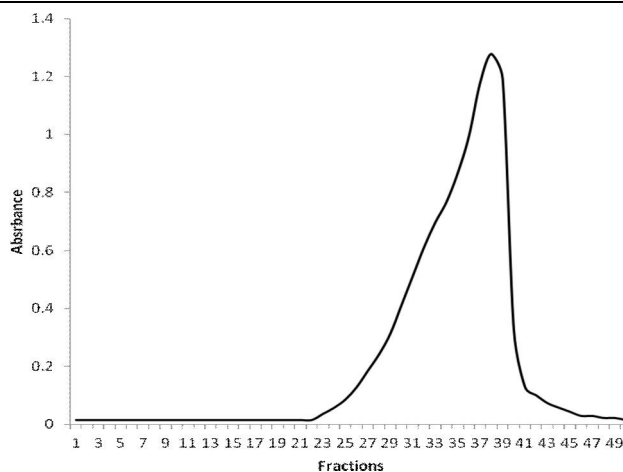


Figure 1: GPC for the produced dextran fractions using TSK G4000 PWXL column produced by *S. cerevisiae* on solid-state fermentation.

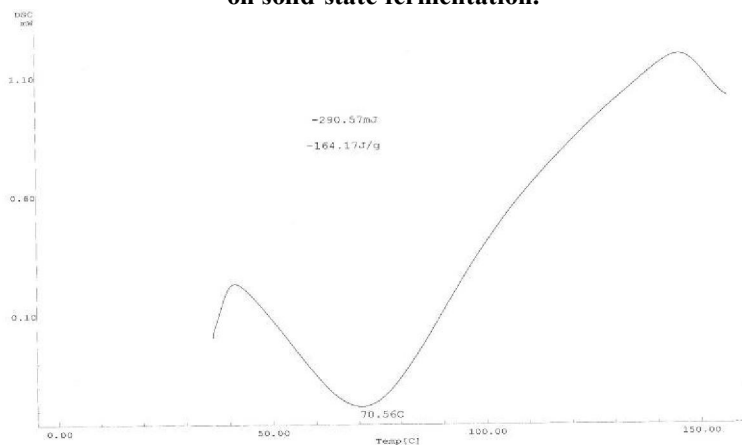


Figure 2: DSC curve for the purified dextran produced by *S. cerevisiae* on solid-state fermentation.

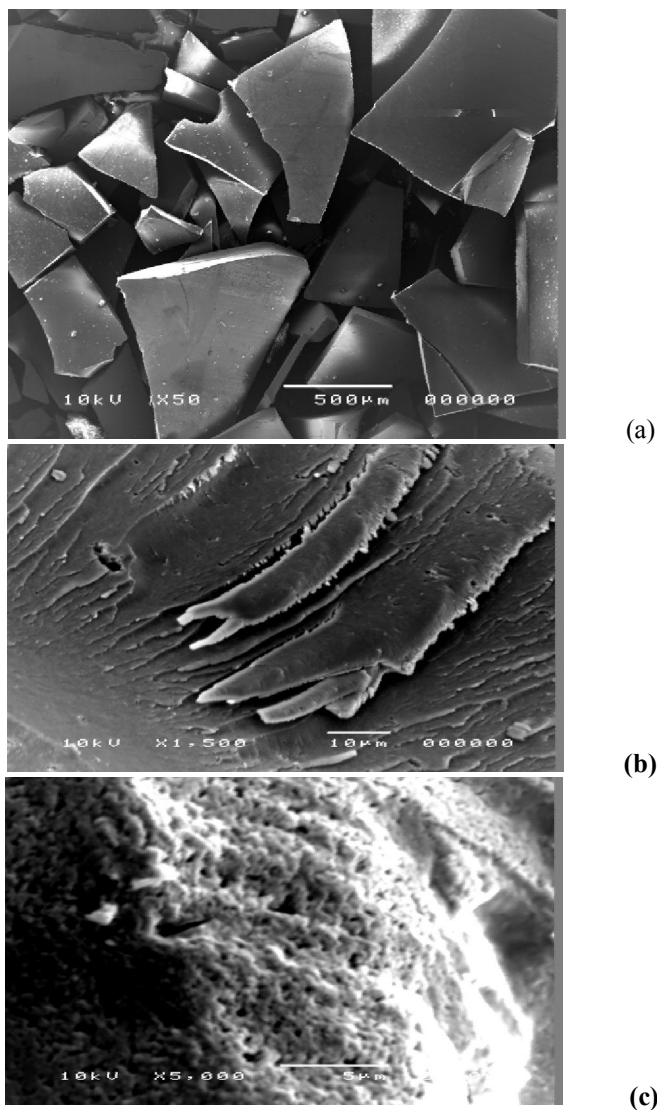
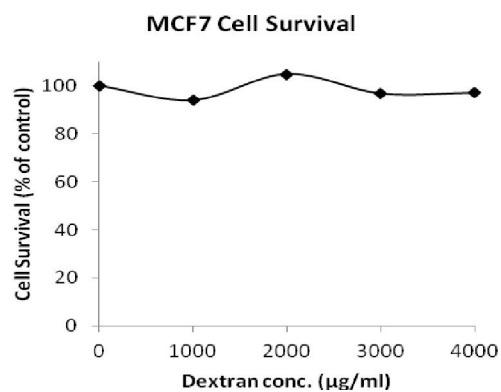
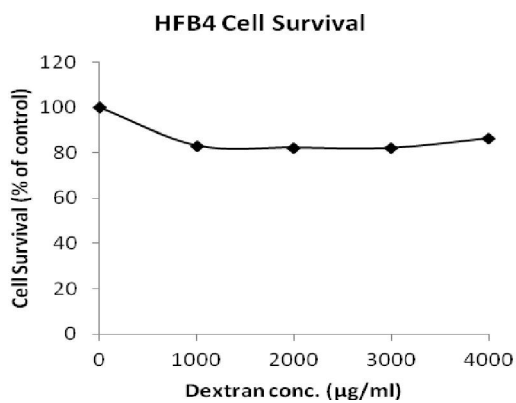


Figure 3: Scanning electron microscopic (SEM) images showing surface morphology of purified dextran from *S. cerevisiae* on solid-state fermentation.



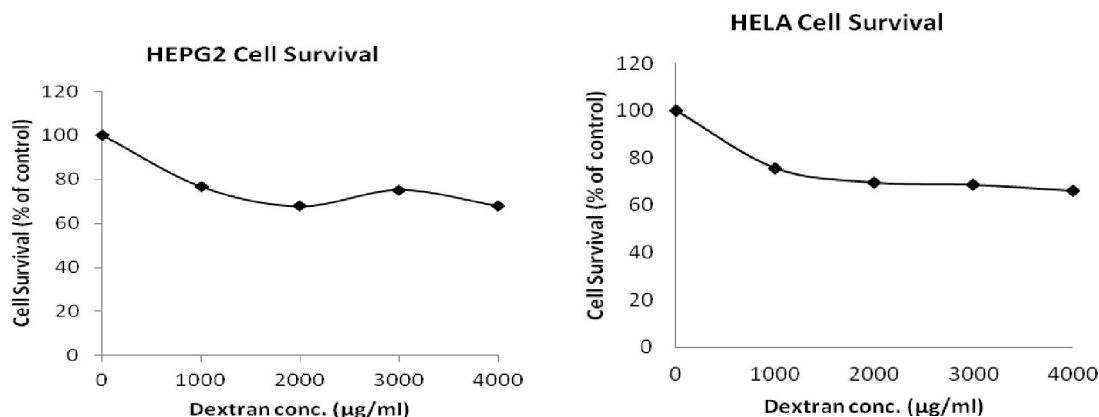


Figure 4: Effect of purified dextran produced by *S. cerevisiae* using solid-state fermentation on cell survival ratio of human normal (HFB 4) and tumor cell lines (MCF 7; breast carcinoma, HEPG 2; liver carcinoma and HELA; cervical carcinoma).

4. Conclusion

Date seeds wastes were successfully utilized by *S. cerevisiae* for production of dextran. Dextran showed thermal stability as well as a crystalline porous structure. Hence, it can be used as a texturing agent in food industry. It had no toxic effect on human normal melanocytes so it can be used safely in biomedical applications. However, it caused a clear decrease in cell survival was observed in case of human liver carcinoma and cervical carcinoma tumor cell lines. The previous result together with the measured molecular weight (67 kDa) renders dextran from *S. cerevisiae* a successful macromolecular drug carrier.

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The Nutritional Status in Patients with Colorectal Cancer Pre and Post Different Modulates of Treatment

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Abstract: Background and Objective: The nutritional status of oncological patients has become a subject of growing scientific interest because of its prognostic significance and the resulting therapeutic possibilities. Colorectal cancer ranks the third highest in cancer incidence and fourth in cancer mortality in both sexes combined worldwide. The role of dietary and other lifestyle factors in colorectal cancer recurrence and survival is largely unknown. The present study aimed to determine the extent of malnutrition in pre and post operative or other treatments of colorectal cancer patients.

Methods: A cross-sectional descriptive study was carried out among (30) Patients, (17) males (56.7%) while the other (13) females (43.3%) at King Abdul Aziz University Hospital (KAUH) with diagnosed colorectal cancer to be included in the study at their first visit to the outpatient Surgery and Oncology department between October 2011 and April 2012 were included in a retrospective review of the patients' medical record. Patients were enrolled consecutively from outpatients 2–4 weeks prior to surgery for study. Demographics characteristics including performance status (PS), assessments included weight history, body mass index (BMI), and percentage of weight loss. Laboratory investigations includes blood analysis, U&E (urine and electrolyte) and albumin, also the CEA (Carcinoembryonic Antigen) as a diagnostic tool. Cancer staging and hospital length of stay were recorded, nutritional status and assigning the level of risk for malnutrition by, using Simple Screening tool for Malnutrition (SSM), were collected and correlated with different modulates of treatment. **Results:** Majority of patients (83.33%) have the tumor in the colon while only (16.66%) in the rectum. About (43.33%) treated with both Surgery and chemotherapy while (26.66%) surgery only, (13.33%) received only chemotherapy, (13.33%) received a combination of Chemotherapy and Radiotherapy, and only (3.33%) treated with both Surgery and Radiotherapy. Malnutrition was defined by full nutritional assessment in the participating patients using SSM which revealed that 21 of the 30 patients (70%) were malnourished before treatment and 20 patients (66.6%) after treatment. SSM had high sensitivity and specificity in detecting patients with colorectal cancer. Declining nutritional status of the patients as seen in serum albumin before and after treatment for all participants which was below reference value of (30.75±0.14 and 29.95±1.93) respectively. The Mean ±SD weight loss (unintentional weight loss) was in male patients (13.61±1.83kg) less than females (15.05±1.75kg). The duration for a unintentional weight loss was (50% of participate) had through 3 months; (16.7%) after 6 months and (16.7%) had change during one year. **Conclusion:** Colorectal cancer Patients does have a real nutritional problem that surely can influence their disease course and length of hospital stay after surgery and long duration of receiving other treatment. Most patients with malignancies are considered to be at risk for malnutrition, and therefore require further nutritional support. Nutritional screening would be beneficial in this group preoperatively to identify weight-losing patients at an early stage in the care pathway when they initially enter the secondary care system. Screening (SSM) for malnutrition in cancer patients is a valid simple approach to define cancer patients for nutritional care. More patients regard themselves in need for nutritional counseling than the number of patients really achieving any.

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Keywords: Colorectal Cancer; Surgery, Radiation therapy, Chemotherapy, malnutrition; weight loss, SSM.

1. Introduction

Colon cancer forms in the tissues of the colon (the longest part of the large intestine). Most colon cancers are adenocarcinoma which begins in cells that make and release mucus and other fluids (**National Cancer Institute, 2011**).

The incidence tends to be low in Asia and intermediate in the southern parts of South America. Although the kingdom of Saudi Arabia (KSA) is

considered a low incidence area for CRC, the disease ranks second, after breast cancer (**National Cancer Registry MOH - 2003**). There were 907 cases of colorectal cancer accounting for 9.9% of all newly diagnosed cases in year 2007 (**National Cancer Registry MOH - 2007**).

Geographic differences for CRC are probably explained by dietary and other environmental exposure (**Parkin et al, 2005**).

Eating less red meat and avoiding processed meat altogether can slash colon cancer risk, consuming less alcohol, boosting fiber intake, exercising, and maintaining a healthy body weight could prevent 45% of all colon cancer cases or more than 64,000 cases of colon cancer each year (**Denise, 2011**). Also, central depositions of adiposity (**Gunter, Leitzmann, 2006**) have a major influence on the risk of CRC (**Giovannucci, 2002**).

The three main types of treatment for colorectal cancer are Surgery, Radiation therapy and Chemotherapy. Depending on the stage of cancer, two or more types of treatment may be used at the same time, or used one after the other (**American Cancer Society, 2011**).

While chemo kills cancer cells, it also damages some normal cells and this can cause side effects. These side effects will depend on the type of drugs given, the amount given, and how long treatment lasts. Side effects could include: Hair loss, Mouth sores, Loss of appetite, Nausea and vomiting, increased chance of infection, Easy bleeding or bruising after minor cuts or injuries and severe tiredness. The radiation therapy also causes side effects which include skin soreness, nausea, diarrhea and others (**American Cancer Society, 2012**).

For the surgery there are several factors predispose patients undergoing surgery for upper GI and colorectal cancer to malnutrition. These factors the catabolic effect of cancer as well as the GI side effects of nausea, vomiting, anorexia, diarrhea and, in some cases, dysphagia and malabsorption (**Nitenberg and Raynard, 2000 and Fettes et al., 2002**).

Nutrition plays major (but not always fully understood) roles in many aspects of cancer development and treatment (**Center, 2009**). Good nutrition practices can help cancer patients maintain weight and the body's nutrition stores, offering relief from nutrition impact symptoms and improving quality of life (**Johansson, 2009**). Poor nutrition practices, which can lead to under nutrition, can contribute to the incidence and severity of treatment side effects and increase the risk of infection, thereby reducing chances for survival (**Bozzetti, 2009**). Quality of Life (QoL) is a subjective multidimensional construct that is increasingly being used as a clinical endpoint in oncology (**Lee, and Chi, 2000**).

The present study has been carried out to evaluate nutritional status among colorectal cancer patients pre and post different treatment modalities.

1. Study sample

A cross-sectional descriptive study was carried out among (30) Patients at King Abdul Aziz University Hospital (KAUH). All patients with diagnosed colorectal cancer were invited to

participate in the study at their first visit to the outpatient Surgery and Oncology department between October 2011 and April 2012 which included in a retrospective review of the patients' medical record. The most common explanation for not participating was that 'people were too sick' or 'the burden of the study was too heavy'. All participants were asked about their usual physical activity. They were all sedentary or had a low physical activity level (PAL). Inclusion criteria for participate patients include aged above the age of 18 years old involving any location from the cecum to the rectum; received any type of treatment. Study participants, 17 (56.7%) males and 13 (43.3%) females were conducted. The mean age for both women and men was 51.96±1.02 years (range from 21-80 years). Patients with other comorbidity were excluded. The aim of the study was explained to the subjects.

2. Methods:

2.1. Study Instruments:

This study carried out to identify the nutritional status of patients with colorectal cancer pre and post operative and other treatments from the data which was collected by an English questionnaire was developed for the purpose of data collection, which was pilot, tested and modified accordingly. A face-to-face interview with each participating patients with diagnosed Colorectal cancer. The interview was of 20 to 30 minutes duration (**Karlsson et al., 2009**). **The questionnaire contains several sections**

2.1.1. Socio-demographic data

This includes questions on basic socio-economic characteristics of the households. It also collects data on individual characteristics as the : age, nationality, marital status, educational status of the patient and the wife / husband (if married), occupational and employment status, working hours, income source, average of household income, place of residence, type of dwelling, number of rooms, number of family members.

2.1.2. Medical history data

This is divided into two divisions: pre and post treatment. Questions in this section includes the location of the primary tumor, signs and symptoms, evidence of metastasis, area affected (if metastatic), family history of the disease, surgical history, medical history, medications, types of treatment, and finally the doses and sessions (if chemo or radiotherapy).

2.1.3. Nutritional assessment

A full nutritional assessment by measurements of BMI, triceps skinfold thickness (TST), mid-arm muscle circumference (MAMC), serum albumin (alb), serum prealbumin (palb), total lymphocyte count (TLC) and unintentional weight loss of more than 5% within the preceding month or 10% or more within the previous 6 months (**Thorsdottir et al., 2001**).

Malnutrition was defined as present when three or more of these seven parameters were subnormal. In addition, weight change from patients' self-reported earlier healthy weight was evaluated (Thorsdottir *et al.*, 2001)

2.1.4. Laboratory data

Laboratory investigations which was divided to two divisions: pre and post treatment, it includes blood analysis, U&E (urine and electrolyte) and blood glucose and albumin to measure the malnutrition level (if malnourished), also the CEA (Carcinoembryonic Antigen) as a diagnostic tool this was collected from the patient's medical records.

2.1.5. Nutritional Screening

The SSM sheet (Fig.1) Thorsdottir *et al.*, 2001 is made up of seven questions covering BMI, weight loss, anorexia, surgery and other variables that may influence nutritional status. No measurements other than weight and height were needed for answering the questions. Each question

gave a score according to the answers. The criterion set for malnutrition was a total score four or more points for cancer patient.

2.2 Biochemical measurements:

Blood tests that are commonly used in diagnosing and staging the disease were obtained from the hospital records and compared with reference standards.

2.2.1. Complete blood count (CBC) (Derrick *et al.*, 2004).

2.2.2. Carcinoembryonic antigen (CEA) assay (National cancer institute, 2011).

2.2.3. The blood test that were used to determine the nutritional status and detect malnutrition:

A. Serum Albumin. (Mahan and Escott-Stump; 2008).

B. Hematocrit. (Bistrrian *et al.*, 1976).

C. U&E (Urea and Electrolyte). (Liaison, 2012).

The results were taken from patient's records of KAAUH and Surgery and Oncology Clinic files.

**NATIONAL UNIVERSITY HOSPITAL Nutritional status of cancer patients
Department of Clinical Nutrition SCREENING FOR MALNUTRITION**

This screening sheet should be used to assess the need for nutritional therapy among adult patients.

Answer the following questions and give score Accordingly

QUESTION ANSWER ASSESSMENT SCORES

1. Height : _____ m BMI: Kg/m² _____
 Weight: _____ kg _____

2. Recent unintentional weight loss? Yes No
 If yes, how much? _____ kg Doesn't
 In what time period? _____ months

3. Age over 65 years? Yes No

4. Problems last weeks or months?
 A. Vomiting lasting more than 3 days?
 B. Daily diarrhea (more than 3 liquid stools per day)?
 C. Continuous loss of appetite or nausea?
 D. Difficulty in chewing or swallowing?

5. Hospitalized for 5 days or more during previous 2
 6. Major surgery in the past month? Yes No
 7. Diseases – 5 points Yes No
 Burn >15 %
 Malnutrition
 Multiple traumas

Completed by _____ Date _____ Sum _____
 Signature Scores _____

PATIENT'S I.D.

>20 0 scores
 18-20: 2 scores
 < 18: 4 score

Unintentional weight loss:
 >5% past month or > 10 % previous 6 mo 4 scores
 5-10% "1-6 mo. 2 score
 Doesn't know 2 scores
 Other 0 scores

Question 3 to 8:
 Yes: 1 scores
 No: 0 scores

know
 Weight loss %

 Yes No _____
 Yes No _____
 months? Yes No
 _____ If yes, list type

If a patient gets 5 or more scores, a referral should be sent to the department of clinical nutrition. For cancer patients and patients with pulmonary diseases use 4 or more scores.

Fig (1): Simple screening tool for malnutrition (SSM).

3. Ethical Considerations:

Permission was attained from the head of department of Surgery and Oncology Clinic in King Abdul-Aziz university hospital (KAAUH). Patient was given consent before the interview.

4. Statistical analysis:

The statistical analysis included:

- A) Descriptive Statistics: arithmetic mean or average and standard deviation.
- B) The results were analyzed by SPSS statistical package version **15 (1994)** and the results were tabulated and used the Harvard graphics packages version 4 for representing the results graphically (**Harvard, 1998**).
- C) Qualitative variables were expressed as percentages and numbers association measures available (**Armitage et al. 2002 and Betty, and Jonathan, 2003**).
- D) Pearson's Correlation Coefficient (r) has been also applied in this study between two quantitative variables. It measures the nature and strength between two variables of the quantitative type. The value of r ranges between -1 and +1 (**Thomas Dietz&Linda Kalof, 2000**)

3. Results:

Table (1) shows the socioeconomic status of the patients participated in the study. The total numbers of the participants were 30 patients 17 males and 13 females. Thirty percent of patients were Illiterate and 20% have elementary and intermediate degree; 23.3 % have high school degree, 26.7 % for the Bachelor's degree and above. The main source of financial was 50% depend on their job, while the type of dwelling where 56.66 % and 43.33 % live in shared house and separate house respectively. The average household income of participant was 10% have a low income of less than 1000 RS / month, 43.33% of the participants have an income between 1000 to 3000RS and 46.66 % between 2000 to 6000 RS and more per month.

Table (2) shows the anthropometric measurements of studied sample of colorectal cancer patients. The mean \pm SD of age was 54, 49.30 for males and females respectively.

Before treatment, the mean \pm SD of weight (kg), and body mass index (BMI) were 72.11, 24.25 and 86.53 and 32.93, for males and females respectively. However, after treatment the mean \pm SD of weight (kg), body mass index (BMI), weight change and weight loss were 69.54, 23.76 \pm 0.14, 12.17, 13.61, and 76.07, 29.3, 13.23 and 15.05, for males and females respectively. Regarding to unintentional weight loss duration, the majority of the patients (50%) had weight change during 3 months followed (16.7%) during 6 months and (16.7%) during 1 year but only (13.3%) had weight change during 1 month.

Table (3) shows the location of the primary tumor and types of cancer treatment of patients participated in the study. About (83.33%) have the tumor in the colon and (16.66 %) in the rectum. The different type of cancer treatment including surgery, chemotherapy and radiotherapy. The majority of the patients (43.33%) treated with both Surgery and chemotherapy while (26.66%) treated by surgery only, (13.33%) received only chemotherapy and other (13.33%) of them received a combination of chemotherapy and radiotherapy, and only (3.33%) treated with both surgery and radiotherapy.

Table (4) demonstrates the statistical evaluation of biochemical analysis for male and female before and after treatment. Through the interpretation the previous data statistically there was significant difference between before and after treatment ($P < 0.05$) in CEA, HB and albumin in male before and after treatments. Regarding to biochemical analysis for female we notice that a significant difference between before and after treatment ($P < 0.05$) in CEA, HB and albumin; but there was a high significant difference in albumin after treatments by ($P < 0.0$)

The evaluation of SSM as single nutritional parameters used in the full nutritional assessment to indicate malnutrition among cancer patients is shown in Table (5) The SSM identified 9 of the 30 patients (30%) as malnourished before treatment and 10 patients (33.34%) after treatment (The criterion set for malnutrition was a total score of 4 or more points). The same table show 23.53% (n= 4) and 38.47% (n= 5) as malnourished before treatment for male and females respectively. However, after treatment (47.06%) (n=8) and (15.39%) (n=2) as malnourished for male and females respectively.

Table (6) verify statistical evaluation of indicators for malnutrition parameters (SSM, BMI, Alb and Unintentional Weight Loss) for male and female colorectal cancer patients before and after treatments, the difference of Mean \pm SD of SSM as indicator for malnutrition for male before and after treatment was significant ($P < 0.05$). However the difference of Mean \pm SD for albumin demonstrates highly significant correlations by ($P < 0.01$) but still low (33.67 \pm 1.2). Regarding to female colorectal cancer patients the difference of mean of SSM before and after treatment was highly significant ($P < 0.01$). However the change of Mean \pm SD of BMI was significant ($P < 0.05$) between before and after treatment. Regarding to the difference of Mean \pm SD before and after treatment decrease (from 25.07 \pm 1.12 to 25.07 \pm 1.12) for albumin which demonstrate highly significant correlations by ($P < 0.01$).

Table (7) demonstrate the Correlation between SSMB and SSMA with anthropometric measurements variables as we can see there was significant correlation between weight before and after treatment

by ($P < 0.01^{**}$) and ($P < 0.05^*$) respectively; regard to the correlation of weight loss before and after was significant similar at ($P < 0.05^*$). The same table and figures (2) showed that BMI change before and after was highly significant ($P < 0.01^{**}$). While figure (3) shows negative correlation between SSMB and SSMA with Body Mass Index and Weight change. Weight change correlation was ($P < 0.05^*$) before and ($P < 0.01^{**}$) after as presented in table (7).

Table (8) represented Sensitivity and specificity of anthropometric measurements and Albumin in relation to SSM-pre and SSM-post treatment. Through

the interpretation of the previous data the SSM had sensitivity and specificity for BMI, Ab, and UWL pre-treatment which improved post-treatment.

The SSM had a sensitivity of 0.38 and the specificity was 0.65. Few individual nutritional parameters had sensitivity above 0.5, and no parameter reached the quality of the SSM. If the patients' earlier self-reported usual healthy weight was used as the reference for unintentional weight loss, this was the single best parameter with high sensitivity

Table (1): Distribution of Socioeconomic characteristic of studied sample of colorectal cancer patients (N= 30).

Parameters	Male (n=17)	%	Female (N=13)	%	All (N=30)	%
Nationality						
Saudi	5	29.4	5	38.5	10	33.3
Non Saudi	12	70.6	8	61.5	20	66.7
Type of certificate degree						
Illiterate	5	29.4	4	30.76	9	30
Elementary	2	11.8	3	23.1	5	16.7
Intermediate	1	5.9	-	-	1	3.3
High School	4	23.5	3	23.1	7	23.3
Bachelor's degree	4	23.5	1	7.7	5	16.7
Diploma	1	5.9	2	15.4	3	10
source of financial Support						
Job	11	64.7	4	30.8	15	50
Husband/ wife	1	5.9	6	46.2	7	23.33
Parents	1	5.9	-	-	1	3.33
Other relatives	1	5.9	2	15.4	3	10
Other	3	17.6	1	7.7	4	13.33
Average household income /RS						
<1000	2	11.8	1	7.7	3	10
1000 to 3000	8	47.1	5	38.5	13	43.33
3000 to 6000	2	11.8	2	15.4	4	13.33
> 6000	5	29.4	5	38.5	10	33.33
Type of dwelling						
Separate	6	35.3	7	53.8	13	43.33
Shared	11	64.7	6	46.2	17	56.66

Table (2): Anthropometric Measurements of Studied sample of colorectal cancer patients (M±SD).

Variables	Male (n=17) M±SD		Female (n=13) M±SD		All	
Age	54±1.93		49.30±1.11		51.96±1.02	
Before Treatment						
Weight (kg)	72.11±1.65		86.53±2.44		78.36±1.12	
Height (cm)	170.76±7.64		161.61±6.15		166.8±8.31	
Body Mass index	24.25±0.21		32.93±0.55		28.01±0.25	
After Treatment						
Weight (kg)	69.54±1.66		76.07±2.01		72.37±1.66	
Height (cm)	170.76±7.64		161.61±6.15		166.8±8.31	
BMI	23.76±0.14		29.3±0.36		26.16±0.16	
Weight change	12.17±0.2		13.23±0.51		12.63±0.18	
Weight Loss	13.61±1.83		15.05±1.75		14.24±1.06	
Weight change duration						
	No	%	No	%	No	%
Non	-	-	1	7.7	1	3.3
1 month	4	23.5	-	-	4	13.3
3 months	9	52.9	6	46.2	15	50.0
6 Months	3	17.6	2	15.4	5	16.7
1 year	1	5.9	4	30.8	5	16.7
Total	17	100	13	100	30	100

Table (3): Distribution of location of the tumor and type of treatment for studied sample (Male &female) of colorectal cancer patients

Parameters	Male (n=17)	%	Female (N=13)	%	All (N=30)	%
Location of the tumor						
Colon	13	76.5	12	92.3	25	83.33
Rectum	4	23.5	1	7.7	5	16.66
Which type of treatment did you receive						
Surgery	4	23.5	4	30.8	8	26.66
Chemotherapy	1	5.9	3	23.1	4	13.33
Surgery + chemotherapy	8	47.1	5	38.5	13	43.33
Surgery + Radiotherapy	1	5.9	-	-	1	3.33
Chemotherapy + Radiotherapy	3	17.7	1	7.7	4	13.33

Table (4): Mean±SD Biochemical Analysis for Male and Female of colorectal cancer patients before and after treatment.

Variables	Male (N=17)				Female (N=13)			
	Before Mean ± SD	After Mean ± SD	T. value	P	Before Mean ± SD	After Mean ± SD	T. value	P
CEA	4.8±0.01	5.81±0.04	2.68	P<0.05*	2.92±0.11	3.22±0.21	2.29	*
WBC	6.72±0.96	6.92±0.73	0.21	NS	7.61±0.03	9.15±0.39	1.94	*
RBC	4.39±0.77	4.25±0.58	0.78	NS	4.2±0.43	3.97±0.54	2.31	*
HB	15.83±1.6	12.08±1.11	2.41	*	10.7±1.53	10.66±1.10	1.61	NS
HCT	35.86±1.74	36.14±1.45	0.95	NS	31.93±1.32	38.06±1.73	2.83	**
MCV	82.25±2.35	85.54±4.51	0.17	NS	74.02±1.56	82.89±4.5	3.16	**
MCH	27.05±0.15	28.71±1.49	1.64	NS	25.5±0.11	27.04±1.2	1.34	NS
Platelet count	280.52±10.33	257.35±6.58	2.37	*	298.61±10.76	255.84±9.7	4.15	***
Albumin	29.55±0.06	33.67±1.2	2.18	*	32.3±0.79	25.07±1.12	2.64	**
Urea	5.09±0.77	4.62±1.82	3.01	*	3.86±0.12	4.14±3.47	1.17	NS
Na	136.05±3.28	137.35±2.95	0.65	NS	135.55±3.24	137.23±4.81	1.5	NS
Crea	82.64±2.83	80±19.55	1.59	NS	69.23±2.07	55.23±22.84	2.44	*
K	4.61±0.25	3.78±0.42	1.91	*	3.64±0.38	3.86±0.34	1.34	NS
Cl	99.05±4.22	101.58±3.75	0.46	NS	99.11±3.12	99.46±4.92	0.23	NS

* P < 0.05 ** P < 0.01 *** P < 0.001 NS: No significant

Table (5): Statistical evaluation of (SSM) for colorectal cancer patients before and after treatment

Parameters	Male (n=17)	%	Female (N=13)	%	All (N=30)	%
Before Treatment						
<4	13	76.47	8	61.53	21	70
≥ 4	4	23.53	5	38.47	9	30
After treatment						
<4	9	52.94	11	84.61	20	66.66
≥ 4	8	47.06	2	15.39	10	33.34

Simple screening tool for malnutrition (SSM)

Table (6): Statistical evaluation of indicators of malnutrition parameters for colorectal cancer (male&female) patients before and after treatment

Variables	Male (N=17)				Female (N=13)			
	Before	After	T. Value	P	Before	After	T. Value	P
SSM	4.47±0.8	3.47±0.37	1.98	*	3.07±0.11	5.81±0.35	3.11	**
BMI	24.25±0.21	23.76±0.14	1.05	NS	32.93±0.55	29.3±0.36	2.16	*
Alb	29.55±0.66	33.67±1.2	2.31	**	32.3±0.79	25.07±1.12	3.25	**
UWL (kg)	-	13.61±1.83	-	-	-	15.05±1.75	-	-

* P < 0.05 ** P < 0.01 *** P < 0.001 NS: No significant

SSM_ screening sheet; BMI_ body mass index; alb_ serum albumin; UWL_ unintentional weight loss.

Table (7): Correlation between SSM-Pre and SSM-Post with anthropometric measurements variables

Measurements	SSM-Pre		SSM-Post	
	R	P-value	R	P-value
WEIGHT	-0.59	P < 0.01**	-0.44	P < 0.05*
HEIGHT	-0.15	P > 0.05(NS)	-0.22	P > 0.05(NS)
BMI	-0.48	P < 0.01**	-0.56	P < 0.01**
W.CHANG	-0.39	P < 0.05*	-0.56	P < 0.01**
W.LOSS	-0.39	P < 0.05*	-0.39	P < 0.05*
DURATION(months)	-0.17	P > 0.05(NS)	-0.23	P > 0.05(NS)

* P < 0.05 ** P < 0.01 SSMB – Simple Screening for malnutrition before treatment SSMA- Simple Screening for malnutrition after treatment.

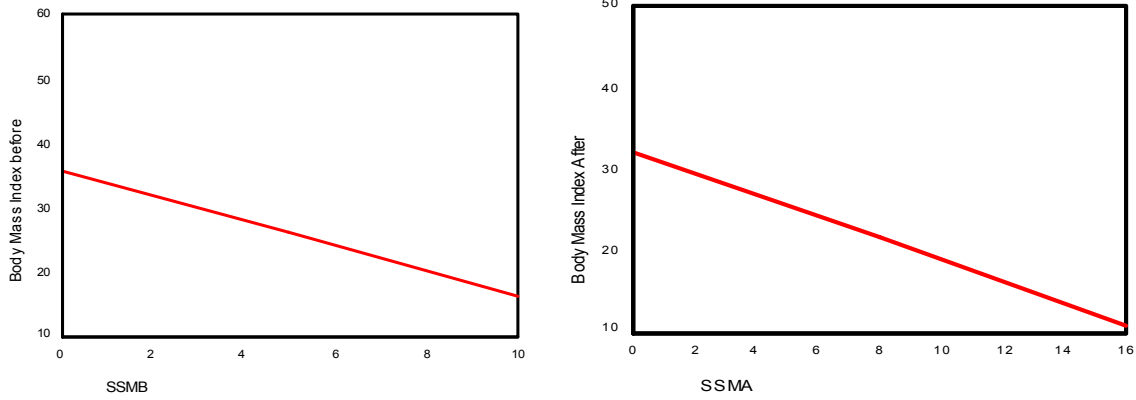


Figure (2): Correlation between SSMB&SSMA and Body Mass Index before

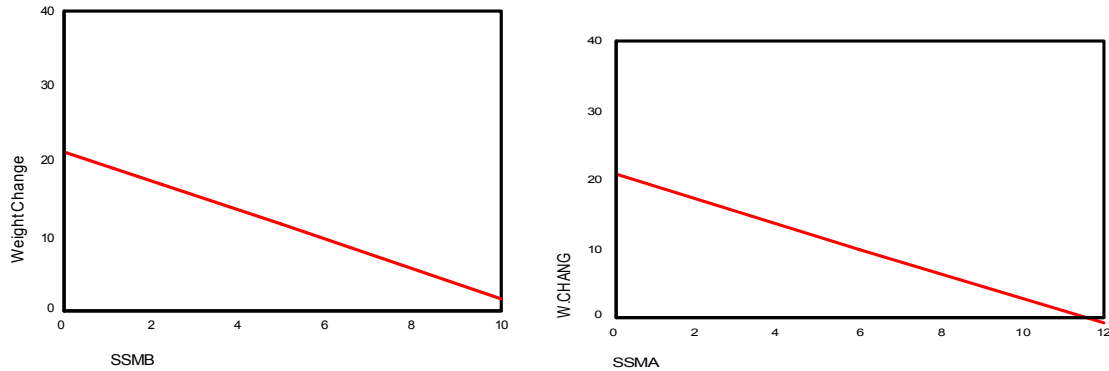


Figure (3): Correlation between SSMB&SSMA and Weight Change

Table (8): Sensitivity and specificity of anthropometric measurements and Albumin in relation to SSM-pre and SSM- post treatment

Test	SSM-pre			SSM-post		
	BMI	Alb (g/L)	UWL (kg)	BMI	Alb (g/L)	UWL (kg)
Sensitivity	0.09	0.55	1.0	0.15	0.54	0.85
Specificity	0.84	0.53	0.21	0.76	0.65	0.12
Positive predictive value	0.25	0.40	0.42	0.33	0.54	0.42
Negative predictive value	0.62	0.67	1.0	0.54	0.65	0.50
False positive	0.75	0.6	0.58	0.67	0.46	0.58
False negative	0.38	0.33	0.0	0.46	0.35	0.5
Misclassification rate	0.04	0.03	0.02	0.03	0.03	0.04

Table (9): Statistical evaluation of some indicators of malnutrition in cancer patients

Tests	SSM	BMI	Alb (g/L)
Sensitivity	0.38	0.17	0.54
Specificity	0.65	0.88	0.53
Positive predictive value	0.45	0.25	0.47
Negative predictive value	0.58	0.81	0.60
False positive	0.55	0.75	0.53
False negative	0.42	0.19	0.40
Misclassification rate	0.03	0.03	0.03

4. Discussion

Colorectal cancer ranks the third highest in cancer incidence and fourth in cancer mortality in both sexes combined worldwide (Jinfu Hu *et al.*, 2010). Hyper metabolism-associated malnutrition, known as protein-calorie malnutrition, is common in cancer patients and

is clearly associated with cytokine production and the systemic inflammatory response (Falconer *et al.*, 1994 and Staal-van den Brekel, *et al.*, 1995). Malnutrition is common among hospitalized patients. However, the nutritional aspect of medical management has not always been given first priority. Cancer patients suffer

from protein energy malnutrition throughout the evolution of their disease with elevated basal energy requirements due to their inherent illness and decreased oral intake due to reduced gustatory senses with elevated basal energy requirements due to their inherent illness and decreased oral intake due to reduced gustatory senses (Sanz et al 2008).

This is the first study that examined the nutritional status for colorectal cancer patient's pre and post different modulates of treatment at the King Abdul-Aziz University Hospital. A cross-sectional descriptive study was carried out among (30) Patients at King Abdul Aziz Hospital (KAAUH) Kingdom Saudi Arabia after an informed consent agreement, with diagnosed colorectal cancer to be included in the study at their first visit to the outpatient surgery and oncology department between October 2011 and April 2012 were included in a retrospective review of the patients' medical record. Inclusion criteria for those Patients aged over the age of 18 years old with colorectal cancer; proven adenocarcinoma of the colon involving any location from the cecum to the rectum; received any type of treatment. Patients with other diagnoses were excluded. The mean age for both women and men was 51.96 ± 1.02 (range 21 – 84 year). The aim of the study was explained to the subjects. Our study likewise the study by **Olof and Inga, 2008** the participants (n_30). The mean age was 55 years (range 29_72year).

An English questionnaire was developed for the purpose of data collection, which was pilot, tested and modified accordingly. A face-to-face interview with each participating Patients with diagnosed Colorectal cancer. The interview was of 20 to 30 minutes duration (**Karlsson et al., 2009**). The questionnaire includes information about Socio-economic status demographic data including; age, sex, social status, housing, educational level, anthropometric measurements (height, weight, calculate BMI, hip, waist circumference and calculate hip/waist ratio) by direct contact face to face or by telephone. In addition to the required laboratory investigations which was collected from the patient's medical records.

Socioeconomic Characteristics

The country of Saudi Arabia is among the richest and highest per capita income countries of the world. This high income combined with food affluence and lack of nutritional awareness has led to a state of over-nutrition of macronutrients and malnutrition of micronutrients among the population (**Madani et al., 2000**). Our result table (1) revealed that about 30% of patient were had more than 6000 RS/ month, however 13.33 had 3000- 6000RS/month and 43% were had 1000 to 3000 RS/month. About 57% from our participate were living in shared dwelling but remain (43%) had separate house. This result verified that

most of our sample in high Socioeconomic status (H-SES).

Nutritional screening

The purpose of nutritional screening is to identify those patients who are at nutritional risk and at higher risk for complications. Early detection of nutritional risk would allow for early intervention and this may prevent later complications. The validity of a screening tool is dependent on its ability to predict outcome. Our study found that there was a significant association between high nutritional risk by the SSM sheet (Fig. 1), (**Thorsdottir et al., 2001**) The evaluation of SSM as single nutritional parameters used in the full nutritional assessment to indicate malnutrition among cancer patients is made up of seven questions covering BMI, weight loss, anorexia, surgery and other variables that may influence nutritional status. The criterion set for malnutrition was a total score of four score or more for cancer patient. This study by SSM identified (30%) as malnourished before treatment and (33.34%) after treatments as shown in table (5). Another study by **Olof and Inga, 2008** which used the SSM sheet showed that 20% of cancer patients in an outpatient clinic with a clinical diagnosis of colon cancer were malnourished. Weight loss and malnutrition are common in patients with advanced malignant diseases that adversely influence patient survival and QoL (**Laviano and Meguid, 1996; Delmore, 1997; and Noursissat et al., 2008**).

Unintentional weight loss has often been reported in cancer patients (**Watson, and Tang, 1980**) and regarded as a stronger variable for detection of malnutrition than BMI (**Lipkin and Bell, 1993 and Orr et al., 1984**). In the present study, unintentional weight loss as indicator for malnutrition in cancer patients showed in table (2) for all participated ($14.24 \pm 1.06\text{kg}$), however unintentional weight loss value ($13.61 \pm 1.83\text{kg}$) and ($15.05 \pm 1.75\text{kg}$) for males and females respectively. In the study by **Olof and Inga, 2008** report that the general unintentional weight loss from patients' self-reported earlier usual healthy weight was found to be the best single parameter for detecting malnutrition. However, it did not reach the quality of the SSM in terms of specificity and misclassification.

The present study as shown in table (4) of biochemical analysis which revealed that a majority of the patients had serum albumin (73.2% before treatment and 71.3% after treatment) below the reference value. This result supported by the data in the table (6) which demonstrated that the difference of Mean \pm SD for albumin as malnutrition indicators in our study was highly significant correlations by ($P < 0.01$) for male and female patients before and after treatments but still low than reference range (34 – 50 g/l). Another Similar study by **Olof and Inga, 2008** found that a majority of the patients had serum albumin

(70%) below the reference value. Previous studies have implicated that pro-inflammatory tumor derived mechanisms influence the hepatic acute phase protein response, which makes measurements of serum albumin and immunocompetence such as TLC of limited value. Serum albumin is the most widely used clinical index of nutrition, but because of its long half-life and affection by stress and illness (**Wong et al., 2001**) it can be regarded as a poor parameter of nutritional status. Also many cancer therapy drugs cause low TLC and serum albumin (**Forse et al., 1985**). This underlines that nutritional status cannot be evaluated from one or two single parameters and supports the need for several measurements as used in the present study.

Medical information and the different types of treatment

The present study as present in table (3) revealed that the majority of the patients (43.33%) treated with both Surgery and chemotherapy while (26.66%) treated by surgery only followed by (13.33%) of the patients received only chemotherapy also other (13.33%) of patients were received a combination of Chemotherapy and Radiotherapy, and only (3.33%) treated with both Surgery and Radiotherapy. Another study by **Olof and Inga, 2008** reported that data from one month screening with SSM indicated that 41% of all cancer patients in chemotherapy were malnourished or in nutritional risk. The majority of the screened patients are regarded themselves in need of nutritional counseling, but only few had received nutritional counseling. Likewise our study showed that (70 %) participated were received chemotherapy or with other treatments (surgery or Radiation) and our data from screening with SSM indicated that (50%) of all cancer patients in chemotherapy were malnourished or in nutritional risk. These studies supported by other reports that nutritional issues are underestimated in diagnostic and therapeutic procedures (**Nitenberg, and Raynard, 2000, Delmore, 1997; and Laviano, and Meguid, 1996**). It has been concluded from the results of other studies that early nutritional support is necessary to improve patient's nutrient status and controlling complications related to food intake which influence patients' QoL (**Ravasco et al., 2007**).

Chemotherapy and radiotherapy are the two important treatment modalities for cancer and can tumor cells and prolong survival time of cancer patients. Patients receiving high-dose chemotherapy need to be supported with parenteral nutrition (**Tartarone et al., 2005**) Nutrition therapy can help cancer patients get the nutrients to maintain body weight and performance status, prevent body tissue from breaking down and rebuild tissues (**Johansen et al., 2004**). Malnutrition can make the patients have more severe chemotherapy-induced toxicity and complications (**Van Cutsem, and Arends, 2005**).

High energy/protein diets help patients tolerate the treatment with fewer side-effects (**Read, 2004 and Khan et al., 2006**) patients with tumors of the gastrointestinal tract have difficulty eating due to side effects of surgery. These patients are weak, tired, and unable to withstand cancer therapies because of malnutrition. The treatment outcome and prognosis of the diseases are associated with the nutritional status of the patients (**Sanford, 2005, Lummen et al, 2006 and Peng et al., 2006**). If the patients get enough calories and protein from their diet when they are not on chemotherapy or radiation therapy, they may have a better prognosis and are able to tolerate higher doses of chemotherapy or radiation therapy (**Bozzetti et al, 1998 and Capra et al, 2001**).

Nutritional assessment

Many researchers have suggested that good nutrition in the patient with cancer may improve quality of life, and the nutrition status of the patient after diagnosis is associated with cancer recurrence and survival rates (**Tian et al., 2008**). The present study as we can see in the table (2) revealed that unintentional weight loss in male patients was more than female. Regard to duration for a unintentional weight loss; the half (50%) for all patient however (52.5% in male & 46.2% in female) had lost weight through 3 months. As we can see after 6 months and 1 year unintentional weight loss was (17.6% and 5.9 respectively for male) and (15.4% and 30.8% respectively for female). We concluded from these results that 3 months don't enough for improvement and patients need 6 months - 1 year under treatment to decrease the percent of unintentional weight loss. Unfortunately that the female were less improvement than male may be due to another factors related gender. Our study in agreement with other studies who's reported that unintentional weight loss has often been reported in cancer patients (**Watson, and Tang, 1980**) and regarded as a stronger variable for detection of malnutrition than BMI (**Orr and Shingleton, 1984 Lipkin & Bell, 1993**). Other study in the Unit of Nutrition Research, National University Hospital, Reykjavik, Iceland by **Olof and Inga, 2008**, found that the unintentional weight change was not significant due to this wide range of patient's weight changes. However, if the patients' self-reported earlier usual healthy weight was found to be the best single parameter for detecting malnutrition. However, it did not reach the quality of the SSM in terms of specificity and misclassification.

The present study as shown in tables (8) there was relation between the sensitivity and specificity of SSM-pre and post treatment with the sensitivity and specificity of BMI, Alb, and UWL before treatment and this relation improved after treatment. The SSM had a sensitivity of 0.38 and the specificity was 0.65 as presented in table (9). Other study by **Olof and Inga, 2008** found that the SSM had high sensitivity (0.87)

and specificity (0.88), and 13% misclassification and few individual nutritional parameters had sensitivity above 0.5 and no parameter reached the quality of the SSM. If the patients' earlier self-reported usual healthy weight was used as the reference for unintentional weight loss, this was the single best parameter with high sensitivity. The SSM have been validated with high sensitivity and are used in routine clinical screening in other departments at Landspítali-University Hospital (**Thorsdottir et al., 2005**). Sensitivity in nutritional screening is very important for realization of the goal of finding malnourished patients, and specificity for preventing well-nourished patients being classified as malnourished. The sensitivity of the SSM was higher in the study by **Olof and Inga, 2008** of cancer patients than found in earlier studies for other patient groups (**Thorsdottir I et al., 2001** and **Bauer J et al., 2002**). Likewise our study verifies that the sensitivity of the SSM was higher as show in table (8).

Anthropometric Data:

According to the National Cancer Institute's "Nutrition in Cancer Care" guidelines, timely identification and treatment of nutrition problems may improve cancer patients' prognosis by helping the patient gain or maintain weight, improving the patient's response to therapy, and reducing the complications of treatment (**Gupta et al., 2006**).

A review **Alina Vrieling and Ellen Kampman, 2010** shows that there is a paucity of published studies on BMI, physical activity, and dietary factors in relation to colorectal cancer recurrence and survival. Because of these small numbers and the large heterogeneity in the type of exposure, timing of exposure assessment, and disease outcomes investigated, summarizing the results and drawing firm conclusions is difficult. Higher BMI or body fatness before or at time of diagnosis may be associated with higher all-cause mortality, colorectal cancer-specific mortality, or recurrence, although results appeared to differ according to sex, tumor location, and the molecular subtype of the tumor. There is suggestive evidence that a higher post diagnosis leisure-time physical activity is associated with lower all-cause and colorectal cancer-specific mortality.

Our results as we can see in table (2) verify that mean of BMI for all colorectal patients was (28.01) before treatments and decrease to (26.16) after treatments. Likewise the results revealed that unintentional weight loss in male patients was more than female. Regard to duration for a unintentional weight loss; the half (50%) of our sample had through 3 months. As we can see in the same table after 6 months and 1 year unintentional weight loss occurs in (17.6%) and (5.9%) from our participated patients respectively. Another study by **Burden et al., 2010** showed that one in five of patients were malnourished

(weight loss >10%) when they first entered the secondary health care system; however, BMI categorized over half of the patients as being overweight or obese. If BMI alone were used as a measure of nutritional status, many CRC patients with malnutrition and weight loss would go unidentified.

Prevalence of malnutrition:

There is a definite interplay between the nutritional status and disease in cancer patients. The altered host metabolism associated with cancer commonly leads to protein calorie malnutrition. In turn, protein calorie malnutrition produces a vicious cycle by interfering with the response to oncological therapy and enhancing morbidity. Protein calorie malnutrition is a common secondary diagnosis in cancer patients. It has an insidious evolution and its detection and treatment is important to the success of oncological therapy and improvement in quality of life. It thus becomes mandatory to develop objective criteria to recognize malnutrition. Anthropometric parameters have long been used in nutrition surveys as markers of malnutrition owing to the ease and simplicity of measurement. Loss of body weight is an important indicator of the presence, severity, and progress of the disease process. Weight is unique in that it is a measurement that many people determine themselves; therefore they can give some estimate of what their weight was when they were well (**Gurpreet Singh and Khanna, 1985**).

Malnutrition is observed in up to 80 % of patients with advanced colorectal cancer (**Karthaus and Frieler, 2004**) and is associated with longer hospital stay, reduced response, and increased overall cost of care, and poor survival. A retrospective analysis study was accomplished in USA on 58 stage III-IV colorectal cancer patients treated at cancer treatment Centers of America concluded that the prevalence of malnutrition, as determined by SGA, was 41% (24 of 58) (**Gupta et al., 2006**).

Another study that was conducted to evaluate a short screening sheet (SSM) for malnutrition and to investigate the nutritional status of patients receiving chemotherapy for cancer of the lungs, colon or breast at an outpatient clinic. The test of SSM in clinical routine showed that 40% of the patients were malnourished (**Olof Gudny and Inga, 2008**). And the prevalence and risk factors of malnutrition among cancer patients according to tumor location and stage in the National Cancer Center in Korea is 61% (**Gyung-Ah et al., 2009**). The present study mentioned that (30%) as malnourished before treatment and (33.34%) after treatment (The criterion set for malnutrition was a total score of 4 or more points by SSM screening) as shows in table (5).

Also our study in table (6) which verify the statistical evaluation of indicators for malnutrition (SSM, BMI, Alb and Unintentional Weight Loss) for

male cancer patients before and after treatments, as we can see the Mean± SD of SSM was 3.47±0.37 and 4.47±0.8, there was significant difference between before and after treatment at * $P < 0.05$. However Mean of second parameters BMI was 24.25±0.21 and 23.76±0.14 but the change was not significant difference between before and after treatment. Regarding to Mean± SD for albumin was 29.55±0.66 and 33.67±1.2 before and after treatment respectively and the difference was highly significant by ** $P < 0.01$.

Unintentional weight loss has often been reported in cancer patients (Watson, 1980) and regarded as a stronger variable for detection of malnutrition than BMI (Lipkin, Bell 1993; Orr *et al.*, 1984). In the present study, general unintentional weight loss was 13.83 for males and 15.05 for females as we can see in table (6).

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Investigation of income smoothing using extraordinary items in firms accepted in Tehran's stock exchange

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Abstract: The purpose of this research is to investigate the informational content of extraordinary items and its effect on income smoothing for firms accepted in Tehran's stock exchange. Income smoothing is defined as management basic interfering in reducing the income's periodic fluctuations. The research data have analyzed using a sample including 96 firms accepted in Tehran's stock exchange for a 7 years period (2003-2009). Ordinary least square regression (OLS), scattering coefficient and determine coefficient models were used for hypothesizes testing. The obtained results suggested that the income smoothing using extraordinary items exists in the under study firms. Also the results revealed that the extraordinary items don't increase the income's informational content.

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Keywords: income smoothing, income management, extraordinary items, income before extraordinary items

1. Introduction and literature

Information play a critical role in economical decision makings and therefore investors cant detect the investing opportunities and risks sufficiently without enough information. The firms' reported incomes are always considered as one the basic criteria for financial decision makings, and the financial analyzers consider income as a basic factor for their investigations and evaluations. Therefore, managers are high motivated to represent a suitable view of their firms and reducing the investment risks and consequently smooth their incomes (Noorvash, et.al 2004) the income smoothing can effects the investors decisions and results in important outcomes specially in inefficient capital markets (Samaee et al. , 2007). The research is organized as follows: first the subject, purposes, and theoretical issues as well as previous related literatures are presented and then the research methodology , hypothesizes , statistical methods and data analyzing , and finally conclusions and recommendation are presented.

1.1. Description and research goal

The accounting international standards regulating board have tried to prevent the presentation of income and expenditure items as extraordinary items in explanatory notes and profit and loss lists. This subject is presented clearly in the articles 14-18 of accounting international standards concluding fundamentals (2008). The board believes that the items considered as extraordinary ones are originated for the business ordinary risks and doesn't need to consider separately in profit and loss lists. The board also believe that all events are originated from the

ordinary activities of enterprises and so classify it as continuous operations. Therefore, the ordinary-unmoral classification is not suitable. Moreover, making distinction between the extraordinary and ordinary items need suitable judgment (Barnea, Ronen, and Sadan,2001).

Although it seems that the new procedure of international board is better due to the low importance of extraordinary items value, but the Britain and American boards have different ideas regarding this issue. Maybe one of the reasons for separately disclosure of extraordinary items is that the presented incomes have more predicting power. Also the extraordinary items can aware investors for the potential risks of their enterprises (Khodadadi, 1996). In accordance with the Iranian standard, the separation of extraordinary items from ordinary ones is due to its reasonable base for investors' decisions and judges. The importance issue is their schedule for income smoothing. Management misuses the extraordinary items due to different reasons such as reducing the agents costs, following the legal requirements like the loans Receiving or other contracts requirements, and marinating the firms profitability process during challengeable periods (Modares 2006, Arabi 2010).

Considering the above motioned notes, it is valuable to investigate the possibility of income smoothing in Iranian firms.. Another important note is their accurate position in profit and loss lists, informational content, and importance in analyzing and predicting the future incomes which are all studied in this research.

The main purpose of this research is to investigate the informational content of extraordinary items and its effect on income smoothing for firms accepted in Tehran's stock exchange. The other purposes are to present the applicable results for income smoothing to the real and potential investors and credit makers for assisting them in financial decision makings.

1.2. Background

Researchers have studied the role of extraordinary items in income smoothing and informational content in several researches. Some obtained results are as follows:

In a research, (Barnea, Ronen, and Sadan,2001) have studied the items suitable for being classified into non continuous (extraordinary) and unordinary groups in USA and evaluated that whether these items can be applied for initial income smoothing before the extraordinary items. The research has performed in a 20 years period for different American industries. The obtained results revealed that managers use extraordinary items classification changes for income smoothing.

Lynn and Guinness (2002) have studied the informational content ability for predicting the income and difference of items number in small and large firms in Hong Kong during a five year period. The obtained results suggested that there is no relation between smoothing and informational content of extraordinary items and the items is more for large firms than small ones . But there wasn't a significant relation between the items numbers and firms size.

Bettie et al (2006) have performed a research on items classification motivation and extraordinary items for income smoothing in 163 Britain firms and concluded that there is a direct relation between the smoothing motivations and importance of classification choice for expected income.

Samadi (2008) has performed a research on effects of smoothing on informational content and concluded that income smoothing increase the abilities of current and past incomes for predicting the operational cash currencies and incomes, while there is no increase for predicting the future promised items through income smoothing.

Khodadadi (1996) have studied the existence, nature, and effects of extraordinary , unordinary , and non-continuous items on income. This research was performed on firms accepted in Tehran's stock exchange during 1991-94. In accordance with his hypothesizes, the following results were obtained: these items have not informational content for predicting firms' future income. These items don't results in income smoothing. There is no direct relationship between

these items and firm size . These are more important in small firms than big ones. There is weak relation between the number of these items and firm size.

1.3. Theoretical fundamentals

Since the industrial revolution and decreasing the final price of goods and services , the investors and owners who were distanced from managers have paid a part of their salary as award(often depends on a percent of shares interest) to motivate them to work better and more responsible. Therefore, managers were working more optimized to gain better awards. After some years, mangers understood that they can use the weak points of different methods and principals of accounting to manipulate different years' income in order to obtain their desired income to present in financial reports . this was the origin of income management or smoothing (Kashipour and Yaghoubi 2006).

This manipulation is possible if the accounting income contains informational content. In other words, investors consider income as an effective factor for decision making.. Ball and Brown (1968) were the establishers of research related to informational content of accounting income, they develop the proving theory. Their research showed that the accounting income changes have a relation with the share price.

The smoothing philosophy is to utilizing form the standards methods flexibility and accounting accepted principals. Of course , different explanations of accounting execution standards is another reason for smoothing. Research showed that managers manipulate the reported incomes deliberately using specific accounting policies , making changes in accounting estimations and promised items to reach their goals (Noorvash, Sepasi, and Nikbakht ,2005). Ranen and Saden , ImHAV, ackel and many other researchers reveal that Hepworth was the first one to introduce smoothing (Defond T and Jiambalvo, 2006). Income smoothing is the goal oriented interference of extra organizational management in financial reporting (Schipper,1989).

1.4. Research hypothesizes

Considering the theoretical fundamentals and background sections presented earlier, two hypothesizes were considered:

hypothesizes 1: extraordinary items is used for income smoothing

hypothesize 2: extraordinary items increase income informational content

2. Methodology

Considering that this research is aimed at investigating the informational content of extraordinary items and how to apply them for income smoothing in firms accepted in Tehran's stock

exchange, so this is an applicable-descriptive research. The research has performed as semi empirical using previous information.

2.1. Data gathering tools

Library ,stock exchange website, and Tadbir Pardaz software were used for data gathering and processing. Therefore, the data have gathered using field study method.

2.2. Statistical population and sampling

The statistical population includes all firms accepted in Tehran's stock exchange during 2003-9, sampling was performed as goal oriented. In every stage, firms which haven't conditioned with the following criteria have been eliminated and finally the remained ones selected as samples:

1. Firms have to be active continuously during the financial year.
2. Firms shouldn't be as agency, investing, lazing, or insurance.
3. The firms' financial year should be terminated by February for ease of comparison
4. The firms accounting should be completed
5. The required data of firms should be available.

Considering these limitations, 96 firms have been qualified for the statistical population. All the qualified firms were considered as the statistical population.

2.3. Data analyzing techniques and research variables

Different tests such as scattering coefficient, regression test, and determination factor R2 were used for performing the research. Software such as Excel and Eviews were used for data processing. Scattering coefficient is one of the statistical indexes which is used for determining the scattering rate from average. It is also called relative criteria or relative scattering. The index is computed as follows:

$$cv = \left(\frac{S}{M} \right) \quad (1)$$

Where, Cv is scattering coefficient, S is standard deviation, and M is mean.

For testing the first hypothesizes and studying the income smoothing by extraordinary items, the scattering coefficient before and after extraordinary items deduction is computed and compared with above equation (Layn and Guinness,2001). For this purpose, first the mean and standard deviation of income before extraordinary items and then the scattering coefficient of income before extraordinary items are computed. Then the mean and standard deviation and scattering coefficient after extraordinary items will be computed. In case of smoothing, it should be expected that the income scattering coefficient become lower after extraordinary items.

For testing the second hypothesizes and studying the informational content of net income before and after extraordinary items , regression models were used as follows:

$$P_{it} = \alpha_0 + \alpha_1 EarnBX_{it} + \alpha_2 FSize_{it} + \alpha_3 CFO_{it} + \alpha_4 MBValue_{it} + e_{it} \quad (2)$$

$$P_{it} = \beta_0 + \beta_1 EarnAX_{it} + \beta_2 FSize_{it} + \beta_3 CFO_{it} + \beta_4 MBValue_{it} + e_{it} \quad (3)$$

The left term P in equations 2 and 3 represents the share price(dependent variable).EarnAX and EarnBX are net income before and after extraordinary items(independent variable), respectively. P_{it} represents the share price at the end of first quarter after the termination of financial year, because this date is the last opportunity of firms to present their financial lists and accounting reports and the information of per share, book value of per share, and operational cash flow in this date can be appeared in shares price (Habib , 2004).

The firms' share price is presented daily in stock exchange. Also the FSize, CFO, and MBValue presents firm size, operational cash flow, and firms' total value or market value ratio to share book value (control variables), respectively.

In the second hypothesizes, first the income informational content before and after extraordinary items is computed for testing the informational content of extraordinary items. For this purpose, the amount of relation and effectiveness of mentioned incomes is compared with the daily price of under study firms. The more the relation between the income and share price, the more the informational content. Then, the informational content before and after extraordinary items will be compared. Three control variables also were used for achieving reliable results from the reasonable relation between the net income before and after extraordinary items and share price. The control variables include firm size, cash flow of operation , and sales growth . these control variable also were used in research of Ronen and Sadan (1981) and Habib (2004). The used variable and their abbreviations are presented in table 1.

Table 1: used variable and their abbreviations

Row	Symbol	Variable and its type
1	EarnAX	Income before extraordinary items deduction
2	EarnBX	Income after extraordinary items deduction
3	P	Share price
4	FSize	Firm size
5	CFO	Cash flow of operation
6	MBValue	Ratio of market value to share book value (firm's value)

3. Findings

3.1. Descriptive statistics

Data are described before analyzing to make better sense for under study population and research variables. Data statistical description is a step toward determining the governing pattern of data and relation between research variables (Hafeznia, 2010). Statistical description of research is presented in table 2.

Table 2: results of statistical description during 2004-10

Variable	mean	Median	Standard deviation	max	Min	Observations number
EarnAX	182/34	216/55	88/01	354/29	12/22	672
EarnBX	180/63	218/39	72/12	329/33	11/41	672
P	8232	10345	6572	28615	1207	672
FSize	5/5678	5/89845	0/4125	6/9044	4/4116	672
CFO	0/183	0/171	0/161	0/649	-0/271	672
MBValue	15/52	8/06	3/14	32/21	0/89	672

3.2. Results of hypothesizes tests

The data of 96 understudy firms during 2004-10 were combined and tests have performed on 672 year-firm for hypothesizes testing . the results of hypothesizes tests for each hypothesizes are presented as follows:

3.2.1. First hypothesizes test

The first hypothesis tries to determine whether the under study firms use extraordinary items for income smoothing. Scattering coefficient index was used for testing this hypothesizes. The related computations are presented for 2004-10 period in table 3.

As it can be seen from table 3, the scattering coefficient (standard deviation to mean ratio) before and after extraordinary items deduction are 0.482 and 0.399, respectively. Considering that the scattering coefficient is much lower after extraordinary items deduction, therefore it can be concluded that these items results in scattering reduction around mean value. In other words, the under study firms have used extraordinary items for income smoothing. Therefore, the first hypothesizes is accepted.

Table 3: computations and results of first hypothesizes test

Description	Results
Period	1382 -1388
Observations	672
μ_{EarnBX}	182/34
μ_{EarnAX}	180/63
σ_{EarnBX}	88/01
σ_{EarnAX}	72/12
CV_{EarnBX}	0/482
CV_{EarnAX}	0/399
Test's result	Accepted

3.2.2. Second hypothesizes test

The second hypothesizes tries to determine whether the extraordinary items increase the income informational content and can predict future incomes. Regression method was used for testing this hypothesizes. The results of regression models estimation 2 and 3 for studying the informational content before and after extraordinary items during 2004-10 are presented in table 4.

Table 4: computations and results of second hypothesizes test

Description	Model 2 test	Model 3 test
Period	1382 -1388	1382 -1388
t-statistics (p-value)	10/43 (0/028)	9/21 (0/041)
Coefficient	0/44	0/38
Observations number	672	672
Modified R ²	0/582	0/393
Relation type	Direct	Direct

Considering the results of models 2 and 3 inserted in table 4, t-statistic of model 2 was significant in error level 0.05 and this means that income had informational content even after extraordinary items deduction. The determination factor R² was 0.582 and 0.393 for testing models 2 and 3, respectively. The more the amount of this factor , the more the relation between the model's dependent and independent variables and consequently the informational content. Comparing the results of two models reveals that the incomes before extraordinary deduction have more informational content than after it. In other words, extraordinary items doesn't increase the income informational content and therefore the second hypothesizes is rejected.

4. Conclusions and recommendations

The role of extraordinary items on income smoothing and increasing the informational content of net income has studied in this research. This research includes two hypothesizes for answering the mentioned questions.

As it was mentioned in first hypothesizes test, the income scattering coefficient before and after extraordinary items deduction were 0.482 and 0.399, respectively. Considering that the income scattering coefficient was much lower after extraordinary items deduction , so it can be concluded that the under study managers have used these items to reduce scattering around mean value. So the first hypothesizes is accepted. The obtained results for the first hypothesizes are consistent with Barnea et al (2001)

and Bettie et al. 2006, while it is different from Lynn and Guinness (2002) and Khodadadi (1997).

Considering the results of second hypothesis, the modified determination factor R^2 for models 2 and 3 were 0.582 and 0.393. Comparing the results obtained from these two tests suggest that income before extraordinary items have more informational content. In other words, extraordinary items don't increase the informational content. Therefore, the second hypothesis is rejected. The obtained results for the second hypothesis are consistent with Barnea et al (2001) and Bettie et al. 2006, while it is different from Lynn and Guinness (2002) and Khodadadi (1997).

There were some limitations for this research. One of these limitations is that some factors effective on research results such as economical factors, political conditions, global economy mode, and regulations were out of the control of the author. The other limitation is that non modification of financial lists can affect the research results through inflation. Considering the research theoretical fundamentals and results, it is recommended that stock exchange and accounting organization make some regulations and standards for optimized control of managers' behaviors for selection among several accounting methods.

4.3. Recommendations

After studying the test results of research hypothesis, the following subjects can be considered in future research:

- a) studying the informational content of other accounting data except extraordinary items such as income per share, cash flow of operation, unspecific income and
- b) Studying income smoothing in firms accepted in Teheran stock exchange using other common methods such as estimations, accounting methods change, transactions scheduling and etc.
- c) Studying the effect of other items of loss and profit list such as exceptional items, stooped operational income, ... on informational content of net income.
- d) making comparison between informational content of net income and comprehensive income and their prediction power.

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Posttraumatic growth, Anxiety, Depression of Stroke Survivors

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Abstract Objective Although some previous studies have suggested that posttraumatic growth (PTG) is comprised of several factors with different properties, few have examined both the association between PTG and anxiety, depression. This study aimed to investigate the status of anxiety, depression and posttraumatic growth among stroke patients, and to study the relationship between them. **Method** This cross-sectional study was performed with 200(190 was effective) stroke survivors at different months post stroke. Data analyzed included self-reporting questionnaire scores on the Posttraumatic Growth Inventory (PTGI), the Hospital Anxiety and Depression Scale(HADS), which is one of the most widely used scales for measuring the level of anxiety, depression. Correlations between scores on the PTGI and anxiety subscale, the PTGI and depression subscale, and they were established by calculating Pearson's correlation coefficients. **Result** The mean score of the anxiety subscale, depression subscale and PTGI were 6.32 ± 4.39 , 7.17 ± 4.59 , and 58.10 ± 13.723 . Anxiety and depressive symptoms in stroke patients were inversely correlated to PTGI, and the correlative coefficient were $r=-0.196$, $P<0.05$, $r=-0.286$, $P<0.01$. New possibility, personal strength, appreciation of life and spiritual change on the PTGI were correlated negatively with anxiety and depression symptoms. Relating to others had no significance correlated with anxiety. **Conclusion** The post-traumatic growth was common in patients with stroke, and anxiety, depression had a negative impacts on it. The nursing should assess the positive psychological changes, and guide patients to adjust the changes, thus the patients' rehabilitation could be promoted.

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Keywords: Stroke; anxiety; depression; posttraumatic growth

1. Introduction

Stroke is a serious traumatic experience for patients. More than 70% of the survivors have a varying degrees of dysfunction(Liu et al, 2007), for example the paralysis, muscle weakness, loss of feeling, speech and language problems, memory problems and indirect social effects, which are often pervasive and indirect social effects, which are often pervasive and persistent. Accompanied by the dysfunction are various prominent psychosocial problems, such as anxiety, depression and so on. These negative emotion problems have seriously effects on the rehabilitation of patients and the improving of quality of life. The literature has tended to emphasize the negative impact of these effects(Yang, 2010; Guo 2010; Li, 2006; Wang,2011). With the development of positive psychology these years, persons are realizing that traumatic event could also contribute to individual's positive changing and growth which is called posttraumatic growth(PTG). Posttraumatic growth were proposed by Tedeschi and Calhoun in 1996. They defined PTG as the individual's experience of significant positive change resulting from the struggle with a major life crisis(Tedeschi and Calhoun, 1996). Tedeschi and Calhoun hold that people facing life crises typically experience distressing emotions,

anxiety depression or specific fears are common negative emotions(Tedeschi and Calhoun, 2004). It is natural to assume that PTG, by definition, would show a negative correlation with anxiety and depression. In fact, recent research suggests that the stroke's psychology may be more mixed and studies from Ostir(2008)and Seale(2010)have confirmed that some correlates of PTG after stroke, and the existence of PTG can promote the rehabilitation of patients and the improving of quality of life. At the same time the anxiety, depression and PTG could exist simultaneously, and there are correlations between them(Gangstad et al, 2009). But we can't find one study about PTG after stroke in China.

The present study, to our best knowledge, is the first to examine the differential impacts of negative and positive effects following stroke in China. So the present study try to examine the samples of people with stroke in center China. The study had two main objectives. First, to explore whether the concept of post-traumatic growth is applicable to the situation of people with stroke in China. Secondly, to explore the relationship between post-traumatic growth, depression and anxiety. Thus the nurse can provide psychological care and support for stroke patients overall.

2. Material and Methods

2.1 Participants and procedure

The study received ethical approval from Ethics Committee of Zhengzhou University. Stroke survivors were recruited from the department of neurology in hospital which is in the Zhengzhou city of middle China. The inclusion and exclusion criteria were as follows. Stroke survivors who attended the department of neurology and were diagnosed of stroke were invited by the researchers to take part in the study. Survivors who were unable to complete the questionnaire because of language dysfunction or cognitive impairment resulting from stroke were excluded. Before the starting of the investigation, the researchers would explain the purpose of the study to the survivors in detail. If we get the consent from the participants, we would gave them a study questionnaire to complete at the department. The researcher would read and explain the problems one by one to the participant who can't complete the questionnaire by self because of reading disability or physical dysfunction. A total of 200 questionnaires were given out, and 190 were retracted. The effective recovery ratio was 95%.

2.2 Measures

The assessments included the following: (a) general socio-demographics, and stroke-related information; (b) the Hospital Anxiety and Depression Scale (HADS); (c) the Posttraumatic Growth Inventory (PTGI).

The HADS(Zigmond and Snaith,1983) is a self-reports scale, and has good reliability and validity. So it is widely used to discover patient's anxiety and depression emotion in general hospital. HADS has 14-item questionnaire and two subscales to measure anxiety and depression. Each subscale contains seven

items scored on 4-point Likert-type scales ranging from 0 to 3 to indicate degree of psychological distress. The subscales scored 0-7 means non-performance; 8-10 points are suspicious, 11-21 are reaction. Reliability and validity of the Chinese version of the HADS have been verified.

The PTGI(Tedeschi and Calhoun, 1996) which is one of the most widely used scales for measuring the degree of change experienced in the aftermath of a traumatic event. It is a 21-item self-rating scale and is comprised of five factors: relating to others, new possibilities, personal strength, spiritual change, and appreciation of life. The degree of PTG for each item is rated on a 6-point response scales ranging from 0 (I did not experience this change as a result of my crisis) to 5 (I experienced this change to a very great degree as a result of my crisis), with high scores indicating positive growth. Reliability and validity of the Chinese version of the PTGI have been verified(Wang et al, 2011). The scale was found to have satisfactory internal reliability (Cronbach's α 0.819) in the present study.

2.3 Statistical Analyses

All data analyses were performed using SPSS statistical software version 13.0 for Windows. Demographic and stroke-related information were analyzed by descriptive statistical respectively. The correlations between the scores on the anxiety, depression and the PTGI were established by calculating Pearson's correlation coefficients because of the anxiety, depression and the PTGI score distributions. All statistical analyses used two-tailed tests. Statistical significance was established at $P < 0.05$.

Table1 The score of anxiety and depression($\bar{X} \pm s$)

	$\bar{X} \pm s$	Score Level (n,%)		
		0-7	8-10	11-21
Anxiety	6.32±4.39	117(61.60)	38(20.00)	35(18.40)
Depression	7.17±4.59	100(52.60)	38(20.00)	52(27.40)

Table 2 Correlations between variables and descriptive values of the variable

	PTGI total	Relating to others	New possibilities	Personal strength	Appreciation of life	Spiritual Change
Anxiety	-0.196	-0.072*	-0.238	-0.145	-0.201	-0.169
Depression	-0.286	-0.152	-0.307	-0.246	-0.286	-0.214
\bar{X}	58.10	9.11	11.12	8.06	17.32	12.09
SD	13.723	2.279	3.233	2.463	4.520	3.204
Range	17-87	4-15	3-20	2-15	5-29	3-20

*Relating to others had no correlated, $P > 0.05$

3. Results

3.1 Sample Characteristics

The total number of participants in the present study was 190 (118 men, 72 women). Participants ranged in age from 24 to 87 years ($M=58.57$, $SD=12.051$). 171 participants were married, and 19 were single or divorced. 114 participants' s course of disease was less than 6 months, and 76 was more than six months. In terms of education level, 35.26% ($N = 67$) were literate (be able to only write and read) and primary school graduate, 25.26% ($N = 48$) were secondary school graduate, 19.47% ($N = 37$) were high school graduate, and 20.00% ($N = 38$) were university graduate.

3.2 Descriptive Statistics and Correlations Analyses between Variables

In addition to the correlation between PTG scores and the other variables, descriptive statistics of all variables included in the present study are presented in Table 1 and 2 respectively. Median score of anxiety, depression and PTGI were 6.32 ± 4.39 , 7.17 ± 4.59 , and 58.10 ± 13.723 (range 17-87) respectively. As it can be seen from the table 2, PTGI was negatively related with anxiety ($r=-0.196$, $P<0.01$) and depression ($r=-0.286$, $P<0.01$). New possibility, personal strength, appreciation of life and spiritual change were correlated negatively with anxiety and depression symptoms. Relating to others had no significance correlated with anxiety.

4. Discussions

4.1 Stroke survivors with anxiety, depression emotions

Stroke is a significant traumatic event to persons, and the damage of the brain also have some impacts on the patient's mental emotion. The existence of negative emotion problems like anxiety and depression have serious impacts on the rehabilitation of stroke survivors. In the present survey, some survivors had anxiety and depression emotions. Suspicious tendencies and manifestations of anxiety and depression account for 20.00% / 18.40%, 20.00% / 27.40% (Table 1) respectively. The results were slightly lower than reported in the literature (Han and Cui, 2011) which were 72.22% and 60.42% in China stroke survivors. The different of the results may be related to many reasons. First the participants were come from different city, and the investigation methods were different for the two studies. In addition, the participants were mostly in the recovery period of the disease when the data collecting. So the serious condition and critical moment had passed. Patients could get a certain degree of psychological comfort from the recovery of the disease. Therefore, the

incidence of anxiety and depression were lower compared to the acute stroke.

4.2 After stroke the phenomenon of post-traumatic growth appeared

This study examined the predictors of posttraumatic growth among survivors after stroke in present study. The previous study (Helgeson et al, 2006) had show that not only the external traumatic events can engender PTG, the occurrence of serious diseases can also engender PTG. The mean score of the PTGI was 58.10 ± 13.723 (table 2) in present study which was considered fairly higher compared with previous literature, the mean score of which was 50.93 ± 19.92 (Gangstad et al, 2009). The differences may be related to many factors. The average age of the participants (58.57 ± 12.051) are old in present study which is significantly lower than previous literature reports (71.67 ± 10.64) (Gangstad et al, 2009). The younger groups were able to experience more growth after traumatic events occurs in cancer survivors (Bellizzi, 2004). This may be related to the young patients need more to adapt the society, so they experience more PTG which is related to self-generated. Second, the Duration of stroke patients in this group are mostly in the 6 months or less, which is significantly lower than the foreign average level of 32.03 months (Gangstad et al, 2009). The finding is consistent with the findings in report of Milam (Milam, 2004) that the patients' PTG had a negative correlation with the duration of disease. In the early stages of the disease, health's recovery may promote the occurrence of PTG. But the patients gradually adapt to the existing of physical condition with time goes on and the recovery of body functions into the chronic stage, so the PTG change is no longer significantly. Third, the huge differences in socio-cultural backgrounds between different countries also affected the level of PTG in the stroke survivors to some extent.

4.3 Anxiety, depression were negatively correlated with PTG

The survey results showed that the total PTGI score of stroke patients was negatively correlated with anxiety and depression (Table 2). Relating to others had no correlated with and anxiety depression, anxiety and depression were negative correlated with other dimension at the different levels. Compared to the other dimensions, anxiety and depression had a relatively high correlation with the dimension new possibilities (Table 2). Anxiety and depression are negative emotions which can lead to unpleasant and painful state for patients. Although the negative emotions have no threat to the disease itself, a series of body discomfort will be accompanied. The discomfort increased the psychological burden of patients and

hindered the rehabilitation of patients seriously. The rehabilitation of the patient's body had a promoting effect to person's PTG, and previous study also showed that positive emotions contribute to returning social life of patients (Gillen, 2005). The results of present study that the negative correlations between PTG and anxiety and depression were consistent with the results of Gangstad (2009) and Helgeson (2006). The result also indicates that the positive mental state can promote the development of PTG to a certain extent. The correlation coefficient between the variables were lower in this survey. So a number of limitations that should be noted. First, the sample size was relatively small. So it is important for future work to expand the sample size. Second, the participants who can't understand the scale well enough maybe too old, so the results have a lower validity.

In summary, anxiety and depression were negatively correlated with stroke PTG in stroke patients, and they can co-exist with the PTG. The results prompted the nurses who should not pay only attention to the negative psychology but also the active and positive changes about stroke survivors at the same time. In clinical work we can take individualized psychological support measures to patients, so that patients could recovery earlier. It takes us a new theoretical framework for the implementation of nursing interventions. From this point we could attempt to reduce the negative psychological emotional and improve the level of PTG.

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A Special Biological Evaluation for Some Food Industrial Wastes

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Abstract: It has been thought that gastric ulcer medication is associated a sort of contradiction to that of hypercholesterolemia. However, additional antioxidant nutrient intervention trials in populations have established an effect relationship from these findings. The biological role of antioxidant content in three most common juice industrial wastes have been implicated in this complicated health issue, ie, the combined health complication therapy of hypercholesterolemia and stomach ulcer. This applying dietary therapy was explored using a 45 rats in nine experimental groups system. This orange (OP), apple (AP) and pomegranate (PP) peel wastes were examined for their content of special antioxidants acts against substances that inevitably lead to oxidative stress hoping that these compounds, or some of them, can support the antioxidant defense and thereby reduce the damaging caused by either a single one or both together these diseases. The peels analysis showed more crude protein in OP, relatively higher both fat and CHO in AP, meanwhile PP contains more fat, ash and had more total polyphenols. In contrast, orange has much more vitamins A, E and β -Carotene. Concerning the other antioxidant nutrients, such as the polyphenols fractions namely p. coumaric, caffeic, caumarin, cinnamic, naringenin, syringic and pyrogallol were found in OP that was effective as a mild hypocholesterolemic dietary agent. More pyrogallol in addition to caffeic acid, p. OH benzoic, vanillic and chlorogenic were currently more shown in PP, which appears more significant against ulceration. Apple is only good source for ferulic acid and salicylic which are absence in OP and make almost their 50% in PP and appeared of relatively less bioactive food treatment. In this evaluation of food industrial waste intervention against ulceration and cholesterolemia the response included volume (V), the pH value, total acidity of gastric juice maintains the ulcer index (mm) of gastric juice using PP, while the influence of OP on serum total cholesterol level can be contributed to the whole antioxidant substances existed in this food waste fraction. Excluding the vitamins and antioxidant nutrients, polyphenols fractions noticed for each peel may play the main intervention role and a special mixer of OP and PP might become a respectable food therapy or alternative therapy in case of such clinical complication.

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1. Introduction

In fact, peptic ulcer is one of the most common gastrointestinal disorders in clinical practice. Most peptic ulcers arise in the two areas exposed to gastric acid and pepsin, as a hole in the gut lining of stomach, duodenum or esophagus (*Anekonda and Reddy, 2005*). Although genesis of ulcers is multifactorial, they are essentially thought to arise due to an imbalance between offensive factors like acid and pepsin secretion, and defensive factors like mucin secretion, cell shedding, cell proliferation, inhibition of gastric mucosal prostaglandin synthesis, disruption of gastric mucosal barrier, reduction of gastric mucosal blood flow, inhibition of gastric mucus and bicarbonate secretion (*Lu and Graham, 2006 ; Ramakrishnan and Salinas, 2007*). Excess gastric acid production in response to food and hormonal stimulation is characteristic of these diseases. Therefore, it was postulated that excess acid production possibly from stress or diet were responsible for formation of ulcers (*Shaw, 1996*). It is

also known that several endogenous factors are related to the pathophysiology of gastroprotection including prostaglandin E_2 (PGE_2), somatostatin, nitric oxide (NO) and sulfhydryl (SH) compounds, delayed gastric emptying, and duodenogastric bile reflux as they associated with gastric mucosal damage (*Tsukimi et al., 2001*). The etiopathogenesis of gastric ulcer involves genetic factors, physiopathological disturbances and environmental factors such as alcohol or coffee consumption, pylorus ligation, steroids, smoking, stress, non-steroidal anti-inflammatory drugs (NSAIDs) and *Helicobacter pylori* (*Konturek et al., 2005*), *Helicobacter pylori* infection (*Levine and Rubesin, 1995*) and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) like aspirin and indomethacin and the augmented acid secretion also contributes to this harmful process, as does the fact that NSAID provokes disturbances in the gastric microcirculation, increases neutrophil infiltration, induces TNF- α expression, and disrupts the balance between NO expression and apoptosis

(Konturek et al., 2002), besides provoking damage to the vascular endothelium, reduction of the blood flow, formation of obstructive micro-thrombi and activation of neutrophils (Guth 1992). Although early trials with nitric oxide donating NSAIDs have not been encouraging, NO-aspirin appears promising. By contrast, protection against ulcer complications by cotherapy with antisecretory drugs, e.g. proton pump inhibitor (PPI) remains unproven and only available double-blind study of a PPI plus an NSAID in high risk NSAID users did not produce encouraging results. It remains to be seen whether the optimism with which these drugs are used for that indication is actually warranted (Lu and Graham, 2006). It has been reported that the major symptom of ulcer is a burning or gnawing feeling in the stomach area that lasts between 30 minutes and 3 hours. This pain is often interpreted as heartburn, indigestion or hunger. The pain usually occurs in the upper abdomen, but sometimes it may occur below the breastbone. In some individuals the pain occurs immediately after eating. In other individuals, the pain may not occur until hours after eating. The pain frequently awakens the person at night. Weeks of pain may be followed by weeks of not having pain. Pain can be relieved by drinking milk, eating, resting, or taking antacids. Appetite and weight loss are other symptoms, but person with duodenal ulcers may experience weight gain because the persons eat more to ease discomfort. Recurrent vomiting, blood in the stool and anemia are other symptoms. An estimation of about 20 percent of cancers of the stomach are of the ulcerating type. It has also been determined that 9 to 10 percent of lesions that can be considered possibly benign ulcers are, or become, malignant. It must therefore be determined by clinical measures (roentgenography, cytological examination of the gastric aspirate), or by surgery and histological examination whether a gastric ulcer is benign or malignant. The differentiation between benign and malignant gastric ulcer can be safely made if accurate observations during a trial management are made and if the patient is followed closely during the year after the first occurrence of the lesion and wisely counseled regarding the significance of possible recurrences (Anekonda & Reddy, 2005 and Lu & Graham, 2006). Earlier, 103 consecutive patients with active radiological proved duodenal ulcer were given alternately regular and bland diets. Daily dietary observations included foods consumed, foods rejected and the reasons for rejection, and foods causing discomfort. With few exceptions, patients in both groups consumed nutritionally adequate diets. Ulcer patients placed on regular diets did not generally select a bland diet from the regular tray served them. Patients previously conditioned by dietary

instructions more frequently rejected food items that were served only on the regular diet as well as food served normally on bland diets. Discomfort following ingestion of a few food items suggests the possibility of poor tolerance by some ulcer patients. Clinical response and rate of healing of duodenal ulcer were the same in the two groups (Buchman et al., 1969). However, evidence is presented which suggests that settings of anxiety and tension can nullify the beneficial effects of a high fat meal on gastric acidity and motility. One should not count very heavily on the inhibitory effects of diet in peptic ulcer when the stomach is under stimulation from stressful situations in the patient's daily life. There is also a great need to study the true effects of certain so-called irritating foods, condiments, and chemicals on the stomach. In a fistulous subject, the direct application of commonly accepted irritants produced fewer and lesser changes in the stomach than on the skin. Similarly, the colon in ulcerative colitis responds more violently to certain situational stimuli than to foods and fecal contents (Wolf, 1954). Antiulcer drugs medication is used for a large variety of complaints, such as functional nonulcer dyspepsia, stomach upset, gastro-esophageal reflux, gastritis, and gastric or duodenal ulcer. Most dyspeptic symptoms are dealt with by the patient without seeking medical advice (Jones et al., 1990; Isolauri and Laippala, 1995; Penston and Pounder, 1996) or by using antacids (Corder et al., 1996). These drugs act via buffering the gastric pH and inactivating the major gastric protease pepsin (McCarthy, 1991). Since the beginning of the 1980s, antacids were to a great extent replaced by H₂-receptor blockers (Peden et al., 1979) and proton pump inhibitors (PPIs) (Richardson et al., 1998). The highly potent, long acting PPIs and H₂-receptor antagonists can almost totally abolish acid secretion (Sharma et al., 1984 and Chiverton et al., 1989), although antisecretory therapy increasing the gastric pH above 3.0 is not necessary for ulcer healing (Burget et al., 1990). Increases of gastric pH might interfere with the physiological gate-keeping function of the stomach, e.g., the protective role of gastric acid against bacterial infections (Cook, 1985; Howden & Hunt 1987 and Hunt 1988). Moreover, gastric acidity is required for the activation of pepsinogens and the initiation of protein digestion. The optimal pH for proteolysis varies for different pepsins in gastric juices, but total enzyme activity has an optimum in the pH range of 1.8-3.2 (Samloff, 1989). Paradoxically, digestion-sensitive food proteins are among the most frequent elicitors of food allergy (Yagami et al., 2000 and Fu et al., 2002). However, Untersmayr et al. (2003) demonstrated in an animal model that antiulcer drugs turned digestion-labile fish proteins into potent elicitors of type I

hypersensitivity by elevating the gastric pH and impairing peptic digestion. Also, *Untersmayr et al. (2005)* strongly suggest that anti-ulcer treatment primes the development of IgE toward dietary compounds in long-term acid-suppressed patients. *Schöll et al. (2005)* suggest that the intake of antiulcer drugs may lead to the induction of immediate-type food hypersensitivity toward hazelnut. *Brunner et al. (2007)* show that parenterally applied sucralfate is able to induce a T helper 2 (Th2) response probably due to the aluminium content. This indicates that orally applied sucralfate may lead to an enhanced risk of food allergy not only by inhibiting peptic digestion but also by acting as a Th2 adjuvant. Moreover, *Schöll et al. (2007)* provided evidence that the anti-acid drug sucralfate supports sensitization against food in pregnant mice and favors a Th 2-milieu in their offspring. *Schöll et al. (2008)* added that anti-acid treatment with sucralfate induces changes in the structure of epithelium and villi, and increases eosinophils and mucus-producing cells in the intestine. Therefore, this medication leads to sensitization against food with changes typical for food allergy also in the intestine. Additionally, acid-suppression medications are frequently used for treatment of dyspeptic disorders. By increasing the gastric pH, they interfere substantially with the digestive function of the stomach, leading to persistence of labile food protein during gastric transit. Moreover, *Andrès et al. (2007)* stated that in elderly people, food-cobalamin malabsorption (vitamin B12 deficiency) syndrome is usually the consequence of atrophic gastritis, related or not to pH. pylori infection, and of the long-term ingestion of antacids and biguanides (in around 60% of patients).

It is also known that hypercholesterolemia is related to endothelial dysfunction at both the macro and microvascular level (*Stokes et al., 2002*). Furthermore, decreasing serum cholesterol levels with exercise, diet and medications has been associated in numerous studies with improved outcome. There were several studies demonstrated that hypercholesterolemia actually has a positive effect in patients with heart failure (*Kalantar-Zadeh et al., 2004*). Furthermore, several studies attempted to improve outcomes with cholesterol lowering medications in patients with heart failure have shown either neutral or negative results. Systematic investigation of genes, environmental factors, and their interactions in explaining the variance of lipoprotein levels indicate that 1) body mass index, smoking, and alcohol intake are strong predictors of blood lipid levels; and 2) their effects are only marginally modified by genetic background. However, clinical and epidemiologic data illustrate the need to expand the scope of therapies to reduce

the residual cardiovascular risk associated with low HDL-C levels and elevated TG levels, even when LDL-C is managed successfully (*Cziraky et al., 2008*).

However, additional antioxidant nutrient intervention trials in populations have established an effect relationship from these findings. Plant foods such as fruit, vegetables and their content of vitamins, minerals, and photochemical have improved antioxidant status and human health. This adequate antioxidant defense is also required to change body's first line of antioxidant defense in both the intra and extracellular compartments. Widespread interest in the possibility that selected foods might promote health has resulted in the coining of the term functional food, although agreement about what is and what is not a functional food is lacking (*Milner, 2000*). Public interest in functional foods is increasing because of higher health care costs; the passage of federal legislation affecting many food categories, including the expanded category of dietary supplements; and recent scientific discoveries linking dietary habits with the development of many diseases, including coronary heart disease and some cancers. A variety of foods have been proposed as providing health benefits by altering one or more physiologic processes. Biomarkers are needed to assess the ability of functional foods or their bioactive components to modify disease and to evaluate the ability of these foods to promote health, growth, and well-being (*Milner, 2000*). For example, polyphenols are abundant micronutrients in our diet and evidence for their role in the prevention of degenerative diseases such as cancer and cardiovascular diseases is emerging. The health effects of polyphenols depend on the amount consumed and on their bioavailability. This appears to differ greatly between the various polyphenols, and the most abundant polyphenols in our diet are not necessarily those that have the best bioavailability profile. A thorough knowledge of the bioavailability of the hundreds of dietary polyphenols will help us to identify those that are most likely to exert protective health effects (*Manach et al., 2004*). Studies on the mechanisms of chemoprotection have focused on the biological activity of plant-based phenols and polyphenols, flavonoids, isoflavones, terpenes, and glucosinolates. Enhancing the phytonutrient content of plant foods through selective breeding or genetic improvement is a potent dietary option for disease prevention. However, most, if not all, of these bioactive compounds are bitter, acrid, or astringent and therefore aversive to the consumer. Some have long been viewed as plant-based toxins. As a result, the food industry routinely removes these compounds from plant foods through selective breeding and a variety of embittering processes. This

posse is a dilemma for the designers of functional foods because increasing the content of bitter phytonutrients for health may be wholly incompatible with consumer acceptance. Studies on phytonutrients and health ought to take sensory factors and food preferences into account (*Drewnowski and Gomez-Carneros, 2000*). For example, nuts are energy-dense foods, rich in total fat and unsaturated fatty acids. Its beneficial effects on vascular reactivity may be ascribed to several constituents of walnuts: l-arginine, the precursor of nitric oxide, α -linolenic acid and phenolic antioxidants. Although more studies are warranted, the emerging picture is that nut consumption beneficially influences cardiovascular risk beyond cholesterol lowering (*Ros, 2009*). More cheap sources of bioactive nutrients are desirable and more practical. Fortunately, antioxidant flavonols and their major food source as black tea have been associated with a lower risk of ischemic heart disease (IHD) and stroke in Dutch men, but was weakly positively related to IHD mortality and cancer mortality while strongly related to total mortality. Men with the highest consumption of tea had better rate of dying in the follow-up period compared with men consuming less. It has been concluded that intake of antioxidant flavonols is not inversely associated with IHD risk in the United Kingdom. The apparent association between tea consumption and increased mortality in this population merits further investigation (*Hertog, et al., 1997*). Furthermore, epidemiologic data indicate that individuals with low plasma concentrations of carotenoids and antioxidant vitamins and those who smoke cigarettes are at increased risk for age-related macular degeneration (AMD). Laboratory data show that carotenoids and antioxidant vitamins help to protect the retina from oxidative damage initiated in part by absorption of light. Primate retinas accumulate two carotenoids, lutein and zeaxanthin, as the macular pigment, which is most dense at the center of the fovea and declines rapidly in more peripheral regions. The retina also distributes alpha-tocopherol (vitamin E) in a non-uniform spatial pattern. The region of monkey retinas where carotenoids and vitamin E are both low corresponds with a locus where early signs of AMD often appear in humans. The combination of evidence suggests that carotenoids and antioxidant vitamins may help to retard some of the destructive processes in the retina and the retinal pigment epithelium that lead to age-related degeneration of the macula (*Snodderly 1995*). As a polyphenol fraction, betalains were recently identified as natural antioxidants. However, little is known about their bioavailability from dietary sources. To evaluate the bioavailability of betalains from dietary sources, plasma kinetics and urinary excretion of betalains were studied in healthy

volunteers to show that cactus pear fruit is a source of bioavailable betalains and suggest that indicaxanthin and betanin may be involved in the observed protection of LDL against ex vivo-induced oxidative modifications (*Tesoriere et al., 2004*).

So far, very short research work is published about more cheap sources of polyphenol or antioxidants in general and their health aspect. Here, polyphenol derived from some food industrial wastes were examined in treating both cholesterolemia and ulcer based on their contradiction during pharmaceutical therapy.

2. Materials and Methods

Three food industrial wastes were collected from corresponding large production project for orange, apple and pomegranate juices in Egyptian delta and used as source samples. The proximate analysis as well as vitamins A and E of these food materials were determined according to the *AOAC (1990)*. In the determination of polyphenols, vitamin C, and β carotene, HPLC techniques according to *Betés-Saura et al., (1996)* were employed. Samples were prepared and their complete extraction are thus accomplished as ran earlier (*Watada, 1982*). Results expressed as mg/mL (*Sánchez-Mata and m 2000*). Quantification was performed by external calibration with standards for undertaken solutes. The total polyphenol content (TPC) determined by Folin-Ciocalteu's reagent was carried out according to the procedure reported in the literature (www.teausa.com) with a modification of working standards gradual at 25, 50, 100, 150, and 200 ppm gallic acid solution prepared freshly each time at room temperature before analysis. Concentrations in ppm of polyphenols in final diluted solutions were measured using x coefficient from the regression analysis correcting for dilution made during procedure.

Liquid chromatographic analysis of β -Carotene: β -Carotene was analyzed following the procedures of *Thayer and Björkman (1990)* using high performance liquid chromatography (HPLC) Agilent 1100 series equipped with auto sampler and quaternary pump, variable wavelength detector set at 254 nm and column compartment set at 35°, the separation was done using Hypersil ODS (250 x 4mm) 5 μ m particle size. The column was equilibrated with degasser solvent A (acetonitrile-methanol-0.1 M Tris, pH 8; 19:3:1, v/v/v) and eluted as follows: solvent A at a flow-rate 1.5 ml/min for 6 min followed by solvent B (methanol-hexane; 4:1, v/v) at 2 ml/min for 10 min and then back to solvent A at 1.5 ml/min for 8 min. Quantification was done against a β -Carotene external standard using peak areas in ppm: mg solute per kg of plant crude powder.

The biological evaluation has been performed as described in Table (1) using nine groups (from G1 to G9) 9X5 = 45 aged albino rats of 364±9 g in the Ophelial experimental animal house, great Cairo. The adaption period 10 days was followed with an

entire length of 30 days. The determination of gastric volume, pH and total acidity were done according to *Denbath et al., (1974)*. Gastric ulceration index was calculating similar to *Robert et al., (1968)*.

Table 1: Dietary description of biological experement.

G	Treatments	Description
1	Negative control (G1)	Basel diet (<i>Bowman et al., 1990</i>).
2	Cholesterol (G2)	G1 + 1% cholesterol. <i>Ahmed et al., (2004)</i> .
3	Ulcer (G3)	Gastric ulcer induction, according to <i>Agrawal et al., (2000)</i> .
4	Cholesterol + Ulcer (G4)	The double treatment, ie, both G2 and G3.
5	Ulcer treatment (G5)	G4 treated with artificial antacid drug.
6	Cholesterol treatment (G6)	G4 treated with artificial hypocholesterolemic drug.
7	OP (G7)	G4 treated with Orange peel 10%.
8	AP (G8)	G4 treated with Apple peel 10%.
9	PP (G9)	G4 treated with Pomegranate peel 10%.

Where: G, animal group; OP, AP and PP: Orange, Apple and Pomegranate peels, respectively.

3. Results and Discussion

As it has been hypnotized that gastric ulcer synthetic medication contradicts that of hypercholesterolemia, dietary therapy might become important way in treating this dilemma. However, additional antioxidant (AO) nutrient intervention trials in populations have established an effect relationship from these findings. Finding new sources for an AO cockatiel of special health aspect is necessary. In Table 2, the proximate chemical composition of three dried fruit peels wastes, as cheap AO sourese were recoded to find that their moisture content are around 10% with more crude protein in orang peel (OP), relatively higher both fat and CHO in appel peel (AP), mainwhile pomegranate peel (PP) gave moer fat and ash. Pomegranate, as in Table 3,

also contained more total polyphenols, meanwhile orange has much more vitamin A, vitamin E and β -carotene.

The polyphenols fractions of ppm in those food waste peels are listed in Table 4. Additional better fractions of polyphenol such as p.coumaric, caffien, caumarin, cinnamic, naringinin, syringic and pyrogallol were also found in orang peel.

However, PP seems to be richer of pyrogallol in addition to caffeic acid, p.OH benzoic, vanillic and chlorogenic. Apple is only good as source of ferulic acid and salycilic which are absence in OP and make almost their 50% in pomegranate peel. They cnseedered to be inactive polyphenol fraction according to their relatively less biological role as meight be extracted from Table 5.

Table (2) Proximate chemical composition of the three dried fruit peels wastes.

#	Plant waste	Moisture%	Crude protein	Fat%	Ash%	Fiber%	CHO%
1	OP	11.42	8.63	4.61	4.24	9.80	61.31
2	AP	9.02	3.78	5.42	2.46	8.05	71.27
3	PP	12.10	5.09	2.80	4.41	11.69	63.65
<i>L.S.D. at 5%</i>		<i>0.447</i>	<i>0.448</i>	<i>0.424</i>	<i>0.124</i>	<i>0.836</i>	<i>0.753</i>
<i>1%</i>		<i>0.742</i>	<i>0.742</i>	<i>0.703</i>	<i>0.206</i>	<i>1.386</i>	<i>2.907</i>

Table (3) Antioxidant composition of some dried fruit peels wastes in ppm.

#	Plant waste	Total Polyphenols	Vitamin A	Vitamin E	β -Carotene
1	OP	6899323.7	161218.9	116.9	3.9
2	AP	2416117.3	86631.6	57.0	0.9
3	PP	9366458.2	101904.9	90.1	0.5
<i>L.S.D. at 5%</i>		<i>30.356</i>	<i>11.258</i>	<i>3.219</i>	<i>0.115</i>
<i>1%</i>		<i>31.627</i>	<i>12.545</i>	<i>3.986</i>	<i>0.191</i>

Table (4) Polyphenols fraction in ppm in some food wastes peels.

#	Polyphenols fraction	Pomegranate peel (PP)	Appel peel (AP)	Orang peel (OP)
1	p.coumaric	111.9	185.4	342.9
2	Ferulic acid	24.7	46.1	0
3	Caffien	643918.0	267897.0	1057941.9
4	Chrsin	0	0	0
5	Caumarin	38216.9	93274.4	757947.4
6	Caffic acid	696565.8	144772.1	252224.3
7	P.OH Benzoic	7970587	1824801	4427384
8	Cinnamic	4556.5	0	211737.4
9	Vanillic	140.8	29.3	58.1
10	Chlorogenic	283	21.4	144.1
11	Naringinin	8728	84980	188526
12	Syringic	44	31	72
13	Pyrogallol	3239	0	2945
14	Salycilic	43	80	0

However, to biologically evaluate these food chemical patterns, ulcer and aged rats with hypercholesterolemia, as most sensitive age cycle for those antioxidant combination were used. Peels addition at dietary level of 10% were examined. Table (5) as mentioned above recorded the effect of these treatments on the volume (V), the pH value, total acidity of gastric juice, the ulcer index (mm) of gastric juice and total cholesterol TC in rats treated for 3wk was conducted. In general, a real sort of metabolic complication upon treating animal ulcer whom suffering hypercholesterolemia can be noticed. Taking in consideration the HDL/TC and ulcer index, OP treatment seems to be the most convenient for both to degenerative diseases followed with PP intervention. In fact, PP is the best in treating ulcer alone and this most probably due to lowering both pH value and total acidity but not gastric juice secretion (Table 5). Likewise, in an experiment undertaken in dogs with midintestinal fistulas to determine whether guar added to a meal of solid food would disrupt gastric sieving and give rise to maldigestion of solid food using an isotope ratio method to determine how

much [14C] triolein was absorbed at midintestine. It has been found that guar in a dose-related fashion increased the weight of chyme collected at midintestine, markedly reduced the percent of triolein absorbed by midintestine from 88 to 38%, and profoundly increased the passage to midintestine of large, poorly digestible pieces of steak and liver solid foods. The viscosity of the guar promoted the GI transit of large, poorly digestible pieces of food but also reduced absorption by other mechanisms (*Meyer and Doty, 1988*). In general discussion and conclusion, PP has been found to be richer than OP in total polyphenol and poorer in containing vitamin E. Earlier, in an animal trial, the photographs were independently rated by three pathologists on a 4-point scale from 1 (no ulceration) to 4 (severe ulceration) to conclude that the mean ulceration rating for the vitamin E group was 1.92, and the rating for the control group was 3.42, indicating that vitamin E has significant preventive properties in relation to the production of stress-induced gastric ulcers in the rat (*Kangas, et al., 1972*).

Table (5): Effect of treatments on the volume (V), the pH value, total acidity of gastric juice and the ulcer index (mm) of gastric juice in rats in 3wk

#	Treatments	V in ml	pH	Total acidity	Ulcer index	Plasma TC	HDL	HDL/TC
1	Negative control (G1)	0.325f	4.542cd	0.175g	0.000e	76.04h	48.97ab	0.645
2	Ulcer (G2)	0.833a	3.168f	0.747a	9.000a	77.82h	46.99c	0.603
3	Cholesterol (G3)	0.550d	4.262d	0.427d	0.833e	163.52a	43.87c	0.268
4	Cholesterol + Ulcer (G4)	0.750b	3.572e	0.617b	7.500b	168.44b	43.95d	0.262
5	Ulcer treatment (G5)	0.325f	5.747a	0.158g	0.667e	168.47b	45.02d	0.268
6	Cholesterol treatment (G6)	0.658c	3.483e	0.585bc	7.500b	89.99g	50.16a	0.556
7	OP 10% (G7)	0.333f	5.292b	0.353e	4.500c	99.54f	48.44bc	0.484
8	AP 10% (G8)	0.592d	4.430cd	0.540c	5.167c	132.11c	47.57bc	0.264
10	PP 10% (G9)	0.350f	5.693a	0.133g	0.833e	116.31e	48.87ab	0.422

LSD at 1% Time 0.113 and 0.151, Treatment 0.086 and 0.370 Interaction NS

Total Cholesterol (TC) LSD at Time 1.851, Treatment 3.207, Interaction 6.413 at 5% and these were 2.440, 4.227 and 8.454 at 1%. Means of time followed by same superscript capital letter(s) are not significantly different at 5% level. Means of treatments followed by same capital letter(s) are not significantly different at 5% level. Means of time followed by same letter(s) are not significantly different at 5% level.

HDL LSD at 5% was Time 0.83, Treatment 1.44, Interaction 2.88, which were 1.09, 1.90 and 3.80 at 1% level, respectively. Means of time followed by same superscript capital letter(s) are not significantly different at 5% level. Means of treatments followed by same capital letter(s) are not significantly different at 5% level. Means of time followed by same letter(s) are not significantly different at 5% level.

This strongly suggests a special role for Polyphenols. The hormonal oxidative balance health role of food and drug was suggested (Ahmed *et al.*, 2003). Moreover, percentage distribution of fatty acids in subcutaneous adipose tissue of patients with peptic ulcer disease was explored. Seidelin *et al.*, (1993) stated that dietary linoleic acid has been implicated in the pathogenesis of peptic ulcer disease because its metabolite arachidonic acid may be converted to cytoprotective prostaglandins. Table 2 shows that OP contains more fat. In addition, it has been suggested that the falling incidence and virulence of duodenal ulcer disease is related to increased dietary polyunsaturated essential fatty acid intake. In the present study the percentage content of linoleic acid in subcutaneous adipose tissue microbiopsies were used to see whether changes in percentage of fatty acids correlate with the presence or absence of an ulcer in individual patients. No significant difference in the adipose tissue content of linoleic acid was found in patients with peptic ulcer disease and matched control subjects (Seidelin *et al.*, 1993). Seemingly, more vitamins A and E in addition to high β -carotene level may be suitable in preventing hypercholesterolemia. This suggests that increased consumption of vitamin A may prove to reduce mortality rates due to heart disease and peptic ulcer. All the investigated mortality rates were in statistically significant positive association with increasing total fat consumption. Mortality rates of ischemic heart disease as well as of hypertensive and cerebrovascular diseases were in positive association with both plant fat and animal fat. These findings suggest that reduced total fat intake may prove to reduce the investigated mortality rates. Diabetes mellitus was in statistically significant inverse association with the average per capital consumption of fruits and vegetables (Palgi, 1981). In connection, artificial drugs severely abundant the complication between the two diseases as seen in Table 5 groups 4 to 6. Evidence suggests that several biomarkers may be useful for distinguishing between diseased and non diseased states and even for predicting future susceptibility to disease. A variety of biomarkers will probably be needed to develop a profile for an individual that reflects the impact of diet on performance and health. The hormonal oxidative balance health role of food and drug, for instance, was suggested (Ahmed *et al.*, 2003). Another area of interest is the interaction of nutrients and their association with genetics. These interactions may account for the inconsistent interrelations observed between specific dietary constituents and the incidence of disease. Greater understanding of how diet influences a person's genetic potential, overall performance, and susceptibility to disease can have

enormous implications for society. As new discoveries are made in this area, consumers will need access to this information so that they can make informed decisions (Milner, 2000). The nature and contents of the various polyphenols in food sources, the influence of agricultural practices and industrial processes, dietary intakes for each class of polyphenols, bioavailability of polyphenols with particular focus on intestinal absorption and the influence of chemical structure, eg, glycosylation, esterification, and polymerization, food matrix, role of microflora in the catabolism of polyphenols and the production of some active metabolites, intestinal and hepatic conjugation, ie, methylation, glucuronidation, sulfation, plasma transport, and elimination in bile and urine, identification of circulating metabolites, cellular uptake, intracellular metabolism with possible deconjugation, biological properties of the conjugated metabolites, and specific accumulation in some target tissues are proposed factors affect polyphenols health role (Manach *et al.*, 2004). Accordingly, the PP action can be attributed to one or more of the polyphenol fractions such as caffeic acid, p-OH benzoic, vanillic, chlorogenic or pyrogallol. The hypocholesterolemic effect of OP might be due to p-coumaric, caffeoyl, caumaroyl, cinnamic, naringenin and syringic or one of them. Both the two distengushale medical effect might be shered with other nutriment like vitamins, mineral ions, fats or, for instance, some dietary fiber. In short, orange peel administration had hypocholesterolemic effect, meanwhile, pomegranate one seems to be effective against ulceration. In fact, both PP and OP as very cheap source of health function when administered together in the dietary pattern of patient suffering of either cholesterolemia or peptic ulcer or both together might introduce a sort of solution for this clinical complication.

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The Response of Replacement of the Yellow Corn with Cull Dates as a Source of Energy on the Productive Performance of Kids Goats

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Abstract: This study was conducted to evaluate the effect of replacing corn with cull dates (CD) on the performance of growing kids. Twelve male kids aged 6 months with an average body weight $16.5 \text{ kg} \pm 0.25 \text{ kg}$ were placed in individual pens and fed with four levels of replacement of corn grain by CD (0, 50, 75 and 100%) during 90 days. Daily live-weight gain, dry matter intake and feed conversion were evaluated. Amino acid of corn grain and cull dates were determined. A digestibility trial was conducted to determine the digestibility coefficients and nutritive value of the tested ration. Rumen parameters were also measured. Results obtained showed that CP, CF and EE contents in four rations were nearly similar. The DM intake of group 4 was higher than the other tested rations. Results of digestibility trial indicated that the difference between all tested rations were not significant. The TDN of 100% cull dates showed insignificant higher than that of the three other groups, concerning the DCP, the control ration showed the highest value compared with the other tested rations. Concerning weight gain, animal fed ration (4) recorded highest gain (105 g) followed by control group (102 g). The group (2) recorded the lowest value (90 g). Ruminant total volatile fatty acids values were significantly higher for goats fed 100% cull dates than control group. Ammonia-nitrogen of treatment 3 (75%) cull dates was higher than values of other groups. In conclusion, group 4 (100% cull dates) could be used to improve animal performance of kids goats without any adverse effect.

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Key words: Replacement; Yellow; Corn; Energy; Productive Performance; Kid; Goat

1. Introduction

Feed is the most important cost items for livestock production. **Taylor and Field (1998)** reported that the feed cost represented 50 to 70% of the total cost of beef cow production. Grains, i.e corn, barley, sorghum and oats are the primary courses of high energy feed for livestock. Yellow corn grains are the most important sources as carbohydrates for rations of ruminants. Because of the shortage and high price of yellow corn grains, one of the alternatives to solve this problem is using non-conventional ingredients as a partial replacement of corn grains in rations of ruminants.

Dates (*Phoenix dactylifera L.*) are very popular in most of the Middle Eastern countries. Over 70% of the total world production are produced in this area and are considered an important national crop in some Arabian countries. A considerable amount (20%) of produced dates is inedible and is not beneficial for human consumption due to their poor quality. Besides, the average weight of dates pits is 10% of the date's weights.

In developing countries, the demand for importing corn grains as an ingredient for animal and poultry industry has been increasing under the

intensive production systems, leading to an increase in its price in the world market. Alternate sources for feed energy have been investigated in many developing countries. Dates are very rich in saccharides, their total sugars may reach up to 87% in the tannin stage and the monosaccharides are mainly 44% glucose and 50% fructose and some sucrose (**Sawaya et al., 1983**). Therefore, dates are considered the highest in energy content among all fruits, for example 1 kg of dates provides over 3000 kcal/kg gross energy, while 1 kg of orange provides 500 Kcal/kg (**Yousif, 1996**). For this reason, dates that are not suitable for human consumption are considered a good source of energy for animals and poultry.

In addition, significant amounts of cull dates (which are unstable for human consumption) are available in Egypt which can be utilized as a cheap non-conventional ingredient in ruminants diets. The annual production of dates in Egypt is estimated by 1.113.270 ton (**Ministry of Agriculture, 2002**). Moreover, the quantity of cull dates is estimated by about 20% of all dates produced (**Al-Yousef et al., 1994**).

The objective of this study is to estimate the value of cull dried dates as an energy substitute for

yellow corn in diets for growing kid goats performance.

2. Materials and Methods

This study was carried out at the Nubaria Experimental Station, Nubaria Governorate and on the Laboratories of Animal Production Department, National Research Center, Dokki, Giza, Egypt.

Feeding trials:

Twelve growing male goats weighed in average 19.3 kg were randomly allocated into four similar groups (3 animals in each). Cull date was incorporated into of the experimental feed mixtures (FM) to replace 0, 50, 75 and 100% of the yellow corn as a source of energy. The formulation and the chemical composition of the feed mixtures and cull dates were shown in Tables (1 and 2).

All ingredients of each ration were well mixed and ground before feeding. The experimental feed mixtures were fed individually *ad libitum* two times daily, at 8 a.m. and 4 p.m., while feed residues were removed and weighed once daily before morning feeding to estimate daily feed intake. Fresh water was freely available all time. Kids weights were recorded at the beginning of the experiment and thereafter at biweekly intervals till the end of the experiment after water and feed were withdrawn for 12 hrs. The feeding trials lasted for 90 days.

Digestibility trials:

At the middle of the feeding trial (45 days), using a grab sample method from each group to determine the nutrients digestibility and feeding value of the experimental rations using acid insoluble ash (AIA) as a internal marker as described by **Van Keulen and Young (1977)**.

Rumen liquor parameters:

During the digestibility trials rumen liquor samples were taken before given the morning rations and at 2 hr after feeding using stomach tube and strained through four layers of cheesecloth. Samples were separated into 2 portions, the first was used for immediate determination of pH values by Orion Research digital pH-meter, model 201. Ammonia-nitrogen (NH₃-N) concentration was determined according to Conway (1962), while the 2nd portion was stored at -20 °C after adding few drops of toluene and a thin layer of parafilm oil till analyzed for total VFA's according to **Warner (1964)**.

Proximate composition

The moisture content of the samples was determined by oven-drying to a constant weight at 105 °C. Crude protein, crude lipid, crude fiber and ash content were determined in accordance with the

standard methods of **AOAC (19905)**. Carbohydrates (nitrogen free extract) were determined by difference.

Amino acid analysis

Amino acid content was determined as described by **Spackman et al. (1958) and Moore et al. (1958)**. The analysis was performed in Central Service Unit, National Research Center, Egypt using LC3000 amino acid analyzer (Eppendorf-Biotronik, Germany). The technique was based on the separation of the amino acids using strong cation exchange chromatography followed by the ninhydrine colour reaction and photometric detection at 570 nm. Samples were hydrolyzed with 6 N HCl at 110 °C in Teflon capped vials for 24 h. After vacuum removal of HCl, the residues were dissolved in a lithium citrate buffer, pH 2.2. Twenty µl of the solution were loaded onto the cation exchange column (pre-equilibrated with the same buffer), then four lithium citrate buffers with pH values of 2.2, 2.8, 3.3 and 3.7, respectively, were successively applied to the column at flow rate 0.2 ml/min. The ninhydrine flow rate was 0.2 ml/min and pressure of 0-150 bar. The pressure of buffer was from 0 to 50 bar; and reaction temperature was 130 °C.

Statistical analysis:

The data of feeding and digestibility trials were statistically analyzed using General linear method of statistical analysis system (**SAS, 1998**). Duncan multiple range test (**Duncan, 1955**) was used to separate among means.

3. Results and Discussion

The proximate chemical analyses of the tested ingredients and experimental rations are shown in Table (2). The results indicated that rations containing dates were nearly similar in DM, CP, EE, CF and NFE contents relative to the control ration. These results are in agreement with those reported by **Al-Dabeeb (2005)**. The experimental data showed that yellow corn was the highest in crude protein (9.85%), while CD was the lowest (4.89%). (**Herms and Al-Homidan, 2004**). The results showed that cull dried dates has lower value of crude protein (4.89%) as compared with yellow corn grains (9.85%), but this value was higher than that obtained by **Awadalla et al., (2002)**, who found that CP of cull dates was 3.62% and the cull dates has nearly similar value of NFE (77.94%) compare to yellow corn grains (77.71%).

The amino acids composition of cull dates and yellow corn grains are presented in Table (3). The results showed that cull dates contains higher amounts of aspartic, threonin, serine, glutamic, glycine, alanine, valine, methionine, isoleucine, leucine, lysine,

histidine and arginine acids compared with yellow corn grains.

Results of feed intake, nutrients digestibility and feeding value are shown in Table (4). The average daily feed intake of the four rations differed between the experimental kids without any significantly ($P < 0.05$). Kids in group (4) consumed more feed (735 g/day) than other three groups.

Results of the digestibility trials are shown in Table (4). The digestibility of all nutrients increased as dates in the rations increased up to 100% CD. Total digestible nutrients (TDN) was higher for animals receiving the diets containing 100% CD compared with the other three rations without any significant. **Ahmed and Al-Dabeeb (2000)** indicated that date supplemented diets may improve the digestibility coefficients of animals. This finding is contrary to the findings of **Al-Hag et al., (1993)**, who reported that high concentrate dates in ration caused a sharp drop in digestion coefficients of CP and CF. The same trend was observed by **Al-Yousef et al., (1994)**.

Results of growth performance for growing kids fed different rations are shown in Table (5). There were no significant differences in daily gain in weight for kids fed the four diets. The kids receiving 100% cull dates recorded the highest value of average daily gain (105 g/head/day). The results of the present study indicated that incorporation of cull dates at 100% of

yellow corn show an improvement in growth rate when compared with the control group. This finding was agree with the findings of **El-Hag et al., (1993)**, who reported that addition of dates to the whole ration was associated with an increase in growth rate of Awassi lambs, while **Al-Dabeeb (2005)** indicated that incorporation of dates in ration did not show an improvement in growth rate when compared with the control group. Values recorded for feed conversion (kg feed intake / kg gain) were nearly the same for the four treatments in terms of DM, TDN or DCP intake / gain.

Rumen fluid parameters of goat kids fed different rations are given in Table (6). Rumen pH decreased as the level of CD increased in the ration. Different between the control and 100% CD is significant, this result agree with that obtained by **Awadalla et al., (2002)**, who reported that rumen pH decrease ($P < 0.05$) tended to increase the levels of CD in the rations. The lower ruminal pH associated with CD feeding was partially a result of higher concentration of total VFA^s. Moreover, the increase in rumen NH₃ N due to CD feeding may indicate high ruminal activity, which was reflected on higher digestibility. There are no interaction between experimental rations and sampling time. **Kholif et al., (1996)**, reported significant decreases in rumen pH with CD inclusion in goat rations.

Table (1): Ingredients proportion (%) used in concentrate mixture.

Ingredients	Treatment			
	0%	50%	75%	100%
Ground corn	40	20	10	-
Cull dried dates	-	20	30	40
Undecorticated cotton seed meal	20	20	20	22
Wheat bran	12	12	12	12
Berseem straw	25	25	25	23
Limestone	2	2	2	2
Sodium chloride	0.7	0.7	0.7	0.7
Vitamins and minerals mixture ^a	0.3	0.3	0.3	0.3

^aEach 3 kg vitamins and minerals mixture contains: Vitamin A 12.000.000 IU, vitamin D₃ 2.200.000 IU, vitamin E 10.000 mg, vitamin K₃ 2.000 mg, vitamin B₁ 1.000 mg, vitamin B₂ 5.000 mg, vitamin B₆ 1.500 mg, vitamin B₁₂ 10 mg, pantothenic acid 10 mg, niacin 30.000 mg, follic acid, 1.000 mg, biotin 50 mg, choline 300.000 mg, manganese 60.000 mg, zinc 50.000 mg, copper 10.000 mg, iron 30.000 mg, iodine 100 mg, selenium 100 mg, cobalt 100 mg, CaCO₃ 3.000g.

Table (2): Chemical composition of the ingredients and experimental rations.

Feed	% DM	Composition (%DM)						
		CP	CF	EE	Ash	NFE	NDF	ADF
Ground corn	89.87	9.85	2.75	4.44	5.25	77.71	9.30	2.1
Cull dates	87.15	4.89	3.60	3.34	10.23	77.94	29.10	13.25
Concentrate 0	88.25	12.25	18.10	2.13	7.99	60.03	51.25	32.10
Concentrate50	86.68	11.72	18.32	2.10	8.21	59.65	52.54	33.25
Concentrate75	86.39	11.31	18.43	2.19	8.21	59.34	54.25	34.57
Concentrate100	86.11	11.10	18.54	2.13	9.14	59.09	56.77	36.00

Table (3): Amino acids composition of cull dates and corn grains.

Amino acids	Cull dates	Corn grains
Aspartic acid	10.94	8.10
Threonine	4.09	3.34
Serine	4.93	4.32
Glutamic acid	24.48	21.13
Glycine	2.90	2.47
Alanine	9.28	7.50
Valine	3.91	3.56
Methionine	1.19	1.08
Isoleucine	4.10	3.89
Leucine	14.76	10.02
Tyrosine	5.72	7.37
Phenylalanine	5.96	8.36
Histidine	3.95	3.17
Lysine	3.59	2.86
Arginine	5.13	4.82

Table (4): Feed intake, nutrients digestibilities and feeding value recorded for kids fed the four rations.

Item	Experimental rations				SE	Sig.
	R1	R2	R3	R4		
No. of animals	3	3	3	3		
Body weight, kg	21.26 ^b	22.38 ^a	25.61 ^a	25.66 ^a	0.75	*
Feed intake, g DM/h/day	715.66 ^a	629.84 ^b	665.00 ^b	735.00 ^a	20.86	*
DM intake, g/kg body weight	33.70	28.47	26.22	28.74	1.31	NS
Nutrients digestibility, %						
DM	65.33	66.55	68.33	68.43	0.93	NS
OM	68.45	66.49	66.53	69.88	1.01	NS
CP	67.73	63.55	64.51	69.62	1.16	NS
CF	54.67	53.63	56.63	59.31	1.31	NS
EE	68.38	66.29	68.04	69.06	1.06	NS
NFE	72.11	71.02	72.91	73.43	1.09	NS
NDF	53.90 ^b	59.58 ^{ab}	62.75 ^a	65.75 ^a	1.65	*
ADF	52.81 ^b	60.25 ^{ab}	64.35 ^a	66.45 ^a	1.91	*
Nutritive values, %						
TDN	64.76	62.76	64.35	65.44	0.15	NS
DCP	8.29	7.44	7.29	7.72	1.65	NS

NS : Not significant.

* : Significant differences at (P<0.05).

Table (5): Growth performance and feed conversion for kids given the different experimental rations.

Item	Experimental Rations				SE	Sig.
	R1	R2	R3	R4		
No. of animals	3	3	3	3		
Body weight, kg						
Initial	16.67	18.33	21.33	20.93	0.78	NS
Final	25.85 ^b	26.43 ^b	29.88 ^a	30.38 ^a	0.74	*
Gain	9.18	8.10	8.55	9.45	0.26	NS
Average body weight gain, g/h/day	102.00	90.00	95.00	105.00	2.98	NS
Feed intake, g/h/day						
DM	715.66	629.84	665.00	735.00	20.86	NS
TDN	461.05 ^a	394.15 ^b	426.94 ^{ab}	480.14 ^a	12.78	*
DCP	55.73	46.71	48.67	55.89	1.95	NS
Feed conversion, kg feed / kg gain						
DM	7.01	7.00	7.00	7.00	0.04	NS
TDN	4.53	4.39	4.50	4.58	0.06	NS
DCP	0.54	0.52	0.51	0.53	0.09	NS

NS : Not significant.

* : Significant differences at (P<0.05).

Table (6): Rumen liquor parameters recorded for kids fed the four rations.

Item	Experimental rations				SE	Sampling time		SE
	R ₁	R ₂	R ₃	R ₄		0 hr.	2 hrs.	
pH	4.83 ^a	4.68 ^{ab}	4.71 ^a	4.45 ^b	0.17*	5.05	4.29	0.09**
Ammonia-N, mg/dl	28.35 ^a	25.55 ^b	32.30 ^c	28.56 ^a	0.94**	32.00	25.37	0.94**
Total VFA's meq/dl	9.70 ^a	11.83 ^b	12.66 ^b	16.18 ^c	0.66**	10.62	14.56	0.66**

* Significant differences at (P<0.05).

** Significant differences at (P<0.01).

Table (7): Effect of incorporation of cull dates in rations on economical efficiency of growing goats

Item	Experimental rations			
	R ₁	R ₂	R ₃	R ₄
Total DM intake, g	715.66	629.84	665.00	735.00
Feed conversions	7.02	6.99	7.00	7.00
Av. daily gain (g/h/day)	102.00	90.00	95.00	105.00
Av. feed cost (h/day, LE*) ¹	1.18	0.98 ^(a)	1.07	1.12
Av. Revenue of daily gain (h/d, LE)	3.06	2.7	2.85 ^(b)	3.15
Net feed revenue (LE/ head) ²	1.88	1.72	1.84	2.03
Economic Feed efficiency (%) ³	1.59	1.76	1.82	1.81
Relative economic efficiency ⁴	1	106.9	114.5	113.8

*LE=Egyptian pounds = 0.164\$ approximately.

1: Calculated according to the local price at 2011 (1900- 1500 - ,2400 - , 1500- and,700 LE for ground corn, cull dates, undecorticated cotton seed meal, wheat bran and berseem straw, respectively.

2: Selling income-total cost x 100.

3: Net revenue/total cost x 100.

4: Economic efficiency for treatment/economic efficiency for control, as assuming that relative economical efficiency of the control group equal 100.

Conclusion

Based on results of the present study, it could be safely concluded that dates could efficiently be used as useful ingredients in the ration of small ruminants taking into account the right proportion of dates added. Therefore, using cull dates in feeding small ruminants could be economically sound in hot climate countries.

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Tissue Doppler Imaging Versus Conventional Echocardiography In Evaluation Of Diastolic Function In Diabetic Patients

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Abstract: modifications and medical interventions could prevent or delay the subsequent development of heart failure in Diabetic patients. Conventional echocardiography was used to screen for and diagnose left ventricular diastolic dysfunction-LVDD- but the results was not satisfactory and underestimate the magnitude of LVDD due to the pseudonormal pattern in grade 2 diastolic dysfunction. Tissue Doppler imaging is considered a better non invasive and more accurate screening modality. **The work aimed a** comparing tissue Doppler imaging to conventional Echocardiography in diagnosing diastolic dysfunction in diabetic patients. **Patients and methods** forty diabetic patients and 20 age matched volunteers – as a control group – were included in this study individuals with IHD,HTN cardiomyopathy or any obvious liver or renal disease were excluded – blood sugar, lipid profile, ECG, conventional echocardiography and tissue Doppler imaging were done for all individuals. **Results** 22 of the 40 diabetic patients had diastolic dysfunction compared to only one of the control group and from those 22 with diastolic dysfunction 13 was diagnosed by both conventional echo and TDI, 1 patient diagnosed only by conventional echo, while 8 patients were diagnosed by TDI and the superiority of TDI in diagnosing LVDD compared to conventional Echocardiography was statistically significant. Also there was a liner correlation between duration of diabetes and the presence of LVDD that was statistically significant. **Conclusion** diabetics especially with longer disease duration are more prone to have diastolic dysfunction even with normal EF and FS and TDI is a better non invasive method in assessing diastolic dysfunction compared to the conventional Echocardiography.

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Keywords: Echocardiography - Tissue Doppler imaging Diastolic dysfunction Diabetes; chemical components.

1. Introduction

Diabetes is one of the most common diseases in the world (1)and its Cardiovascular complications are known to be the main cause of death and morbidity in diabetic patients, as over 75% of all diabetic patients die from cardiovascular events. There is an increased rate of ischemic heart disease and cardiomyopathy, which may lead to congestive heart failure in the absence of coronary artery disease (1,2)

A number of potential mechanisms have been proposed to explain abnormal myocardial function in diabetes. First, small vessel disease both due to structural abnormalities in the vessels as well as functional disturbances (including endothelial dysfunction) may lead to reduced substrate delivery. Second, myocyte function may be abnormal due to alterations of substrate supply and utilization, including disturbances of glucose transporters, free fatty acids, and calcium homeostasis. Third, both apoptosis and myocardial fibrosis have been identified in diabetic subjects, reflecting changes in the hormonal milieu, particularly involving Angiotensin and Aldosterone. Finally, diabetic autonomic neuropathy has been widely described and appears to be associated with left ventricular dysfunction (3,4,5)

The traditional measurements of diastolic function, the Doppler derived mitral valve inflow velocity pattern and its derivatives, have proved difficult to interpret because of the pseudonormal pattern that defines grade 2 dysfunction, but may be mistaken for the normal pattern unless differentiation by the Valsalva maneuver or by assessing pulmonary vein flow is performed. While the clinical course of diastolic dysfunction is characterized by decreasing effectiveness of myocardial relaxation and extension associated with increasing left atrial pressure and size, the respective developments of pressure and filling cannot be mirrored by the traditional Doppler parameters. An even more important limitation, however, is the non-quantitative pattern recognition used for assessing diastolic function and the changes in the course of disease and during preventive therapy.(6)

Tissue Doppler imaging is a robust and reproducible ultrasound technique employing the low-frequency and high-amplitude ultrasound signals reflected from the myocardium.

Pulsed tissue Doppler imaging for Detection of systolic or diastolic dysfunction depends on the sensitivity and specificity of the diagnostic technique

used. Tissue Doppler imaging has demonstrated that the systolic myocardial velocity S' is a more sensitive measure of systolic function than ejection fraction and that the early diastolic myocardial velocity E' and E/E' have the best correlation with left ventricular relaxation and compliance indexes.

Regional left ventricular function is quantified as the myocardial velocity of long-axis motion in cm/s during systole (S'), early diastole (E) and late diastole (A).

Left ventricular global function is the average of these segmental velocities, obtained either at the mitral annulus or very basal myocardium in the apical four- and two-chamber views. (7,8)

The aim of this work is comparing tissue Doppler imaging to conventional echocardiography in diagnosing diastolic dysfunction in diabetic patients.

2. Patients and methods:

The study included 40 diabetic patients from Fayoum university hospital presented to the out patient clinic for controlling their blood sugar and 20 age and sex matched healthy volunteers as a control group. Patients who had valvular heart disease, Ischemic heart disease (excluded by history and ECG, absence of SWMA by Echo), congestive heart failure, overt renal disease or overt renal impairment were excluded from this study the following were done for all individuals Careful history taking, full clinical examination, laboratory investigations include: FBS, 2HPP, lipid profile liver enzymes as well as serum creatinine Echocardiography (using Siemens - Acuson CV70 - system equipped with TDI technology) was performed to all subjects in the left lateral position and 2D & M- mode techniques were used for measurement of the following parameters LVEDD LVESD, EF, FS, LA size, isovolumic relaxation time (IVRT) & DT as well as exclusion of any wall motion abnormalities. Transmitral flow pattern: Using PW Doppler across the mitral inflow tract, two waves

were measured :the early E wave corresponding to early ventricular filling and A wave which reflect atrial contraction was typically measured by placing a 2 mm sample volume at the mitral leaflet tips in the four chamber apical view. Tissue Doppler imaging mitral annular velocity was obtained by placing a 5 mm sample volume over the lateral or septal mitral annulus and also Systolic S' (Sa), early diastolic E (Ea) and the late diastolic velocities A' (Aa) were measured.

Statistical analysis:

Data were analysed using SPSS version 10. Variables as age, sex, duration of diabetes mellitus, EF, FS, Mitral inflow velocities, isovolumic relaxation time and mitral E wave deceleration time on Doppler echocardiography and mean diastolic mitral annular velocities on TDI were compared and data were expressed as mean \pm standard deviation and in percentages.

3. Results

This study included 40 diabetic patients and 20 healthy age and sex matched control persons their age ranged between 18-55 years old.

(Table - 1): Distribution of study groups according to type of diabetes, and type of treatment among cases.

variable	Case (n=40)	
	No.	%
Type of diabetes		
• Type 1	11	27.5%
• Type 2	29	72.5%
Type of treatment		
• Insulin	14	35%
• Oral hypoglycemic	26	65%

The percentage of type 1 diabetics was 27.5 % while type 2 was 72.5% The percentage of patients treated with insulin was 35% while those on oral hypoglycemic drugs was 65 %.

(Table--2) Comparison between study groups according to anthropometric measures and investigations.

Variables	Case (n=40)		Control (n=20)		p-value	Sig.
	Mean	\pm SD	Mean	\pm SD		
Weight	79.2	\pm 14.6	71.7	\pm 12.8	0.2	NS
BMI	28.6	\pm 4.7	28.6	\pm 10.8	0.9	NS
SBP	<u>126.3</u>	\pm 9.5	119.5	\pm 6.9	0.003	HS
DBP	<u>80</u>	\pm 10.6	73.8	\pm 5.8	0.02	S
FBS	<u>187.4</u>	\pm 89.7	89.6	\pm 7.6	<0.001	HS
2HPP	<u>297</u>	\pm 111	175.4	\pm 16.9	<0.001	HS
Creatinine	1.03	\pm 1.2	0.77	\pm 0.1	0.3	NS

- Systolic blood pressure was highly significant in diabetic group as compared with control group (126.3 \pm 9.5 vs 119.5 \pm 6.9, p value = 0.003)
- Diastolic blood pressure was significantly higher in diabetic group as compared with control group (80 \pm 10.6 vs 73.8 \pm 5.8, p value = 0.02)
- FBS & 2HPP were highly significant in diabetic group as compared with control group with p value was <0.001 in both.

(Table 3): Comparison between study groups according to lipid profile

Variables	Case (n=40)		Control (n=20)		p value	Sig.
	Mean	±SD	Mean	±SD		
LDL	103.4	±31	86.7	±7.4	0.002	HS
HDL	56.2	±9.7	46.2	±4.5	<0.001	HS
Cholesterol	193.2	±40.5	139.2	±23.8	<0.001	HS
TG	196.6	±81.7	144.6	±39.9	0.002	HS

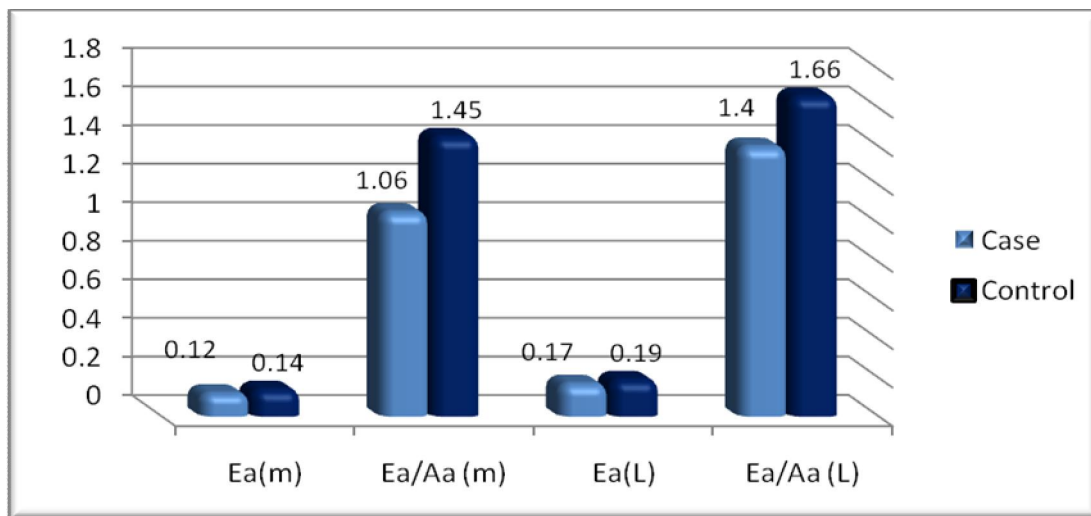
Lipid profile including LDL, HDL, Cholesterol, TG were highly significant in diabetic group as compared with control group as presented in table 3.

(Table 4): Comparison between study groups according to Echocardiography findings

Variables	Case (n=40)		Control (n=20)		p value	Sig.
	Mean	±SD	Mean	±SD		
LVPWd	9.3	±1.5	8.12	±1.4	0.004	HS
LVIDd	47.3	±4.4	43.8	±13.5	0.1	NS
IVSd	8.4	±1.8	9.9	±8.3	0.3	NS
LVIDS	30.9	±3.3	30.6	±4.4	0.7	NS
EF	0.63	±0.05	0.64	±0.07	0.4	NS
FS	0.34	±0.03	0.35	±0.05	0.5	NS
LA size	32.6	±4.6	30.3	±3.7	0.06	NS
E(m/s)	0.78	±0.2	0.8	±0.2	0.6	NS
A(m/s)	0.72	±0.2	0.53	±0.1	<0.001	HS
E/A	1.12	±0.29	1.5	±0.3	<0.001	HS
DT	190.5	±53.5	173.2	±34.7	0.2	NS
IVRT	83.8	±18.4	81.6	±12.6	0.6	NS

Data derived from Echocardiography showed that the left ventricular posterior wall diameter (LVPWd), A wave velocity were significantly higher in diabetic group as compared with control group (p value =0.004, <0.001 respectively).

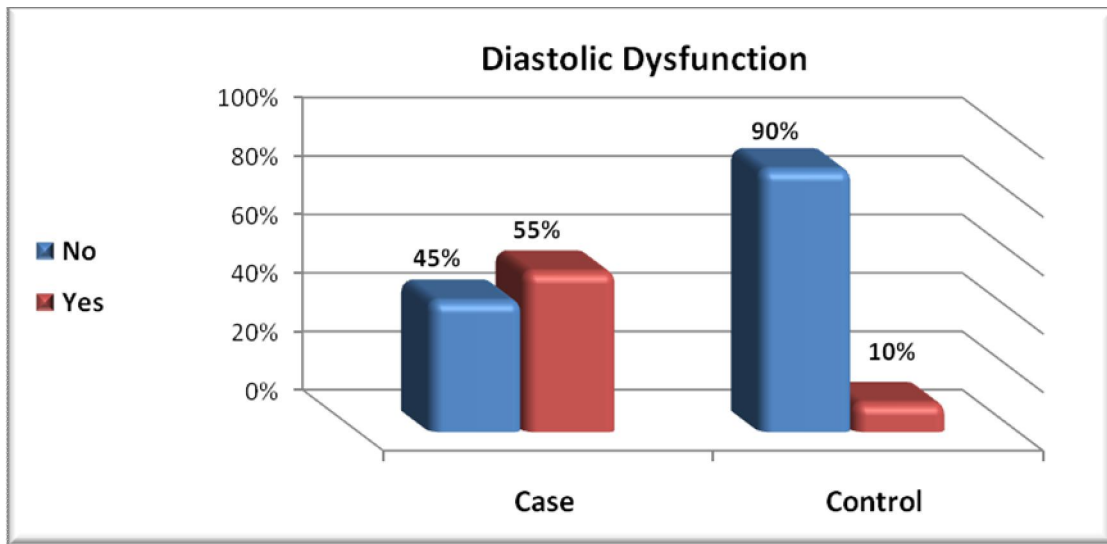
A / E ratio was lower in diabetic group as compared with study group persons with statistically high significance. (p value <0.001).



(Figure-1): Comparison between study groups according to Tissue Doppler finding

- Septal Ea(m) velocity was highly significant lower in diabetic subjects as compared with control persons with (p value <0.001).
- Septal Aa (m) velocity was highly significant higher in diabetic subjects as compared with control persons with (p value <0.001).
- Ea/Aa (m) was highly significant lower in diabetic subjects as compared with control persons with (p value < 0.001).
- Lateral Aa(L) velocity was significantly higher in diabetic subjects as compared with control persons with (p value =0.01).

Ea/Aa (L) was significantly lower in diabetic subjects as compared with control persons with (p value = 0.03)



(figure-2) Comparison between study groups according to presence of diastolic dysfunction

From 40 diabetic patients there were 22 patients have diastolic dysfunction with a percentage of 55% while from 20 control persons there were only 2 persons have diastolic dysfunction with a percentage of 10%, this means that there was a highly significant statistical difference (p value = 0.001)

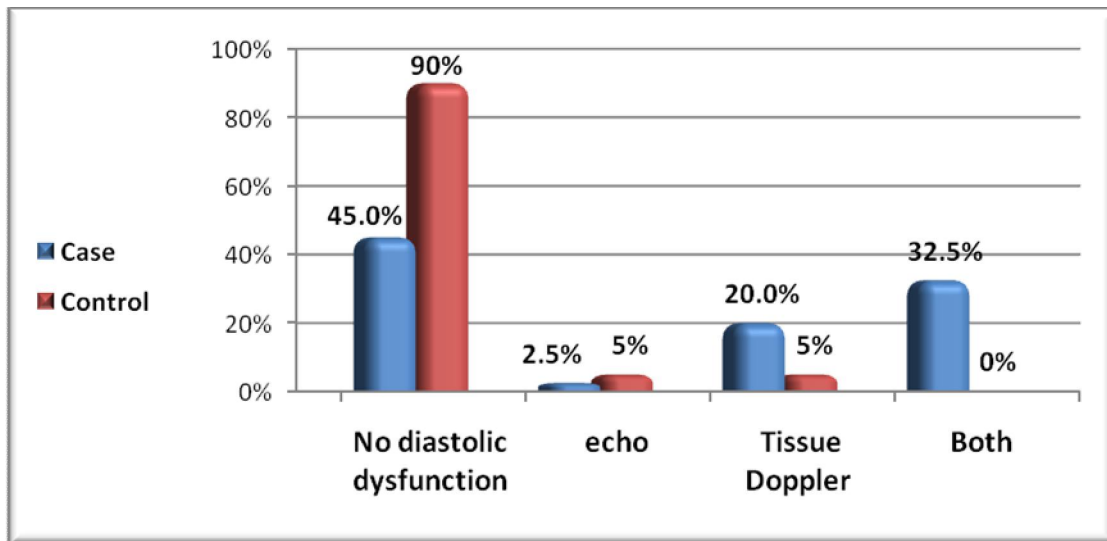


Figure-3 : Comparison between study groups according to diagnostic tools used for detection of diastolic dysfunction

Within 22 diabetic subjects having diastolic dysfunction, there were only one patient detected by conventional echocardiography only, 8 patients detected by tissue TDI only AND 13 patients detected by both. This means statistically that tissue Doppler as a tool used in detection of diastolic dysfunction is highly significant more valuable as a diagnostic method than conventional echocardiography. (p value = 0.004).

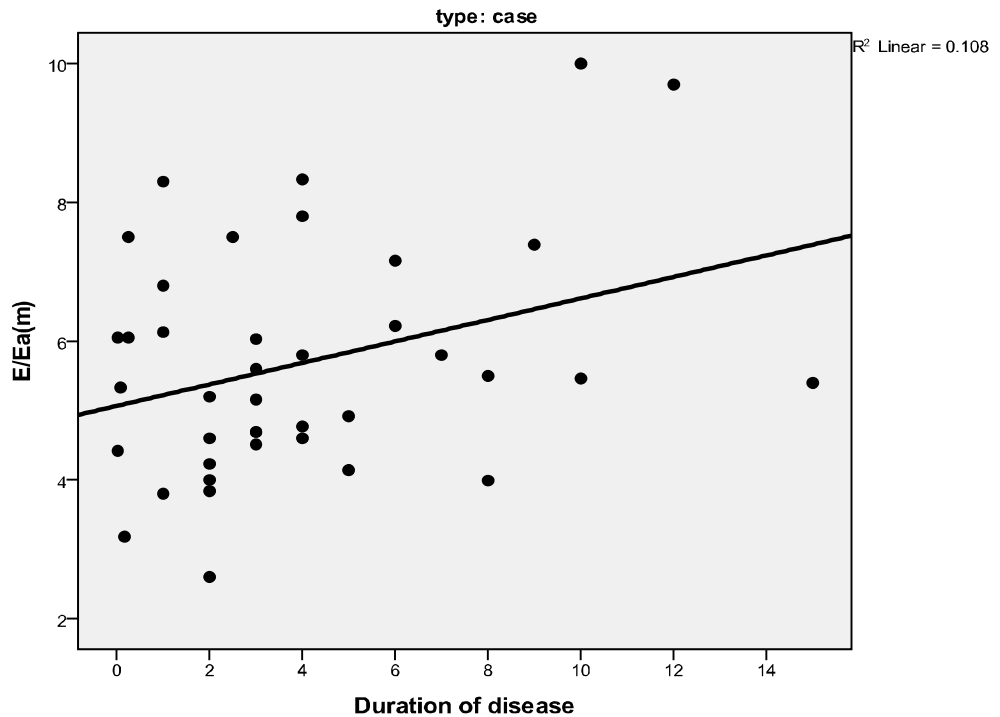


Figure-4 Correlation between duration of DM diastolic dysfunction in TDI measurements.

This figure shows that there is a + correlation which is statistically significant between the duration of the disease and diastolic dysfunction (E / Ea) with ($r : + 0.3$) and (P value = 0.03).

4. Discussion

Early detection of diabetic heart disease is of importance, Numerous studies have attempted to determine the prevalence of left ventricular diastolic dysfunction in asymptomatic diabetic subjects with normal left ventricular systolic function using Doppler assessment of transmitral flow velocity, have underestimated the prevalence of LVDD. The Doppler-derived mitral valve inflow velocity pattern and its derivatives, have proved difficult to interpret because of the pseudo normal pattern, that defines grade 2 diastolic dysfunction, may be mistaken for the normal pattern. Unless differentiation by the Valsalva maneuver or by assessing pulmonary vein flow is performed. Also loading conditions, especially preload, influence the indices obtained from these velocity patterns.. Tissue Doppler imaging (TDI) of mitral annular motion has been proposed as an improved (load-independent) noninvasive method of assessing diastolic function via echocardiography and it does not possess the substantial limitations of previous traditional noninvasive techniques. So TDI appears to be extremely effective for the identification of subclinical left ventricular diastolic dysfunction in diabetic patients.

In this study it was found that when using the conventional echocardiography in screening for LVDD there were 14 diabetic patients out of 40 found to have LVDD versus a single case in the control group out of 20 and the **A wave velocity** was $(0.72 \text{ (m/s)} \pm 0.2)$ in diabetics while it was $(0.53 \text{ (m/s)} \pm 0.1)$ in control group, this means that the A wave velocity is higher in diabetic patient than in the control persons and this was highly statistically significant (p value < 0.001). **E / A ratio** was 1.12 ± 0.29 in diabetics, while it was 1.5 ± 0.3 in control group, this means that E / A ratio is lower in diabetic patient than in the control persons and this was highly statistically significant (p value < 0.001) Both study and control groups have normal systolic function with normal EF.

And when using in screening for LVDD 21 diabetics were found to have LVDD out of 40 versus a single case in the control group out of 20 and **the Ea wave velocity** was $0.12 \text{ (m/s)} \pm 0.04$ in the diabetics while it was $0.14 \text{ (m/s)} \pm 0.02$ in control group, this means that Ea(m) wave velocity is lower in diabetic patient than in the control persons this was highly statistically significant (p value < 0.001). **Ea/ Aa ratio** was 1.06 ± 0.38 in diabetics, while it 1.45 ± 0.35 in control group, this means that Ea / Aa ratio is lower in

diabetic patient than in the control persons and this was highly statistically significant (p value < 0.001).

- **Aa(I) wave velocity** was 0.13 ± 0.03 in diabetics while it was 0.12 ± 0.01 in control group, this means that Aa (I) wave velocity is higher in diabetic patient than in the control persons with statistically significant difference (p value = 0.01).
- **Ea/ Aa(I) ratio** was : 1.4 ± 0.44 in case group, while it was 1.66 ± 0.5 in control group, this means that Ea / Aa ratio is lower in diabetic patient than the control persons with statistically significant difference (p value = 0.03)
- ❖ Also our study showed that from 22 diabetic patients having left ventricular diastolic dysfunction there were one patient only was detected by conventional echocardiography alone, 8 patients were detected by TDI alone, and 13 patients by both. This reflect that Tissue Doppler imaging is more valuable in detection of diastolic dysfunction than conventional Echocardiography with statistically significant difference with (p value = 0.004).
- ❖ These results support the existence of a distinct diabetic cardiomyopathy that causes diastolic dysfunction formerly. In addition, diastolic dysfunction has been shown to precede systolic dysfunction in diabetics, and even before the presence of pathological findings on clinical examination. Thus, impairment of diastolic parameters may be used as an early preclinical manifestation of diabetic cardiomyopathy

Our results agrees with that found by **Virendra, 2011** who assess Diastolic dysfunction in 127 asymptomatic type 2 diabetes mellitus with normal systolic function and 100 healthy subjects and found that of the total 127 subjects, 69 (54.33%) from the case group had diastolic dysfunction, and 11% amongst 100 subjects in the control group population showed the diastolic dysfunction ($P < 0.001$). also found that Patients with a longer duration of DM (of 11 to 15 years) had a higher prevalence of diastolic dysfunction ($P < 0.02$). and so this study reveals high incidence of diastolic dysfunction in asymptomatic diabetic subjects. (9)

Diamant et al. (2003) stated that early (E) acceleration peak, deceleration peak, peak filling rate, and E/A ratio, and all other indices of diastolic function, were significantly decreased in patients with recently diagnosed, well-controlled and uncomplicated type 2 diabetes compared with the controls ($P < 0.02$). These findings are similar to our results. (10)

Also **Boyer et al., (2004)** who assess the Prevalence of ventricular diastolic dysfunction in asymptomatic, normotensive patients with type two

diabetes mellitus stated that the prevalence of LV diastolic dysfunction in these subjects is high. Diastolic dysfunction was found in 75% subjects. They also found that, TDI detected diastolic dysfunction more often than any other Echocardiographic parameter.(11)

Our results agree with what was found by **Kamile Gul et al. (2009)** who assess early left ventricular dysfunction in 81 patients with type 1 diabetes mellitus and 51 healthy volunteers using Tissue Doppler imaging and found that type 1 DM subjects are characterized with impaired diastolic parameters. In addition, DD has been shown to precede systolic dysfunction in diabetics, even before the presence of pathological findings on clinical examination. And that PW Doppler is limited in the setting of pseudo-normal pattern, which can be unmasked by preload reducing conditions such as Valsalva maneuver So TDI is useful to overcome this outstanding problem. Furthermore, addition of TDI to PW Doppler has been reported to improve the Echocardiographic diagnosis of diastolic impairment in diabetic population.,(12).

Finally our study demonstrates that the prevalence of pre-clinical diastolic dysfunction is high among the diabetic subjects. and that Tissue Doppler imaging is more valuable than conventional Echocardiographic parameters in diagnosis of this preclinical diastolic dysfunction in diabetic patient.

Study limitations

- We did not perform coronary angiography to exclude coronary artery disease on ethical grounds. So, we carefully excluded the patients with obvious ischemic symptoms, ECG changes, and Echocardiography
- Evaluation of glycemic control on the basis of HbA1c measurement was another limitation in this study due to resources limitations.

5. Conclusion

- DM is a strong independent factor for LV diastolic dysfunction even in absence of ischemic, hypertensive or valvular heart diseases
- Early detection of subclinical cardiac involvement in diabetics may provide an approach for identifying high-risk patients who are likely to benefit from an earlier intervention. And institution of treatment for diastolic dysfunction
- TDI may permit early identification of this subclinical diastolic dysfunction in the presence of normal diastolic function indices by conventional echocardiography.

Recommendations

Diabetic patients should be evaluated early for diastolic function even in the absence of

manifestation of diastolic heart failure.. Diastolic function of diabetic patients can be easily and practically assessed by TDI. Which seems to be more valuable than conventional Echocardiography. The assessment of early myocardial relaxation velocities provides an additional window on LV diastolic function in a manner complementary to evaluation of mitral inflow.

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Serological and Molecular Typing of *Clostridium Perfringens* and Its Toxins Recovered from Weaned Rabbit's Flocks in Egypt

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Abstract: This study was carried out for serological and molecular typing of *Clostridium perfringens* (*C. perfringens*) and its toxins recovered from apparently healthy, diseased and dead weaned rabbits, as well as their feed and water. Identified 42 *C. perfringens* organisms representing 35 from rabbits and 7 from feed and water were subjected for determination of toxigenicity by intravenous inoculation (I/V) in Swiss mice. Toxigenic *C. perfringens* organisms were typed serologically using Nagler's test, dermonecrotic reaction in albino Guinea pigs and toxin antitoxin serum neutralization test (SNT) in Swiss mice. For confirmation of serological results, detection of alpha gene of *C. perfringens* was done using conventional polymerase chain reaction (PCR), followed by using of multiplex PCR to detect the toxin's types. Distribution of different *C. perfringens* types of surveyed rabbit's farms at different Egyptian governorate was carried out. In addition, the *in-vitro* antibiotic sensitivity of different *C. perfringens* types against different antimicrobial agents was performed. The results showed that 34 (97.14%) of *C. perfringens* recovered from rabbits were toxigenic, while 1.0 (2.86%) was none. Four out of 6 (66.66%) *C. perfringens* isolates from feed was toxigenic and 2 (33.33%) isolates was non-toxigenic. Only one (100%) *C. perfringens* isolate from water was toxigenic. Identical proving results were obtained using serological typing tests. Single and mixed types of toxigenic *C. perfringens* constituted 17 out of 35 (48.57%) for each, whereas only one type was none (2.86%). Single *C. perfringens* was representing 8 (22.85%) type A, 3 (8.57%) type B, 4 (11.43%) type D and 2 (5.71%) type E, whereas mixed types were 11 (31.42%) types (A and D), 2 (5.71%) types (A and E) and 4 (11.42%) types (B and D). Four *C. perfringens* isolates from feed was 3 type A (50%) and 1.0 type D (16.6%). The only *C. perfringens* isolate from water was type A (100%). Conventional PCR proved detection of alpha gene of *C. perfringens*, whereas multiplex PCR proved that *C. perfringens* type (A) was positive for alpha toxin at 324 base pair (bp), type (B) was positive for alpha toxin at (324 bp), beta toxin at (196 bp) and epsilon toxin at (655 bp), type (D) was positive for alpha toxin at (324 bp) and epsilon toxin at (655 bp) while type (E) was positive for alpha toxin at (324 bp) and iota toxin at (446 bp). The result of distribution of different *C. perfringens* types at different Egyptian governorate was recorded. *In vitro* antibiotic sensitivity test of single or mixed types of identified *C. perfringens* revealed sensitivity to amoxicillin/ clavulanic acid and ampicillin and resistance to colistine, erythromycin and lincomycine.

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Keywords: Weaned rabbits; *Clostridium* species; Egypt; Serotyping; PCR; Sensitivity test.

1. Introduction

Rabbits are animals of an economic importance. The rabbit meat has many advantages as it is nearly white, fine grained, palatable, flavored, high in good quality protein content, low fat and caloric contents, contains a higher percent of minerals than other meats, nearly of the same nutritive value as beef meat, good meat-to-bone ratio and it is acceptable to the general consumer in most countries of the world (Reddy *et al.*, 1977; Lukefahr *et al.*, 1989). Weaning is considered as a stressful period for rabbits caused by abrupt changes of diet and environment. An immature immune system together with a transient decrease of nutrient digestibility places the animal in adverse conditions where digestive pathologies might take place (de Blas *et al.*, 2012).

Enteritis in rabbits is considered to be a major cause of disease, mortality and economic loss in

domestic rabbits, particularly in younger ones (Peeters *et al.*, 1984).

There are many infectious agents known to play a role in inducing enteritis in rabbits, including intestinal and hepatic *Eimeria*, and infections with bacteria such as *Escherichia coli*, *Clostridium* species (spp.) and *Bacillus piliformis*. Dietary and management factors are also recognized to have an effect on the incidence of enteric disease (Carman *et al.*, 1948; Patton *et al.*, 1978; Percy *et al.*, 1993).

Clostridium perfringens (*C. perfringens*) is the most widely occurring pathogenic bacterium and is certainly the most important cause of *Clostridial* enteric disease in domestic rabbits (Smith and Williams, 1984). Some types of *C. perfringens* (mainly type A) are consistently recovered both from the intestinal tracts of animals and from the environment, while others (types B, C, D, and E) are less common in the intestinal tracts of animals (Carter and Chengappa,

1991) and can occasionally be found in the environment in areas where disease produced by these organisms is enzootic (Niilo, 1980). *Clostridial* toxins are main pathogenic virulence factor of *C. perfringens* that have been associated with a wide range of diseases in both humans and domestic animals (Jin Zeng *et al.*, 2011).

Typing of *C. perfringens* into types A, B, C, D and E is based on production of four major toxins namely alpha, beta, epsilon and iota as determined by *in vivo* protection tests performed by intradermal injection of Guinea pigs or intravenous inoculation of mice (McDonel, 1980; Walker, 1990; Songer, 1996). Strains of *C. perfringens* type A produces alpha toxin which is the principle lethal toxin producing enterotoxaemia in rabbits, type B produces alpha, beta and epsilon toxins, type C induces alpha and beta toxins, type D produces alpha and epsilon toxins, while type E induces alpha and iota toxins (Kunstyr *et al.*, 1975; Molloy, 1978)

Routine diagnostic bacteriological cultivation of intestinal samples for *C. perfringens* followed by polymerase chain reaction (PCR) based genotyping colonies, also multiplex real-time PCR for detection of toxins were previously done by Albini *et al.*, (2008).

Antimicrobial therapy continues to be important in reducing losses due to *Clostridial* infections. Susceptibility, resistance and antibiotic profile of different antimicrobial agents against *C. perfringens* strains isolated during surveillance studies of *Clostridial* enteritis in rabbits were investigated by Agnoletti *et al.*, (2007); Marien *et al.*, (2008); Richez *et al.*, (2008); Saggiolato *et al.*, (2008).

So, the purpose of this study was typing of *C. perfringens* and its toxins serologically and molecularly, and also testing the sensitivity of different *C. perfringens* type's *in-vitro* to different antimicrobial agents.

2. Materials and Methods

Clostridial strains:

Morphologically and biochemically identified 42 field isolates of *C. perfringens* that isolated from apparently healthy, diseased and dead weaned rabbits as well as their feed and water were kindly obtained from Poultry and Rabbits Diseases Department, Faculty of Veterinary Medicine, Cairo University, Egypt.

Determination of toxigenic strains of Clostridium spp. by intravenous (I/V) inoculation in Swiss mice:

This test was carried out according to the method of Mariano *et al.*, (2007). From recovered toxigenic isolates of *C. perfringens*, about 5ml of 24 hrs cooked meat cultures of toxigenic strains of *C. perfringens* was added to 50 ml of toxin production medium for types A, B and C and incubated for 5-6 hrs. Another 5ml

from the same 24 hrs cooked meat cultures was added to 50 ml of toxin production medium for types D and E, incubated for 48 hrs., then trypsinized to a final concentration of 0.1% and then incubated at 37°C for an hr. The cultures were centrifuged at 3000 rpm for 20 min. and 0.1 ml from the clear supernatant fluid was I/V inoculated in the tail vein of each of Swiss mouse. Mice were kept under observation for 48 hr. If the mice died during 48 hrs observation period, it will consider as highly toxigenic *C. perfringens*.

Nagler's test by half antitoxin plate:

This test was carried out according to the method of Smith and Holdman, (1968). It was done by spreading *C. perfringens* types A, B, C, D and E antitoxin separately on half of egg yolk agar plate and allowed to dry in incubator for half an hr. The suspected colonies were streaked across the plate starting from the half of plate without antitoxin and ending to side containing antitoxin. The plate was incubated anaerobically at 37°C for 24 hrs. The release of alpha toxin that produced by all types of *C. perfringens* on lecithin was inhibited by the alpha antitoxin. In positive cases; opalescence should be clear on the side of the plate without antitoxin.

Typing of C. perfringens toxins by dermonecrotic test in albino Guinea pigs:

Preparation of the toxins was done according to Bullen, (1952). Application and interpretation of the test in albino Guinea pigs were adopted after Oakley and Warrack, (1953) and Quinn *et al.*, (2002).

Toxin antitoxin serum neutralization test (SNT) in Swiss mice:

It was done as the method described by Smith and Holdman, (1968).

All the experiments on animals such as inoculation in Swiss mice, dermonecrotic reaction in albino Guinea pigs and toxin antitoxin SNT in Swiss mice was carried out according to the National regulations on animal welfare and Institutional Animal Ethical Committee (IAEC).

Genotyping of C. perfringens using polymerase chain reaction (PCR):

Identified pure colonies of *C. perfringens* were grown over night in 5 ml brain heart infusion broth supplemented with 1% sodium thioglycolate at 37°C under anaerobic condition. The process of DNA extraction was done as Sheedy *et al.*, (2004). The concentration of DNA in µg /ml was measured at 260 and 280 nanometer (nm) by ultra-violet spectrophotometer and then the ratio of 260/280 was calculated. Pure DNA should have ratio of >1:8 that contamination with protein resulted in a significantly lower value. The DNA solution was kept at -20° C

until used. DNA samples were amplified according to the method of Tong and Labbe, (2003). Primers used for conventional and multiplex PCR was showed in Tables (1 and 2). DNA samples were amplified according to the method of August ynowicz et al.,

(2000). Cycling program of PCR was performed in the thermal cyclor as in Tables (3 and 4). Specific amplicons were observed under ultraviolet trans illumination, compared with the marker and photographed by a digital camera.

Table (1): Primer of alpha toxin gene of *C. perfringens* used in conventional PCR

Primer name and direction	Nucleotide sequence
cpa: Forward	GCTAATGTTACTGCCGTTGA
Reverse	CCTCTGATACATCGTGTAAG`

Cpa: *C. perfringens* alpha toxin

Table (2): Primers for the four toxins genes of *C. perfringens* used in multiplex PCR

Primer name and direction	Nucleotide sequence
cpa: Forward	GCTAATGTTACTGCCGTTGA
Reverse	CCTCTGATACATCGTGTAAG`
cpb: Forward	GCGAATATGCTGAATCATCTA
Reverse	GCAGGAACATTAGTATATCTTC`
etx: Forward	GCGGTGATATCCATCTATTC
Reverse	CCACTTACTTGTCTACTAAC
iA: Forward	ACTACTCTCAGACAAGACAG
Reverse	CTTTCCTTCTATTACTATACG`

Cpa: *C. perfringens* alpha toxin, Cpb: *C. perfringens* beta toxin,
etx: *C. perfringens* epsilon toxin, iA: *C. perfringens* iota toxin

Table (3): PCR cycling protocol for alpha gene of *C. perfringens* using conventional PCR

Amplified DNA	Initial denaturation	Actual cycles	Final extension	Amplified product size (bp)
<i>C. perfringens</i> (alpha) toxin gene	94° C for 5 min.	35 cycles of : Denaturation: 94° C for 1 min. Annealing: 53° C for 1 min. Extension: 72° C for 1 min.	72° C for 5 min.	cpa: 324

Table (4): PCR cycling protocol for four toxins genes of *C. perfringens* using multiplex PCR

Amplified DNA	Initial denaturation	Actual cycles	Final extension	Amplified product size (bp)
<i>C. perfringens</i> toxin genes (alpha, beta, epsilon and iota)	94° C for 3 min.	30 cycles of : Denaturation: 94° C for 1 min. Annealing: 55° C for 1 min. Extension: 72° C for 1 min.	72° C for 5 min.	cpa: 324 cpb: 196 etx: 655 iA: 446

In vitro antibiotic sensitivity test:

The in-vitro antibiotic sensitivity test of single or mixed types of *C. perfringens* using disc diffusion technique was applied to according National Committee for Clinical Laboratory Standards (NCCLS), (1998).

3. Results and Discussion

Enteric diseases in weaned rabbits constitutes a great problem resulted in high morbidity and mortality as well as growth depression. *C. perfringens* is a widely occurring pathogenic bacterium in enteric diseases of domestic rabbits and its pathogenicity

comes from the production of potent exotoxins (**Romero et al., 2011**).

Since *C. perfringens* represents an intestinal commensal organism (Petit *et al.*, 1999), so we should differentiate between toxigenic and non toxigenic ones. Table (5) revealed the results of the prevalence of toxigenic and non- toxigenic types of *C. perfringens* recovered from surveyed rabbits and from feed and water at different Egyptian governorates. A total of 35 *C. perfringens* isolated from rabbits that previously identified morphologically and biochemically were subjected for determination of toxigenicity by I/V inoculation in Swiss mice. The results revealed that 34

out of 35 (97.14%) of *C. perfringens* were toxigenic, while 1.0 (2.86%) was none. The obtained results nearly agree with that proved by Abdel-Rahman *et al.*, (2006) who recorded that the incidence of toxigenic *C. perfringens* was 81.82% while, the non toxigenic ones was 18.18%. On the other hand, Mostafa, (1992) recovered 54.1% toxigenic *C. perfringens* and 45.9% non toxigenic ones. Moreover, Heba, (2010) found 67.3% and 32.7% toxigenic and non toxigenic *C. perfringens*, respectively. The differences in the recovery percentages may be attributed to the difference in samples types or the status of the host.

Four out of 6 (66.66%) *C. perfringens* isolates from feed was toxigenic and 2 (33.33%) isolates was non-toxigenic. The only isolated *C. perfringens* isolate (100%) from water was toxigenic. This result accord with that recorded by Heba, (2010) who isolated *C. perfringens* from feed and water samples obtained from surveyed rabbit farms.

Recovered *C. perfringens* isolates from rabbits, feed and water were typed serologically using Nagler's test, dermonecrotic test in albino Guinea pigs and toxin antitoxin SNT in Swiss mice.

The results revealed that 34 out of 35 *C. perfringens* isolates from rabbits were positive for Nagler's reaction which appeared as opalescence on the plate's side without antitoxins indicating the toxigenicity of these isolates, whereas one isolate showed clear zone representing the non toxigenicity of that isolate (Fig. 1). The toxigenic 34 *C. perfringens* strains exhibited clear zone versus to side of the plate with antitoxin indicating that these strains produce alpha toxin which is secreted by all *C. perfringens* types. That result cleared a preliminary serological typing of the isolated *C. perfringens*. Many investigators used Nagler's reaction as a serological tool for testing the toxigenicity and typing of *C. perfringens* only (Smith, 1955; Hartwigk and Ghenitir, 1969; Mostafa, 1992; Heba, 2010).

Dermonecrotic reaction in albino Guinea pigs was used for differentiation of different *C. perfringens* types. The results demonstrated that 17 out of 35 isolates of *C. perfringens* were single type (48.57%) which were as follow; 8 type (A) (22.85%) as they showed irregular areas of yellowish to green necrosis and the lesions tend to spread downward (Fig. 2A), 3 type (B) (8.57%) as they induced purplish yellow hemorrhagic necrosis (Fig. 2B), 4 type (D) (11.43%) as they showed circular white necrosis which were fully developed within in 24 hrs surrounded by small areas of purplish hemorrhagic necrosis (Fig. 2C) and 2 type (E) (5.71%) as they revealed irregular purplish hemorrhagic necrosis (Fig. 2D). In addition, 17 isolates were mixed types representing 11 types (A and D) (31.42%), 2 types (A and E) (5.71%) and 4 types (B and D) (11.42%). Finally, one isolate proved to be non toxigenic as it did not induce any reaction in Guinea

pigs' skins. Similarly, Singh and Malik, (1968) revealed that out of 18 *C. perfringens* strains, 4 were type A, 2 were type C, 5 were type E and 4 were non toxigenic, also Mostafa, (1992) used dermonecrotic reaction for typing of *C. perfringens* and found types A, B, D and E, respectively at percentages of 15.65, 4.45, 8.89 and 71.11%, while mixed types (A and D) was isolated in percentage of 5%. Furthermore, Heba, (2010) isolated *C. perfringens* types A and D with percentages 47.3 and 20.0%, respectively using the same test.

As well, 4 toxigenic *C. perfringens* feed isolates were 3 type (A) (50%) and 1.0 type (D) (16.6%), while the toxigenic water strain was type A (100%) (Table, 6).

Single 17 toxigenic *C. perfringens* were examined serologically using toxin antitoxin SNT in Swiss mice. The results showed that all mice inoculated with each toxin and its corresponding antitoxin as well as negative control ones were still a life after 3 days observation period, while positive control mice were died within 24 hrs. The results of *C. perfringens* typing which obtained by SNT in Swiss mice were identical and confirmatory to the results of dermonecrotic reaction in albino Guinea pigs as reported by Roskopf *et al.*, (2004) who applied toxin neutralization test in mice to confirm *C. perfringens* types B and D.

The PCR techniques in this study were used for as a recent, rapid and an accurate diagnostic tool for detection and typing of *C. perfringens* (Uzal *et al.*, 1997). Four *C. perfringens* types A, B, D and E were subjected for molecular confirmation of *C. perfringens* and its common toxin (alpha) using conventional PCR. The results illustrated that all tested types were positive for Cp alpha toxin at (324 bp) (Fig., 3A).

Multiplex PCR is a protocol for genotyping of *C. perfringens* as a reliable and specific test for detection of *C. perfringens* toxin genes alpha (Cpa), beta (Cpb), epsilon (etx), iota (iA), enterotoxin (Cpe) and beta-2 toxin (Baums *et al.*, 2004), so we used that technique as a final step for molecular typing of *C. perfringens* and its toxins. The results of multiplex PCR demonstrated that *C. perfringens* type (A) was positive for Cp alpha toxin at (324 bp), *C. perfringens* type (B) was positive for Cp alpha toxin at (324 bp), beta toxin at (196 bp) and epsilon toxin at (655 bp), *C. perfringens* type (D) was positive for Cp alpha toxin at (324 bp) and epsilon toxin at (655 bp) and *C. perfringens* type (E) was positive for Cp alpha toxin at (324 bp) and iota toxin at (446 bp) (Fig. 3B). Parallel results were found by Songer *et al.*, (1993); Songer and Ralph, (1996); Augustynowicz *et al.*, (2000) and Piatti *et al.*, (2004) who developed a PCR assay for detecting of *C. perfringens* alpha toxin gene which gave a characteristic band at 324 bp, however, many authors as Fach and Guillou, (1993); Augustynowicz *et al.*,

(2002); Eman *et al.*, (2006) and Heba, (2010) recorded that *C. perfringens* type A contained alpha toxin gene which gave a characteristic band at 1167 bp. That difference between our results and the others attributed to usage of different oligonucleotide primers. The results of molecular typing of different *C. perfringens* types and its toxins accurately cleared the toxin type which is disagree with that reported by Wang, (1985) and Percy *et al.*, (1993) who mentioned the absence of information on the toxin type. This disagreement may be related to the advances in application of PCR techniques as a recent, rapid, reliable and an accurate method for typing of *C. perfringens* types and its toxins.

Most *C. perfringens* strains carrying the enterotoxin gene (Cpe) are classified as type A isolates. The Cpe gene can be present on either the chromosome or on a large plasmid (Collie and McClane, 1998). Discovered by Gibert *et al.*, (1997), toxin b2 is encoded from the Cpb2 gene, carried on plasmid. The Cpb2 gene can be found in all *C. perfringens* toxin types (Bueschel *et al.*, 2003).

Table (7) summarized the distribution of different types of isolated *C. perfringens* among surveyed rabbit's farms at different Egyptian governorates. The results indicated that, the total number of single type, mixed types as well as, non toxigenic type of *C. perfringens* was 35 representing 12 (Giza), 6 (El-Qaliubiya), 3 (El-Sharkia), 3 (Cairo), 3 (Port-Said), 3 (El-Fayoum), 3 (El-Menoufia) and 1 (Beni Suef). Reviewing available literatures, there was no recorded data about the distribution of different *C. perfringens* types at different Egyptian governorates.

The *in-vitro* sensitivity of the most prevalent toxigenic types of *C. perfringens* that recovered from surveyed rabbit's farms at different governorates of

Egypt to different antibiotics was tabulated in Table (8). All types of *C. perfringens* were highly sensitive for amoxicillin/clavulanic acid and ampicillin. Strains of *C. perfringens* types (E, A and E), (A and E) and (B and D) showed sensitivity to nalidixic acid. Also, all types of *C. perfringens* revealed intermediate sensitivity to enrofloxacin, doxycycline and penicillin, whereas resistance to colistine, erythromycin and lincomycine. These results are nearly similar to these recorded by Secasiu and Pastarnac, (1993) who tested the *in-vitro* the sensitivity of 78 strains of *C. perfringens* isolated from rabbits to some antimicrobial drugs and found that, they were sensitive to penicillin and ampicillin, Abdel-Rahman *et al.*, (2006) who observed that *C. perfringens* isolated from diarrheic rabbits was sensitive to ampicillin and resistant to gentamycin, Agnoletti *et al.*, (2010) who detected that rabbit's *C. perfringens* isolates were sensitive to tylosin and oxytetracyclin and Heba, (2010) who demonstrated that *Clostridial* isolates from diarrheic rabbits were highly sensitive to penicillin and tylosin. On the other hand, our results disagree with Mostafa, (1992) who reported sensitivity of *Clostridial* spp. to colistin sulphate and sulphaquinoxaline/ trimethoprim and resistance to penicillin and tetracycline, Abdel-Rahman *et al.*, (2006) who found that *C. perfringens* isolates were resistance to gentamicin, Heba, (2010) who recorded on resistance of *Clostridial* strains to nalidixic acid, gentamycin, ampicillin, oxytetracycline and doxycycline and Catalán *et al.*, (2010) who observed that strain H28 *C. perfringens* showed resistance to penicillin, ampicillin and tetracycline. This disagreement with other Egyptian investigators may be due to the hazardous usage of different antimicrobial agents, the difference of surveyed governorates and the time of surveillance.

Table (5): Prevalence of toxigenic and non toxigenic types of *C. perfringens* recovered from surveyed rabbits farms as well as from feed and water samples at different Egyptian governorates

No. of recovered <i>C. perfringens</i> examined rabbits	35	Toxigenic <i>C. perfringens</i>		Non-toxigenic <i>C. perfringens</i>	
		No.	%	No.	%
examined rabbits	35	34	97.14	1	2.86
feed samples	6	4	66.66	2	33.33
water samples	1	1	100	-	0

Table (6): Prevalence of *C. perfringens* isolated from feed and water samples in examined rabbit's farms

Types of samples	Recovered <i>C. perfringens</i>	Non- toxigenic <i>C. perfringens</i>		Toxigenic <i>C. perfringens</i>		Types of toxigenic <i>C. perfringens</i>			
	No.	No.	%	No.	%	A		D	
Feed	6	2	33.33	4	66.66	No.	%	No.	%
						3	50	1	16.6
Water	1	-	0	1	100	1	100	-	-

Table (7): Distribution of different types of *C. perfringens* among surveyed rabbit's farms at different Egyptian governorates

Governorates	No. of farms	non-toxicogenic <i>C. perfringens</i> isolates		toxicogenic <i>C. perfringens</i> isolates		<i>C. perfringens</i> types						
		No.	%	No.	%	A	B	D	E	A and D	A and E	B and D
Port-said	2	-	0	3	8.57	-	-	1	-	2	-	-
Giza	4	-	0	12	34.28	3	-	2	1	3	1	2
Cairo	2	-	0	3	8.57	1	-	1	-	1	-	-
Beni Suef	2	-	0	1	2.86	-	1	-	-	-	-	-
El-Fayoum	3	-	0	3	8.57	1	-	-	1	1	-	-
El-Qaliubiya	4	1	2.86	6	17.14	1	-	-	-	2	1	2
El-Sharkia	1	-	0	3	8.57	1	1	-	-	1	-	-
El-Menoufia	1	-	0	3	8.57	1	1	-	-	1	-	-
Total	19	1	2.86	34	97.14	8	3	4	2	11	2	4

%= Percentages were calculated according to the total No. of typed *C. perfringens* (35).

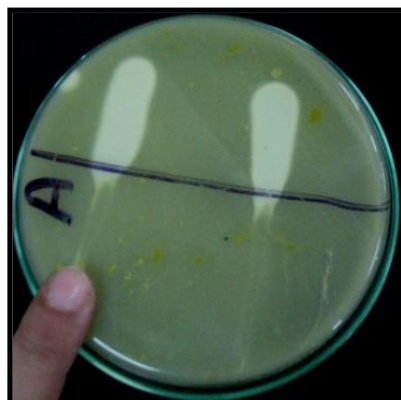
Table (8): *In-vitro* antibiotic sensitivity test of different *C. perfringens* types recovered from surveyed rabbit's farms at different Egyptian governorates.

Active principle	<i>C. perfringens</i> types																				
	A			B			D			E			A and E			A and D			B and D		
	R	IS	S	R	IS	S	R	IS	S	R	IS	S	R	IS	S	R	IS	S	R	IS	S
Amoxicillin / Clavulanic acid (2:1)			+			+			+			+			+			+			+
Cloxacillin		+			+			+			+			+			+			+	
Erythromycin	+				+			+			+			+			+			+	
Gentamicin	+				+			+			+			+			+			+	
Oxytetracycline			+		+			+			+			+			+			+	
Penicillin G		+			+			+			+			+			+			+	
Sulphadoxine / Trimethoprim		+			+			+			+			+			+			+	
Kanamycin		+			+			+			+			+			+			+	
Enrofloxacin		+			+			+			+			+			+			+	
Doxycycline		+			+			+			+			+			+			+	
Ampicillin			+		+			+			+			+			+			+	
Colistine	+				+			+			+			+			+			+	
Lincomycin	+				+			+			+			+			+			+	
Tylosine			+		+			+			+			+			+			+	
Tetracycline		+			+			+			+			+			+			+	
Chlorotetracycline		+			+			+			+			+			+			+	
Nalidixic Acid			+	+				+			+			+			+			+	
Metronidazole		+			+			+			+			+			+			+	

R: Resistance

IS: Intermediated sensitivity

S: Sensitivity

**Fig. (1):** Positive result of Nagler's reaction appears as opalescence on the plate's side without antitoxin and as clear zone on the another side of the plate with antitoxin

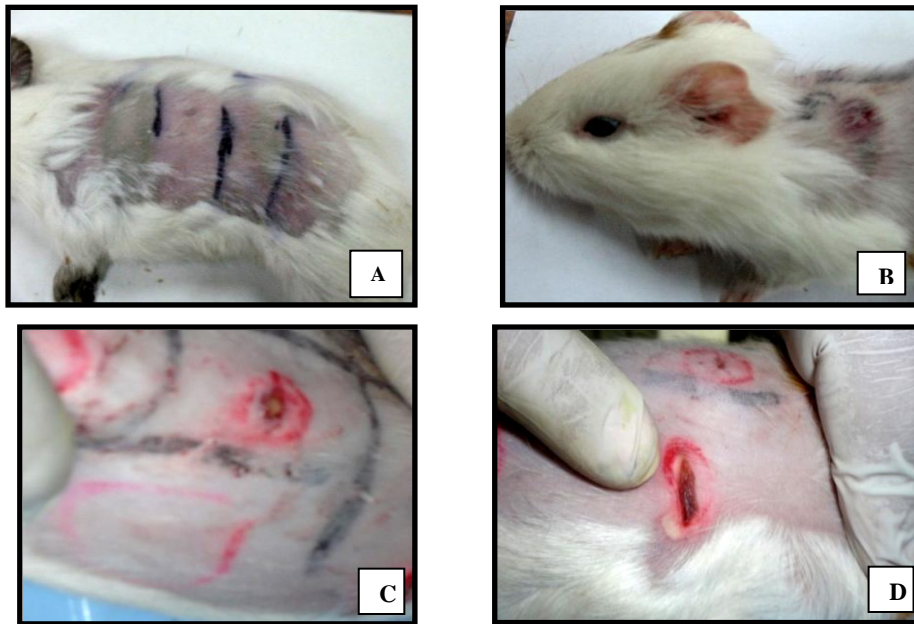


Fig. (2): Results of dermonecrotic reaction in Guinea pigs as the follow; **A:** *C. perfringens* type (A) shows irregular areas of yellowish to green necrosis and the lesions tend to spread downward, **B:** *C. perfringens* type (B) induces purplish yellow hemorrhagic necrosis, **C:** *C. perfringens* type (D) shows circular white necrosis which are fully developed within in 24 hrs surrounded by small areas of purplish hemorrhagic necrosis and **D:** *C. perfringens* type (E) reveals irregular purplish hemorrhagic necrosis.

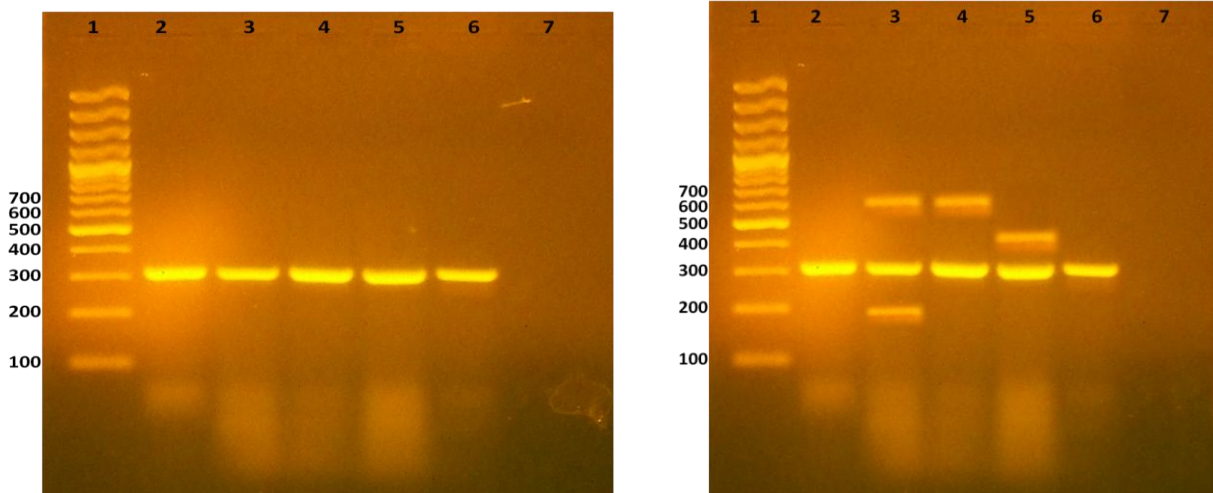


Fig. (3 A): Agarose gel photodocumentation of conventional PCR on genetic material extracted from *C. perfringens* types A, B, D and E. **lane 1**, molecular weight marker (1kb); **lane 2-5**, the samples are positive for Cp alpha toxin (324bp); **lane 6**, positive control (alpha) and **lane 7**, negative control.

Fig. (3 B): Agarose gel photodocumentation of multiplex PCR on genetic material extracted from *C. perfringens* types A, B, D and E. **lane 1**, molecular weight marker (1kb); **lane 2**, CpA sample is positive alpha toxin (324bp); **lane 3**, Cp B sample positive is for alpha toxin (324bp), beta toxin (196bp) and epsilon toxin (655bp); **lane 4**, Cp D sample is positive for alpha toxin (324bp) and epsilon toxin (655bp); **lane 5**, Cp E sample is positive for alpha toxin (324bp) and iota toxin (446bp); **lane 6**, is positive control (alpha toxin) and **lane 7**, is negative control.

Conclusion

In conclusion, the detection of toxigenicity of the isolated *C. perfringens* circulating strains in the Egyptian field is very important as some of them are non toxigenic. Also, accurate, rapid and reliable serological and molecular methods of diagnosis must be applied. It is very important to through light on the role of feed and water as an epidemiological source of infection for early weaned rabbits. Latterly, it is the must to carry out *in vitro* sensitivity test of rabbits *Clostridial* strains to different antimicrobial agents as there are resistance to the common antibiotics used for prevention and control f *Clostridial* enteritis in rabbits.

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Recent Status of *Clostridial* Enteritis Affecting Early Weaned Rabbits in Egypt

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Abstract: A surveillance study for diagnosis of *Clostridial* enteritis affecting early weaned rabbits was carried out on eight Egyptian governorates. Diagnosis based on history, clinical examination, palpation, post-mortem lesions, histopathological examination, as well as isolation of different *Clostridial* species (spp.) causing *Clostridial* enteritis. Two samples representing rectal swabs, liver and intestine were collected from each examined rabbits. A total of 718 samples expressing 329 surveyed rabbits (95 apparently healthy, 204 clinically affected and 30 freshly dead ones). Equal number (19) of feed and water samples were collected from each surveyed farm. All the samples were subjected for *Clostridial* isolation and spp. identification after cultural and biochemical characterization. Tissue samples from liver and intestine of freshly dead rabbits were subjected for histopathological examination. Results revealed that, the most prevalent observed signs were severe diarrhea, bloat accompanied with variable mortalities. Post-mortem lesions were severe enteritis and typhlitis with different degrees of necrosis and hemorrhages associated with gaseous contents. Both kidneys and livers showed congestion and enlargement with peripheral hepatic necrosis. The rate of isolation of *Clostridial* spp. recovered from 756 rabbits, feed and water samples was 311 (41.13%). Only 135 (41.03%) out of 329 examined rabbits was positive for *Clostridial* spp. that was distributed as the following; 109 (80.74%) exhibited single *Clostridial* spp., 4 (2.96%) showed mixed infection with more than one *Clostridial* spp. and 22 (16.29%) were un-typable. From 135 positive *Clostridial* spp.; *Clostridium perfringens* (*C. perfringens*), *C. tertium*, *C. sporogenes*, *C. bifementans*, *C. septicum* and *C. difficile* were recovered as 35 (25.92%), 32 (23.70%), 19 (14.07%), 14 (10.37%), 5 (3.70%) and 4 (2.96%), respectively. Mixed types (*C. perfringens* and *C. tertium*) were represented as 2 (1.48%), (*C. perfringens* and *C. sporogenes*) 1 (0.74%) as well as (*C. perfringens* and *C. difficile*) 1 (0.74%). Seven (18.42%) out of 38 examined feed and water samples was positive for *Clostridial* spp. where *C. perfringens* was the only *Clostridial* spp. that isolated at a rate of 6/19 (31.57%) from feed and 1.0/19 (5.26%) from water samples. The distribution of *Clostridial* spp. among surveyed rabbit's farms at different Egyptian governorates was detected. On histopathological examination, fibrosis in the portal area of liver as well as infiltration with inflammatory cells, and also diffuse inflammatory cells, oedema and necrosis was observed in intestines.

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Keywords: Weaned rabbits; Enteritis; *Clostridium* species; Egypt.

1. Introduction:

Rabbits industry is one of the small livestock industries that play a considerable role in solving the problem of meat shortage in developing countries (Lepas *et al.*, 1997). The domestic rabbits when compared with other livestock animals are characterized by early sexual maturity, high prolificacy, relatively short gestation length, short generation interval, high productive potential, rapid growth, good ability to utilize forages and fibrous plant materials, more efficient feed conversion, lower cost per breeding female and its profitability for small-scale production system (Cheecke, 1986; Finzi and Amici, 1991).

Enteritis in rabbits mainly after weaning is the major cause of economic losses in commercial rabbitaries as it induces high mortalities about 27-50% at 5-7 weeks of age (Scharmann and Wolff, 1985). The epizootic rabbit enteropathy (ERE) has

become a threat to the industry as it can cause between 20 - 70% mortality and up to 100% morbidity in European rabbit commercial farms (de Blas *et al.*, 2012).

Many causes are claimed in induction of enteritis in rabbits as *Clostridium* species (spp.), *Escherichia coli*, *Staphylococcus aureus*, *Salmonella* spp. and *Vibrio* spp. (Hara-Kudo *et al.*, 1996). *Clostridium* spp. are the most important one (Szemerédi *et al.*, 1983) as they adversely affecting rabbit's industry all over the world (Diab *et al.*, 2003).

Clostridial organisms are widely distributed pathogens commonly isolated from the environment and the gastrointestinal tract of rabbits (Hein and Timms, 1972). *Clostridium perfringens* (*C. perfringens*), *C. piliformis*, *C. spiroforme* and *C. difficile* are the most common bacterial causes of enteritis complex in rabbits (Tzika and Saoulidis,

2004). *C. perfringens* is one of the most widely distributed and the most dangerous spp. members of the genus *Clostridium* that affecting rabbit's farms (Timoney *et al.*, 1988). *C. perfringens* vegetative cells cause both histotoxic infections (e.g. gas gangrene) and diseases originating in the intestines (e.g. hemorrhagic necrotizing enteritis or lethal enterotoxemia) (Menglin *et al.*, 2011). Toxigenic types of *C. perfringens* are significant causative agents of enteric disease in domestic animals (Miyashiro *et al.*, 2009).

Severe *C. difficile* toxin- induce rabbit enteritis which characterized by exuberant intestinal tissue inflammation, epithelial disruption and diarrhea (Cirle *et al.*, 2012).

From the above mentioned, this work was designed to through light on the recent status of *Clostridial* enteritis affecting early weaned rabbits and the role of feed and water in transmission of such infection at different Egyptian governorates.

2. Materials and Methods

Field diagnosis of Clostridial enteritis among examined weaned rabbit farms at different Egyptian governorates:

Field diagnosis of Clostridial enteritis based on clinical examination including flock history and palpation of the examined rabbits for detection of abnormal intestinal contents and excessive gases (bloat) was carried out according to Ivanics *et al.*, (1982).

Sampling:

It was applied as Cruickshank *et al.*, (1975). Equal two samples (rectal swabs, liver and intestine) from a total of 718 samples expressing 329 examined rabbits (95 apparently healthy, 204 clinically affected and 30 freshly dead ones) were collected from each examined rabbits in separate sterile bag with serial number corresponding to each flock. Moreover, equal number (19) of feed and water samples were also collected from each examined farm in identified and labeled sterile plastic cups with a serial number corresponding to each flock. All rabbit's samples were rapidly transferred to the laboratory on ice for isolation of *Clostridium* spp. One sample was used for isolation of *C. perfringens*, whereas the other one was used for isolation of spp. other than *C. perfringens*.

Isolation of Clostridium spp.

The method was adopted as Smith and Holdman, (1968). Each sample was transferred aseptically into two separate sterile test tubes containing cooked meat media. The media were previously heated in boiling water bath for 10 min.

To drive off any dissolved oxygen and then rapidly cooled in a cold bath just prior to their inoculation with the samples. Immediate inoculation of samples was done to ensure that cultures were placed under anaerobic conditions. One of the inoculated tubes was heated at 80° C for 10 min. In a water bath with a depth of water more than the level of the tube content to eliminate non spore forming aerobes and allow heat resistant spore former *Clostridium* spp. to grow, while the other tube was left unheated. Both heated and unheated inoculated tubes were incubated at 37° C for 48 hrs. under anaerobic conditions (Gas Pack Jar). A loopful from unheated tubes was then streaked on neomycin sulfate 10% sheep blood agar plate, while the other loopful was taken from heated culture and streaked onto 10% sheep blood agar plates. All the inoculated plates were incubated anaerobically at 37°C for 24-48 hrs. Sub-culturing of the identified culture was restored in cooked meat media and then kept in the refrigerator for purification and further identification.

Identification of Clostridial isolates:

Colonial morphology:

Suspected different Clostridial colonies were examined morphologically (Vaikosen and Muller, 2001).

Microscopical examination:

Smears from suspected Clostridial colonies were stained with Gram's stain and examined microscopically for detection of morphological characters of Clostridial microorganisms (Cruickshank *et al.*, 1975).

Biochemical reactions:

Suspected purified Clostridial isolates were identified biochemically using catalogs, sugar fermentation, gelatin liquefaction, indole, urease, lecithinase and meat digestion as well as motility test according to the schemes of Koneman *et al.*, (1992) and Macfaddin, (2000).

Histopathological examination:

Tissue samples were taken from livers as well as intestines of naturally infected weaned rabbits showed characteristic Clostridial post-mortem lesions and then processed for histopathological examination according to Banchroft *et al.*, (1996).

3. Results and Discussion

Rabbit's industry and production have been developed and expanded all over the world to fill the gap between available and required animal protein for human being. Great attention is directed to the

diseases causing economic losses to this industry from time to time (Finzi and Amici, 1991).

The history of examining rabbit's farms at different Egyptian governorates revealed that, the examined breeds were floundering, Belgian, French, Erks, Hi-plus, Native, New Zealand, Chinchilla, Gabali and Moshtohor with ages ranged from 3 - 9 weeks. The total number of rabbits per farm ranged from 35- 800 rabbits, however, the number of dead rabbits at each examined farm at day of examination ranged from 1.0 to 20. The system of housing of examined rabbits was battery and ground breeding systems. All examined rabbits were fed on commercial ration. Most of examined flocks were vaccinated with rabbit haemorrhagic disease virus vaccine and formalized polyvalent rabbit pasteurellosis vaccine. Also, antibacterial agents were used on some examined farms.

The most commonly observed clinical signs on examined early weaned rabbits at the time of visiting the farm were severe bloat associated with offensive odour doughy brownish diarrhea (Fig. 1) that soil the regions around anuses and hind quarters, inability to walk, depression and ruffled fur. Similar signs on naturally infected rabbits with *Clostridial* organisms were observed by Baskerville *et al.*, (1980); Ivanics *et al.*, (1982); Nagi *et al.*, (1988); Hunter *et al.*, (1992) and Mostafa (1992).

Palpation of the clinically affected rabbits exhibited pain response on palpation of their abdomens which were distended with gases.

The recorded post-mortem lesions of *Clostridial* enteritis in the examined freshly dead rabbits were severe enteritis, typhlitis, ballooning with offensive odour doughy brownish or bloody stained contents mixed with gases, different degrees of necrosis and hemorrhages of the mucosa and the mesenteric blood vessels were engorged with blood (Fig. 2 and 3). Similar findings were recorded by Prescott, (1977). The liver showed congestion, enlargement with sub-capsular hemorrhages, necrosis especially at its margins (Fig. 4) and friability as well as distended gall bladder. Kunstyr *et al.*, (1975) found similar hepatic lesions in rabbits infected with *Clostridial* enteritis. The kidneys were congested and enlarged (Fig. 5) and the urinary bladder was distended with urine (Fig. 6). Our results about kidney lesions resembled these recorded by Baskerville *et al.*, (1980); Nagi *et al.*, (1988); Abdel-Rahman *et al.*, (2006) and Shi Xi Shan *et al.*, (2008) in dead rabbits with different *Clostridial* enteritis.

The results of isolation rate of *Clostridial* spp. from examined rabbit's farms at different Egyptian governorates were observed in Table (1). The results demonstrated that a total of 311 (41.13%) *Clostridial* spp. was isolated from 756 examined samples which

recovered from 329 surveyed rabbits as well as 38 feed and water samples. The obtained isolation rate (41.13%) was higher than McDonal and Duncan, (1975) 37.6%, Szemerédi *et al.*, (1983) 39.0% and Mostafa, (1992) 35.2%. This difference in the isolation rate between this study and the others may be related to the difference in the date of surveillance, season, locality, feeding and housing system.

A total of 135 *Clostridial* isolates recovered from 329 examined rabbits (41.03%) were subjected for spp. identification on the basis of colonial appearance on blood agar, microscopical appearance and biochemical identification. The prevalence of *C. perfringens* and *Clostridial* spp. other than *C. perfringens* isolated from examined rabbits was illustrated in Table (2). The results showed that 109 (80.74%) out of 135 isolated *Clostridial* organisms exhibited single infection, but 4 (2.96%) showed mixed infection with more than *Clostridial* spp., whereas 22 (16.29%) were un-typable spp.

C. perfringens constituted the higher incidence (25.92%), followed by *C. tertium* (23.70%), *C. sporogenes* (14.07%), *C. bifermentans* (10.37%), *C. septicum* (3.70%), *C. difficile* (2.96%) and untypable (16.29%) spp. Nearly similar finding was reported by Mostafa, (1992) who isolated *C. perfringens* in percentage of 23%. However, higher incidences were recorded by Lee *et al.*, (1991) 76.5 %, Abdel-Rahman *et al.*, (2006) 39.3% and Heba, (2010) 86%. That difference between us and others may be attributed to the state of examining rabbits, as *C. perfringens* is one of the most widely distributed and the most dangerous spp. members of the genus *Clostridium* that affecting rabbit's farms (Timoney *et al.*, 1988).

The incidence of *C. tertium* and *C. difficile* in this study were 23.70 and 2.96%, respectively which were nearly comparable to that recorded by Hughes *et al.*, (1983) who recovered *C. tertium* and *C. difficile* in percentages of 25.7 and 2.5%, respectively. Also, Bano *et al.*, (2008) isolated *C. difficile* from the content of the small intestine and impacted caecum of 319 diseased rabbits and 80 apparent healthy ones. On the other hand, the obtained results are disagree with that of Mostafa, (1992) who recorded lower incidence rate of *C. tertium* (0.83%) and *C. difficile* (0.90%) from 358 diseased and apparently healthy surveyed rabbits. In addition, higher percentage (10%) of *C. difficile* isolation from dead rabbits with intestinal pathological lesions was reported by El-Rahman and Atwa, (2006). This disagreement may be owing to the hazardous adopted hygienic measures and the system of housing in the surveyed farms.

This work succeeded in isolation of *C. sporogenes*, *C. bifermentans* and *C. septicum* in rabbits which

causing *Clostridial* enteritis of the surveyed early weaned rabbits. Similarly, Peeters *et al.*, (1986) isolated *C. sporogenes*, *C. bifermentans* and *C. septicum* from rabbit's intestine.

Mixed types between *C. perfringens* and spp. other than *C. perfringens* were *C. perfringens* and *C. tertium* (1.48%), *C. perfringens* and *C. sporogenes* (0.74%) as well as *C. perfringens* and *C. difficile* (0.74%).

Table (3) declared that 7 out of 38 (18.42%) examined feed and water samples was positive for *Clostridial* spp. where *C. perfringens* was the only *Clostridial* spp. that isolated at a rate of 6/19 (31.57%) from feed and 1.0/19 (5.26%) from water samples. No *Clostridial* spp. other than *C. perfringens* was recovered from feed and water. Our results agree with that recorded by Heba, (2010) who recovered *C. perfringens* from feed and water of rabbits.

The distribution of different types of isolated single and un-typable *Clostridial* spp. among surveyed rabbit's farms at Port-Said, Giza, Cairo, Beni Suef, El-Fayoum, El-Qaliubiya, El-Sharkia and El-Menoufia governorates was represented in Table (4). Other Egyptian researchers like Heba, (2010) found that the incidence of *C. perfringens* infection in Giza governorate was 86%, meanwhile, El-Rahman and Atwa, (2006) demonstrated that the incidence rates of *C. perfringens* were 30, 18 and 10% from the intestines, livers and fecal samples, respectively from 300 diseased and died 4-12 weeks old rabbits in El-Menoufia governorate. Moreover, Abdel-Rahman *et*

al., (2006) detected that the incidence rate of *C. perfringens* that isolated from 140 rectal swabs from apparently healthy, diarrheic and dead weaned rabbits was 39.30% in El-Menia and Assuit governorates. This difference in spp. isolation may be attributed to the difference in governorates, season, state of examined rabbits and the usage of antibiotics.

The histopathological examination of livers collected from freshly dead weaned rabbits showed fibrosis of the portal area with newly formed bile ducts (Fig. 7. A), associated with diffuse kupffer cells proliferation and inflammatory cells infiltration in between the hepatocytes (Fig. 7. B). Severe congestion was observed in the central vein while the surrounding hepatic parenchyma was brown pigmented material (Fig. 7. C). Prescott, (1977) and Heba, (2010) found similar histopathological alterations in dead rabbits due to *Clostridial* organisms. The findings of small intestine revealed necrosis involving the mucosal layer with desquamation of the lining epithelium while the underlying sub-mucosa showed oedema, inflammatory cells infiltration and congested blood vessels and capillaries (Fig. 7. D, E and F). Microscopic lesions observed in the large intestine were diffuse mucosal necrosis and ulceration all over the lining epithelium with inflammatory cells infiltration in the lamina propria (Fig. 7. G). The same microscopic changes in the small and large intestine of *C. perfringens* naturally infected dead rabbits were observed by Badagliacca *et al.*, (2010) and Francisco *et al.*, (2012).

Table (1): The isolation rate of *Clostridial* spp. from surveyed rabbit's farms at different Egyptian governorates

Governorate	No. of examined farms	Examined samples			Isolation of <i>Clostridial</i> spp.			
					<i>Clostridial</i> positive samples		<i>Clostridial</i> negative samples	
		Swabs and organs	Feed and water	Total	No.	%	No.	%
Port Said	2	78	4	82	30	36.58	52	63.42
Giza	4	200	8	208	83	39.9	125	60.10
Cairo	2	32	4	36	16	44.44	20	55.55
Beni Suef	2	36	4	40	17	42.5	23	57.5
El-Fayoum	3	128	6	134	59	44.02	75	55.97
El-Qaliubiya	4	120	8	128	55	42.97	73	57.03
El-Sharkia	1	48	2	50	20	40	30	60
EL-Menoufia	1	76	2	78	31	39.74	47	60.26
Total	19	718	38	756	311	41.13	445	58.87

Table (2): Prevalence of *C. perfringens* and *Clostridial* spp. other than *C. perfringens* isolated from examined rabbits at different Egyptian governorates.

No. of examined rabbits	<i>Clostridial</i> spp.	No. of identified <i>Clostridial</i> spp.	%
329	Single types	109	80.74
	<i>C. perfringens</i>	35	25.92
	<i>C. tertium</i>	32	23.70
	<i>C. sporogenes</i>	19	14.07
	<i>C. bifermentans</i>	14	10.37
	<i>C. septicum</i>	5	3.70
	<i>C. difficile</i>	4	2.96
	Mixed types	4	2.96
	<i>C. perfringens</i> + <i>C. tertium</i>	2	1.48
	<i>C. perfringens</i> + <i>C. sporogenes</i>	1	0.74
<i>C. perfringens</i> + <i>C. difficile</i>	1	0.74	
	Un-tytable	22	16.29
Total		135	

Table (3): Prevalence of *C. perfringens* isolated from feed and water samples in examined rabbit's farms at different Egyptian governorates

Type of sample	No. of samples	Recovered <i>C. perfringens</i>	
		No.	%
Feed	19	6	31.57
Water	19	1	5.26
Total	38	7	18.42

Table (4): Distribution of single and un-tytable *Clostridial* spp. among surveyed rabbit's farms at different Egyptian governorates

Governorate	No. of examined farms	<i>C. perfringens</i>	<i>C. tertium</i>	<i>C. sporogenes</i>	<i>C. bifermentans</i>	<i>C. septicum</i>	<i>C. difficile</i>	Un-tytable <i>Clostridial</i> spp.
Port Said	2	3	5	1	2	-	1	9
Giza	4	12	10	7	3	1	1	2
Cairo	2	4	1	-	1	2	-	4
Beni Suef	2	3	3	1	-	1	1	2
El-Fayoum	3	7	4	6	5	-	1	1
El-Qaliubiya	4	3	2	2	1	-	-	2
El-Sharkia	1	2	3	1	2	-	-	1
El-Menoufia	1	1	4	1	-	1	-	1
Total	19	35	32	19	14	5	4	22

**Fig. (1):** A rabbit shows severe bloat and doughy brownish diarrhea.**Fig. (2):** Large intestine of rabbit exhibited ballooning and filled with gases**Fig. (3):** Small intestine of a rabbit shows different degrees of enteritis, the intestine distended with gases and the mesenteric blood vessels are engorged with blood.



Fig. (4): A rabbit's liver reveals congestion, enlargement, sub-capsular hemorrhage and necrosis especially at liver's margins (arrow)

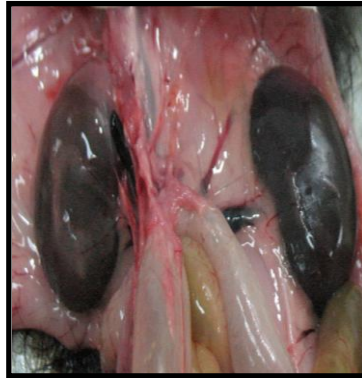


Fig. (5): Congested and enlargement of a rabbit's kidneys.



Fig. (6): A rabbit with severely distended urinary bladder with urine.

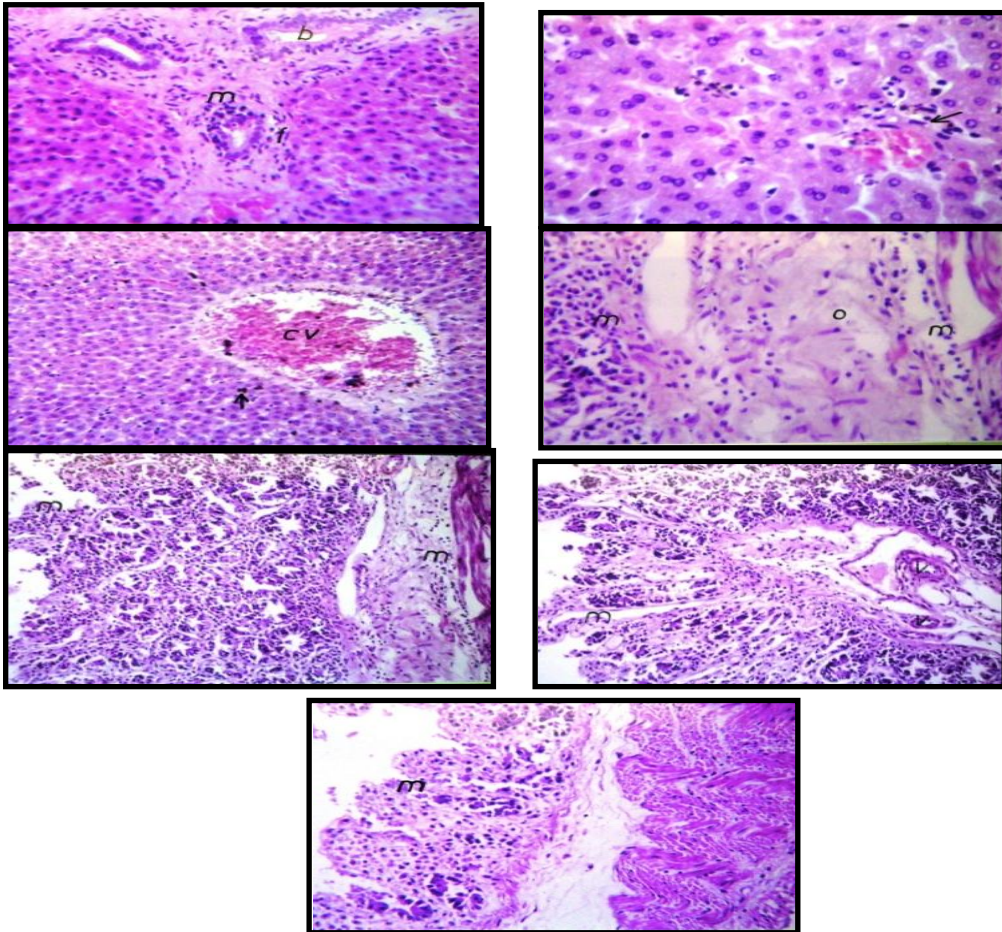


Fig. (7): The histopathological findings are as follow; (A): Liver of a rabbit showing fibrosis in the portal area (f) with multiple newly formed bile ducts (b). **H&E X 64**, (B): Liver of a rabbit showing diffuse Kupffer cells proliferation (arrow) with inflammatory cells infiltration in between the hepatocytes. **H&E X 80**, (C): Liver of a rabbit showing severe congestion in central vein (cv) with diffuse brown pigmented material (arrow) in between hepatocytes. **H&E X 40**, (D): Small intestine of a rabbit showing diffuse inflammatory cells infiltration (m) and oedema (O) in submucosal layer. **H&E X 40**, (E): Small intestine of a rabbit showing diffuse inflammatory cells infiltration (m) and oedema in submucosal layer. **H&E X 80**, (F): Small intestine of a rabbit showing mucosal necrosis (m) with oedema and congestion in blood vessels (v) of submucosa. **H&E X 40** and (G): Large intestine of a rabbit showing necrosis in the mucosal layer (m) and ulceration with inflammatory cell in lamina propria. **H&E X 64**.

Conclusion

Finally, it could be concluded that *Clostridial* spp. are incriminated in the induction of enteritis problem in rabbits with high percentages. There are different types of *Clostridial* spp. circulating in weaned rabbit's farms at different Egyptian governorates, so it should be taken into consideration during the research work. In addition, contamination of feed and water with *C. perfringens* plays a prominent role in the fulmination of this problem, so it is recommended developing of new management strategies including testing feed ingredients periodically for spore contamination and also checking the water sources for monitoring management programs.

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Determination of Factors Affecting on Risk Incidence in State's Civil Projects: Case Study of Tehran and Zanzan Provinces

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Abstract: Improper designing, technological complexities, higher number of organizations and individuals involving in a project, diversity of the required specialties and extensive scope of the activities are among the reasons cause the state's civil project not to be completed within the time and cost as determined initially. So, the application of a well-organized system to optimize the investment in the civil project seems inevitable. The optimization procedures which cause the project to be completed within the initial time and cost may play a key role to eliminate the adverse and negative effects of the above-mentioned factors. This research is intended to examine the effect of application of risk management on elimination of such problems. According to the results, the contracting companies working in Zanzan and Tehran provinces have sometimes applied the techniques of project management and different factors such as the lack of adequate arrangement specifically, in Zanzan province, too many errors in feasibility and designing phases, contradiction and changes of regulations, variations and economic as well as political crises and disregard of project management standards are among main issues affecting on risk incidence in civil projects.

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1. Introduction

Civil projects are essential prerequisites for development and industrialization of the developing countries. Annual budget deficit, higher rate of inflation, irregularities existing in performance procedures, failure to achieve the ultimate goals of the project, the lack of competent consulting and contracting companies, failure to achieve the modern technology and to discontinue the under construction projects in the developing countries are among issues cause the costs required for completion the projects to be become doubled or tripled than the costs as expected initially. The lack of adequate management to allocate the budget for civil projects and improper as well as inaccurate performance of the project will impose a huge expense during commissioning period and cause the quality and efficiency of the project to be impaired. These issues will result to adverse cycle's altogether which aggravate each other and threaten the development of the countries as well. Each year, a significant part of national income is dedicated to investment in civil and infrastructure projects. Nowadays, given Improper designing, technological complexities, higher number of organizations and individuals involving in a project, diversity of the required specialties and extensive scope of the activities, the executors and designers of civil projects

found themselves confronted by many problems to achieve their predetermined goals and consequently these projects will not be completed within the time and costs as determined initially.

According to the studies, the main reason of these problems may be attributed to the lack of prediction of probable risks throughout the life of project. Today, implementation of risk management as one of nine clauses of PMBOK Standard is considered as a requirement in advanced countries to be met during construction projects. Given the effect of different factors on this issue specifically in huge investment public projects as well the sensitivity of the governmental, Non-governmental and supervisory organizations is of an extraordinary importance. Risk management, in fact, includes a series of activities such as determination of risk factors, risk analysis, determination of risk probability and its influence, examination of different scenarios of reaction to risk and control of risk. This paper intends to scrutinize the problems of civil projects and risk management technique. Then, the status of application of risk management in civil projects of Zanzan and Tehran provinces will be examined statistically using a field study and the effect of implementation of risk management to eliminate a part of state civil projects' problems will be examined statistically. Finally, the

results and findings of the researchers are analyzed and the authors will provide their own suggestions.

2. Status of State's Civil Projects

First of all, the status of state's civil projects will be studied from planning organization and strategic management standpoint and according to the reports issued in 2005. The results achieved in this way will help the researchers to formulate the objectives and research-related hypotheses. Since the reports on civil projects have not been issued after 2005, the examination of these reports is not possible.

2.1. Delay in Execution of State's Civil Project

Taking into consideration of the delay reasons of projects which their execution has fallen behind the time schedule are among the factors have a key role to determine the weaknesses of civil projects. Here, the major reasons of delay and their influence upon the projects have fallen behind the time schedule will be studied. In all issued reports, the delay factors are classified into three categories as follows: administrative factors (administrative organization, contractor, designing advisor and supervising advisor), credit-related factors (approved credit, budget allocation, payment made by the treasury and budget absorption) and problems resulting from environmental and social factors (shortage of materials, social problems, land and other similar factors. According to our findings, the highest rate of delays in administrative, credit and environmental and social factors are for administrative organizations (11.8%), budget deficit (30.2%) and land preparation (5.5%), respectively. In connection with the problems resulting from the weakness of administrative organizations, Islamic Revolution Housing Foundation has contributed to more delays with 21%.

About 60 % of delays in the projects run by Presidency Institution are attributed to the problems resulting from budget allocation deficit, while in connection with the problems resulting from credit-related factors, more than 42.1% of the projects handled by the Islamic Revolution Housing Foundation found them confronted by the approved credit deficit. Nearly 6.7% of delays caused in the civil projects run by the Ministry of Power are attributed to land preparation which is the highest rate among major administrative organizations, while the rate of delays caused in the civil projects run by the Ministry of Road & Transportation is only 6.4%.

2.2. The Quality of Execution of State's Civil Projects

According to the results obtained from supervisory visits' data as well as given the indicators as defined for the quality of civil projects, the execution quality values of 20.4%, 50.2%, 22.2% and 7.1% are evaluated as excellent, good, medium and weak quality, respectively. The quality of 33% of the projects run by the Ministry of Industries and Mines is evaluated as

excellent and the quality of 59.7% of the projects run by the Ministry of Science, Research and Technology is evaluated as good which in comparison with similar values in major administrative organization are considered as the highest values of quality execution.

2.3. Status of Execution of State's Civil Projects from Statistical Standpoint

Out of 3513 under supervision projects, it was supposed that the numbers of 1484 projects to be completed till the end of 2008. The results of supervisory visits indicate that the numbers of 613 projects (i.e. 41.3%) have been completed. The rate of completed projects replaced by the new one is 96.7%. It means that the numbers of 96.7 projects has been launched in comparison with each one hundred completed projects [1]. Among the major administrative organizations, the percent of projects completed by the Ministry of Industries and Mines (i.e. 12.5%) is considered as the highest value and the Presidency Institution with 11.1% has fallen behind the time schedule.

2.4. Weighted Average of Execution Duration of State's Civil Projects

Since the duration of execution of new projects has been evaluated 2.6 years and the weighted average of duration of execution of completed projects has been evaluated 10.7 years, so the administrative organizations have to consider all necessary factors in their executive planning in order to achieve their predicted objectives during execution phases through a proper resources management. By comparison of the average of duration of execution of new projects with the average of duration of completion of the projects in administrative organizations, it seems that the said organizations have not paid any attention to real duration of execution and instead have focused the concentration on the sustainability of the projects and commencement of new ones.

2.5. Examination of Status of State's Civil Projects as well as Target Provinces (Tehran & Zanjan) in 2007 and their Comparison

Given the performance of administrative organizations, the results of evaluation of national civil projects in different provinces of the country are as follows (Table 1).

As shown in the Table (1), Markazi Province has achieved the first rank with the point of 77, while Gilan province has achieved the last rank with the point of 30.4. The indicator of completion fulfillment of the projects shows that about 72.7% of predicted goals of national projects of Qazvin province in 2007 have been fulfilled. The value of latter indicator in Kohkilooyeh and Boyerahmad province is 12.5% which is the least value. The examination of the quality of execution of national civil projects as one of the most effective indicators demonstrates that the quality of the projects

of Zanjan province as one of targeted provinces of the present research is more ideal than other provinces. The highest value of indicator of achievement of one-year objectives relates to Zanjan province (107.3) and the lowest value is related to Ilam province (23.6). Since the quality of execution plays a key role in achieving the civil objectives of the state and makes possible to optimize the productivity of the resources, the elements' points of execution quality of national civil projects have been provided in terms of the province. This section includes general specifications of national civil projects in 2007 which are separated in terms of the provinces and includes the number and the amount of credit allocated to civil projects of state's provinces.

In 2007, more than 1696 agreements on civil project operation have been executed and within these agreements a credit more than Rls 191.3 thousands billion has been allocated for execution of 5014 civil projects. With 751 civil projects (15% out of total civil projects), Tehran province has the highest numbers of national civil projects among the different provinces of the country. In terms of credit allocation, Tehran province has absorbed a credit amounts to Rls 14.8 thousands billion (equal to 7.7% of total credits approved). Zanjan province has observed a credit amounts to Rls 1.2 thousands billion (equal to 1.7% of total credits approved).

Table1. , the results of evaluation of national civil projects in different provinces of the country

Province	% of Completion Fulfilled	Execution Quality	Achievement of One-year Objectives	Term of Execution	Method of work assignment	Delay Causes	Points
Zanjan	39.4	94.2	107.3	29.5	76.8	82.5	73.4
Qazvin	72.7	84.8	81.3	29.8	71.6	82.4	72
East Azerbaijan	44.1	88.6	50	48.6	78.6	71.7	66.4
Tehran	48.5	83.3	60.6	39.4	48.7	84.7	64.9
Hamedan	62.5	80.1	44.8	28.3	71.3	63.7	60.8
Semnan	34.1	77.6	40.5	39.1	61.4	88.2	58.4
Kordestan	48	82.5	35.5	31.6	67.7	22.8	54.4
Mazandaran	44.7	60.8	50.6	31.4	68	47.3	50.8
Ardebil	50	67.4	45.1	31	68.3	14.9	50
Gilan	31.7	10.9	32.5	27.9	74.6	76.3	30.4

For the purpose of calculation, Evaluation point of 100 has been considered.

2.6. Risk Management

There are many definitions of risk that vary by different application domains. In economic theory, risk refers to situations where the decision maker can assign probabilities to different possible outcomes (Knight, 1921). Similarly, in decision theory, risk is the fact that the decision is made under the condition of known probability over the states of nature (Luce and Raiffa, 1957). In project management, there is no consistent definition for risk (Ward and Chapman, 2003; Perminova et al., 2008). In the project management body of knowledge (Project Management Institute, 2004), risk is considered as "an uncertain event or condition that, if it occurs, has a positive (opportunity) or negative (threat) impact on project objectives." However, many practitioners and researchers in project management still consider risk to be more related to adverse effects on project performance (Williams, 1995; Boehm and DeMarco, 1997; Smith and Merritt, 2002; Ward and Chapman, 2003). From this perspective, project risk management seems to be about identifying and managing threats to the project. There is no doubt that risk is one of the factors give rise to above-mentioned problems and inadequacies. Literally, risk has been likened to two sides of a coin which one of its side represents the risk and its other side represents the damage. In other words, risk is a

multidimensional cube which each of its dimensions represents damage and intensity of damage, unreliability and risk level. It means that risk includes all above-mentioned concepts and this is for the reason that other words have been used instead of risk and all of them include the risk. Project risk management, one of the main subjects of project management (Raz & Michael, 2001), is the planning, organization, monitoring and control of all aspects of a project and it consists of risk identification, risk qualification, risk response development, and risk response control (Saynisch, 2005). Miller and Lessard (2001) pointed out that understanding and managing project risks in large engineering projects are challenging tasks at the early phase.

3. Methodology

It defines the approach, tools and data resources may be used for risk management in the project. The sufficiency of data availability and the flexibility existed in risk management and various types of measurements depend on the phase of project.

Roles and Responsibilities:

To take any action in connection with risk management planning, the leader will appoint the supporter and the members of risk management team. Risk management teams do not have any role to run the project and accordingly they can independently analyze

the project risks more fairly than project's investing team.

Budgeting:

The budget needed for risk management of the project is determined through budgeting.

Time Frequency:

It means that how often will risk management processes apply throughout the cycle of a project life. In order to make an effective decision, the results have to be prepared as early as possible. These decisions have to be checked periodically during the execution of the project.

Factoring and Interpretation:

Given the type and time frequency of qualitative and quantitative analysis of a risk, factoring and proper interpretation methods are applied. To ensure the compatibility, the methods and factoring have to be determined in advance.

Threshold:

It is considered as a measure on the basis of which a necessary action is taken. (By whom and how). Any employer, customer or a project investor may have a different threshold of risk. An acceptable threshold as an indicator helps the project team to measure the ratio of efficacy of execution of a reaction plan to a risk.

Reporting formats:

It describes the content and format of reaction plan to a risk. Reporting formats will determine how the results of risk management processes are documented, analyzed and transferred to the project team, internal and external beneficiaries, investors and others.

Follow-up:

It documents all the aspects of risky activities to be used in current projects. Those audited and not audited risk processes and their auditing methods are documented.

Field Study

As mentioned earlier, arrangement and distribution of standard questionnaires among statistical society of the research is one of the main tools for collecting the required information to examine the status of risk management in state's civil projects and determine the effect of risk management on eliminating of some of problems of such projects and collect the ideas of respective experts in this regard. The structure and questions of such questionnaires are designed on the basis of second part's library studies, authors' experiences; research hypotheses as well as the findings of other researchers. The final and main result of such questionnaires has a key role to determine the objectives of the research.

3.1 Statistical Population

Statistical Population of this research is consisted of a group of experts who have Bachelor's degree or higher and have some valuable experiences in

executing the state's civil project as the member of employer, consultant or contractor. Given their involvement in civil and industrial projects and direct participation in the projects, they can provide the research with proper and valuable information. Consequently, a single questionnaire is presented to each respondent personally and the number of completed questionnaires is considered as the result of follow-up made by the authors.

3.2. The Objectives of the Research

The main objective of arranging such questionnaires is to examine the status of risk management in state's civil projects and determine the effect of risk management on eliminating of some of problems of such projects.

3.3. Questions of Questionnaire:

This questionnaire consists of three kinds of questions as follows:

First type questions:

Some questions on the specifications and experiences of respondent. These questions are as follows: Age, work experience, educational degree, field of study and executive position.

Second type questions:

Examination of the condition of civil projects of Zanjan and Tehran provinces in terms of application of techniques and approaches is one of the objectives followed by the researchers. These techniques and approaches may directly and or indirectly improve the risk management in the projects. For instance, insurance, consultant, standard, software, information systems and project management team working as well as quantitative techniques of risk management, value engineering, and value added engineering and hierarchical analysis may directly and or indirectly improve the risk management in the projects.

Work experience, educational degree, field of study and executive position may be regarded as the requirements and prerequisite of implementation of risk management system in the construction-related projects.

Third type questions:

These questions are regarded as the main questions of questionnaire and all hypotheses of the research are based on them. These questions intend to gather the opinions and views of statistical society about the factors affecting on increasing the project risk. These questions will examine the factors affecting on increasing the project risk in terms of three dimensions of time, cost and quality. Two hypotheses out of set of hypotheses of the research are hidden in these questions.

4. Research Hypotheses

- 1- Inadequacies of designing phase may give rise to risk occurrence in time, quality and cost of execution of the projects. (f1)

- 2- Selection of an incompetent consultant may give rise to risk occurrence in time, quality and cost of execution of the projects. (f2)
- 3- Failure to do the feasibility studies (technical, social, economic, financial, organizational, political and funding the project) may give rise to risk occurrence in time, quality and cost of execution of the projects. (f3)
- 4- Ignorance of expectations of the beneficiaries or the customer may give rise to risk occurrence in time, quality and cost of execution of the projects. (f4)
- 5- Any contradictions and inconsistencies between regulations of construction by-laws (civil projects) may give rise to risk occurrence in time, quality and cost of execution of the projects. (f5)
- 6- The economic and social issues and crises may give rise to risk occurrence in time, quality and cost of execution of the projects. (f6)
- 7- Frequent changes of the laws and procedures may give rise to risk occurrence in time, quality and cost of execution of the projects. (f7)
- 8- Many disagreements and contradictions between the executors of the project (such as consultant, contractor and employer) may give rise to risk occurrence in time, quality and cost of execution of the projects. (f8)
- 9- Improper use of project's planning and controlling systems may give rise to risk occurrence in time, quality and cost of execution of the projects. (f9)
- 10- The necessary requirements to implement risk management in civil projects of Tehran and Zanjan Cities are met. (f20)
- 11- The effect of the factors cause the cost-related risks of civil projects to be increased (f30)
- 12- The effect of the factors cause the time-related risks of civil projects to be increased (f31)
- 13- The effect of the factors cause the quality-related risks of civil projects to be increased (f32)

4.1. Analysis of Questionnaires

After extensive follow-up, the numbers of 35 questionnaires were obtained from the researchers. The

measurement criteria of questionnaires of second and third types include five choices as Likert as follows. Here, three parts of this questionnaire will be considered:

Criteria	1	2	3	4	5
2 nd Type	In most times	Always	Sometimes	Seldom	Never
3 rd Type	Very much	Much	Middle	Little	Very little

Questions about the Specifications of the Respondents:

Work Experience	Age	City	Valid	N
30	30	30		
0	0	0	Missing	
7.33	31.57	1.57	Mean	
1	24	1	Minimum	
18	49	2	Maximum	

Second Type Questions: Status Evaluation of Civil Projects of Tehran and Zanjan Provinces:

- 1- To place different insurance policies in construction industry;
- 2- Use of project management consultant;
- 3- Application of project management knowledge;
- 4- Application of project management software;
- 5- Use of information systems of project management;
- 6- Use of specialized committee during different processes of the project (team working);
- 7- Application of risk management techniques such as Monte Carlo Method;
- 8- Use of Value Engineering Technique;
- 9- Application of Value Added Management techniques;
- 10- Application of hierarchical analysis technique.

	Valid N	Missing	Mean	Std. Deviation	Skewness	Std. Error of Skewness
To place different insurance policies in construction industry	30	0	3.80	1.031	0.178	0.427
Use of project management consultant	30	0	3.57	1.073	0.095	0.427
Application of project management knowledge	30	0	3.30	1.022	0.378	0.427
Application of project management software	30	0	3.23	1.165	0.212	0.427
Use of information systems of project management	30	0	3.13	1.106	0.539	0.427
Use of specialized committee during different processes of the project	30	0	2.63	1.066	0.084	0.427
Application of risk management techniques such as Monte Carlo Method	30	0	2.77	1.040	0.110	0.427
Use of Value Engineering Technique	30	0	2.97	1.033	0.070	0.427
Application of Value Added Management techniques	30	0	3.23	1.278	0.061	0.427
Application of hierarchical analysis technique	30	0	3.40	1.102	0.106	0.427

Prior to analyze the hypotheses and in order to examine the condition of the civil projects of Tehran and Zanjan provinces in terms of application of the risks, approaches and software related to project's risk management, the researchers of the present research have asked some questions from the statistical society. The statistical society has claimed that it has placed insurance policies in relation to construction industry generally. Similarly, it has sometimes used the problems of project management and project management knowledge as well as project control software. Of course, given the knowledge the researchers have about the atmosphere of state's civil projects, these statistics have to be adjusted and to be decreased by one degree at least. Because, it is likely that the pride issue and supporting the project have affected upon answering these questions. However, these statistics may provide us with a criterion although with a minor error for judgment. As shown in the above table, the statistical society has stated that risk management technique, value engineering and value added management have been applied seldom to sometimes in civil projects. Risk management is considered in details in the present essay. Value engineering is regarded as a technique which has been used for last 50 years to decrease the costs or eliminate the problems in some of projects and has brought about brilliant results. Value added management technique is regarded as a technique which examines the time progress, cost progress and physical progress of the projects altogether. It determines the condition and weaknesses of the project and examines the future of the project as well. These three techniques are always used in major projects in advanced countries.

The Main Questions of the Questionnaire (Hypotheses No.: 1 to 13)

Uniform Distribution Test

There are various methods to do sampling. Here, simple random sampling method is used. Prior to test the hypotheses, we test the questionnaire using uniform test method to find out that the sample selected from the statistical society is randomly or uniformly.

The simplest discrete probability distribution is that distribution whose random variable has equal probability. Such distribution is referred to uniform distribution. For instance, if the values of random variable of $x (x_1, x_2, \dots, x)$ select an equal probability, then its discrete uniform distribution is given as follows:

$$F(x;k)=1/k \quad x=x_1, x_2, \dots, x_k$$

Here, we intend to demonstrate whether each six measures of the questionnaire, i.e., 1) very ineffective, 2) low effective, 3) relatively ineffective, 4) relatively effective, 5) effective, 6) very effective has equal probability or not. In other words, $f(x;6)=1/6$?

To do this, Kolmogorov-Smirnov Uniform Test will be used. As shown in the table, since output sig of the table is lower than 0.05 for all variables except for hypothesis of f20, then we can conclude that any of our variables except for variables of second type questions do not follow a uniform distribution pattern. In other words, the probability of each six measures to be selected will be varied.

The results of Kolmogorov-Smirnov Uniform Test are shown in the following table.

f32	f31	f30	f20	f10	f9	f7	f6	f5	f4	f3	f2	f1		
30	30	30	30	30	30	30	30	30	30	30	30	30	N	
2.00	2.00	2.00	2.00	2	2	2	2	2	2	2	2	2	Minimum	Uniform Parameters(a,b)
4.00	4.00	5.00	5.00	5	5	5	4	5	5	5	4	5	Maximum	
.433	.567	.433	.233	.400	.300	.367	.433	.367	.267	.300	.433	.400	Absolute	Most Extreme Differences
.100	.033	.300	.233	.167	.167	.300	.100	.233	.233	.300	.167	.200	Positive	
-.433	-.567	-.433	-.167	-.400	-.300	-.367	-.433	-.367	-.267	-.300	-.433	-.400	Negative	
2.373	3.104	2.373	1.278	2.191	1.643	2.008	2.373	2.008	1.461	1.643	2.373	2.191	Kolmogorov-Smirnov Z	
.000	.000	.000	.076	.000	.009	.001	.000	.001	.028	.009	.000	.000	Asymp. Sig. (2-tailed)	

a: Test distribution is Uniform.

b: Calculated from data.

Determination of Questionnaire's Error:

Prior to commence the analysis, the questionnaire's error has to be determined given the size of the sample and statistical society. Hypotheses used for calculation of the error are as follows:

Acceptable range is %95.

As a result:

$$Z_{\alpha/2}=1.67$$

$$n=30$$

$$P=1/2$$

$$N=160$$

The questionnaire's error is calculated according to the following equation:

$$n = \frac{N(Z\alpha/2)2p(1-P)}{(N-1)\epsilon^2 + (Z\alpha/2)P(1-P)}$$

By substituting the values, the value of ϵ is equal to 14.5%. Since we have chosen 95% for our project as well as given the cost-related limitations of the project, this value of 14.5% will be acceptable.

Validation of the Questionnaires:

To validate the questionnaires, SPSS13 software has been used. Cronbach's Alpha factor is used for this purpose. After validation of the questionnaire taking into consideration of Cronbach's

Alpha factor and each of the questions, it became evident that the general factor of Cronbach's Alpha is 0.858.

Table: Questions of the questionnaire

Table 6. Reliability Statistics		
N of items	Cronbach's Alpha based on standardized items	Cronbach's Alpha
13	0.880	0.858

Cronbach's Alpha if Item Deleted	Squared Multiple Correlation	Corrected Item-Total Correlation	Scale Variance if Item Deleted	Scale Mean if Item Deleted	
.839	.719	.659	27.237	42.7333	f1
.843	.703	.593	27.390	43.3000	f2
.847	.754	.536	28.585	42.9667	f3
.842	.628	.616	26.961	43.0667	f4
.841	.745	.619	26.809	42.8667	f5
.848	.566	.526	28.392	43.2333	f6
.845	.703	.595	28.395	42.8667	f7
.859	.512	.353	28.993	42.8000	f9
.855	.647	.414	28.409	42.7333	f10
.888	.401	.072	30.626	43.1667	f20
.834	.834	.819	27.338	42.8000	f30
.833	.904	.826	27.275	43.0333	f31
.843	.704	.618	28.185	43.2333	f32

Description of Research:

As stated at the outset of this part, prior to duplication and distribution of the questionnaire, a final sample was completed by two qualified members of the statistical society on experimental basis and its probable problems were eliminated. Then the corrected questionnaire was seen by the esteemed professor and the respective consultant and approved accordingly. The context of the research was related prior to distribution of the research as described above. Then, the questionnaires were collected and for the purpose of examination of the questionnaire's relation, a structural relation method has been used. According to this method, the questions are classified based on the hypotheses and through SPSS13 Software; factor-based analysis was made for each classes.

Descriptive Test of Hypotheses:

Now, the hypotheses are coded once again according to their respective questions. Consequently, the hypotheses of 1 to 13 are changed into the codes of f1 to f13.

When the hypotheses are coded, they are examined individually in terms of whether they follow normal distribution or not. To do this, Kolmogorov-

Smirnov test is used. This method is based on maximum difference between two observed cumulative distributions in two groups. Given the output signification, it would become clear that which variable complies with normal distribution. If the output signification (p-value) shown as sig is known, there would be no need to know the statistical value of t and refer to t probable table for determination or proving zero assumption.

P-value shows the value of the area located under the curve (t) at the right side of (t) point and at left side of (-t) point. Here, n-1 stands for freedom of degree and $|t| > 1/96$. When (sig < 0/05), then H_1 assumption is rejected. In this case, we say that "the test is significant". Now, if the distance between the significant value and the value of 0.05 increases (or is lesser), the intensity of test signification will be more. It means that we will reject the H_0 more reliably.

Given the above explanations as well as the output of Kolmogorov-Smirnov test, it would become clear that only variable of f20 follows the normal distribution and H_0 assumption is rejected for other variables.

$$H_0 : \text{oki } \text{SIG} < 0.05$$

Opposite Assumption: H₁

If we intend to use normal distribution for our test and where we want to know whether a sample is belonged to a particular society, its average as well as its standard deviation has to be known. But often we

do not know anything about its standard deviation and then it is necessary to obtain it from the sample's standard deviation, provided that this distribution is near to normal distribution.

f32	f31	f30	f20	f10	f9	f7	f6	f5	f4	f3	f2	f1		
30	30	30	30	30	30	30	30	30	30	30	30	30	N	
3.3333	3.5333	3.7667	3.4000	3.83	3.77	3.70	3.33	3.70	3.50	3.60	3.27	3.83	Mean	Normal Parameters (a,b)
.60648	.57135	.56832	1.03724	.791	.774	.596	.661	.794	.777	.621	.740	.699	Std. Deviation	
.309	.360	.426	.185	.317	.252	.393	.277	.347	.273	.340	.273	.328	Absolute	Most Extreme Differences
.309	.258	.307	.183	.250	.215	.274	.260	.253	.273	.233	.207	.272	Positive	
-.264	-.360	-.426	-.185	-.317	-.252	-.393	-.277	-.347	-.207	-.340	-.273	-.328	Negative	
1.691	1.970	2.333	1.014	1.735	1.379	2.151	1.516	1.901	1.498	1.863	1.493	1.794	Kolmogorov-Smirnov Z	
.007	.001	.000	.255	.005	.045	.000	.020	.001	.023	.002	.023	.003	Asymp. Sig. (2-tailed)	

- a: Test distribution is Normal.
- b: Calculated from data.

To do this, we have used t- distribution. It is similar to normal distribution, but the area located at under the curve is greater at two extremes and its shape will vary based on the number of the samples. In other words, whenever the numbers of the samples are increased, t-distribution is more similar to normal distribution.

Now, we consider again our main assumptions:
 H₀= μ=3
 H₁= μ≠3

$$\bar{X} = \frac{\sum f_i X_i}{n} = 1/6\{1 + 2 + 3 + 4 + 5\} = 3$$

Generally speaking, we are going to know what the answers of the respondents are alike. Are they upper than the average of the codes? "Effective" or lower than the average of the codes. "Ineffective".

Test of Hypothesis of f20 (Inferential)

As stated before, since the significant value of above hypothesis for variable f20 is equal to 0.255, then the assumption of H₀, i.e. the normality of f20 is accepted. It means that the test is significant. Since, f20 follows a normal distribution, then a unilateral t-test has to be used for examination of I assumption. Given the output of t test, since, the significant value is equal to 0.000, then H₀ assumption in I test is rejected. It means that the questions included in the questionnaire were important for the respondents.

Std. Error Mean	Std. Deviation	Mean	N	
.18937	1.03724	3.4000	30	f20

Test Value = 0					
95% Confidence Interval of the Difference		Mean Difference	Sig. (2-tailed)	df	t
Upper	Lower				
3.7873	3.0127	3.40000	.000	29	17.954

Table 3-7 show T- Distribution.

Now, we have to find the direction of this significance. Effective or Ineffective? To do this, descriptive statistics are used. In other words, the skewness has to be determined.

Positive Skewness: Positive skewness relates that the length of tail is directed to the right side, i.e. accumulation of data is directed to the left side. In other words, codes of 1, 2 and 3. Ineffective and or low effective.

Negative Skewness: Negative skewness relates that the length of tail is directed to the left side, i.e. accumulation of data is directed to the right side. In other words, codes of 4, 5 and 6. High effective.

Given the average of 3.4, assumption of f20 is accepted. It means that all requirements of implementation of risk management in civil projects of Tehran and Zanjan provinces are sometimes to generally meet. Of course, we cannot accept this assumption more reliably. If we want to compare the condition of Tehran and Zanjan provinces, we will find out that (according to assumption of f20), the said assumption has been accepted more reliably in Tehran province (average of 3.92) while this average in Zanjan province is just 3. It means that all requirements for implementation of risk management in Tehran province have always been met in most of the projects, while these requirements have sometimes been met in Zanjan province.

Test Value = 0					
95% Confidence Interval of the Difference		Mean Difference	Sig. (2-tailed)	df	t
Upper	Lower				
4.3821	3.4641	3.92308	.000	12	18.623

Test Value = 0					
95% Confidence Interval of the Difference		Mean Difference	Sig. (2-tailed)	df	t
Upper	Lower				
3.5453	2.4547	3.00000	.000	16	11.662

Test of other Hypotheses (Inferential)

Those tests we are going to use in this part are called "Non-Parametric" test, because data distribution is not normal.

When we analyze the data, some cases may be happened in which we may be far away the required assumptions seriously. In such cases, we may need some procedures which require fewer hypotheses concerning the society. These procedures are generally called non-distribution or non-parametric tests. These procedures do not require a particular distribution, although some of them do require few hypotheses about the form of distribution. One of the disadvantages of non-parametric tests is that discovering real difference is less likely. In other words, the strength of non-parametric tests is not the same as those tests which require the normality of society as an assumption such as t-test.

f32	f31	f30	f10	f9	f7	f6	f5	f4	f3	f2	f1	Valid	N
30	30	30	30	30	30	30	30	30	30	30	30	Missing	
0	0	0	0	0	0	0	0	0	0	0	0	Mean	
3.3333	3.5333	3.7667	3.83	3.77	3.70	3.33	3.70	3.50	3.60	3.27	3.83	Std. Error of Mean	
.11073	.10431	.10376	.145	.141	.109	.121	.145	.142	.113	.135	.128	Median	
3.0000	4.0000	4.0000	4.00	4.00	4.00	3.00	4.00	3.00	4.00	3.00	4.00	Mode	
3.00	4.00	4.00	4	4	4	3	4	3	4	4	4	Std. Deviation	
.60648	.57135	.56832	.791	.774	.596	.661	.794	.777	.621	.740	.699	Variance	
.368	.326	.323	.626	.599	.355	.437	.631	.603	.386	.547	.489	Skewness	
-.294	-.732	-1.220	-.580	-.037	-.859	-.484	-.716	.236	-.406	-.480	-.409	Std. Error of Skewness	
.427	.427	.427	.427	.427	.427	.427	.427	.427	.427	.427	.427	Range	
2.00	2.00	3.00	3	3	3	2	3	3	3	2	3		

As mentioned earlier, the variables in hypotheses of f1, f2, f3, f4, f5, f6, f7, f9, f10, f30, f31 and f32 have not specific distribution. So, non-parametric methods are used for testing the hypotheses. When the samples are small in size, they are used frequently. It is true in the present questionnaire.

$$\left\{ \begin{array}{l} H_1 : \mu_i \neq \mu_j \\ H_0 : \mu_1 = \mu_2 = \mu_3 = \mu_4 = \mu_6 = \mu_7 = \mu_8 = \mu_9 \end{array} \right.$$

KRU	
87.957	Chi-Square
15	Df
.000	Asymp. Sig.

As stated before, to test averages' equality, a non-parametric test will be required. Kruskal-Wallis test is regarded as a non-parametric synonymous test through which a unilateral variance is analyzed. If you are going to test zero hypotheses, the data has to be selected from single samples of the societies which their forms are the same. Given the output of this test,

since the sig. value of the test is 0.000, then H₀ hypothesis is rejected. It means that there is a significant difference and since sig. value is differed from the value of 0.05 greatly, then the equality of averages is rejected more reliably.

Here, a question is raised: To which direction this inequality approaches? As stated before, we will descriptive statistics again for this case. Given the Skewness line as indicated in Table 8-3, we can identify different types of skewnesses. For negative skewnesses, the length of the tail is directed to the left side. In other words, the data are accumulated in the right side and the hypotheses are accepted accordingly. For positive skewnesses, the length of the tail is directed to the right side. In other words, the data are accumulated in the left side and the hypotheses are rejected accordingly. As shown in the table, all the hypotheses, except for f4 hypotheses have been accepted.

5. Analysis & Conclusion

Hypothesis: Assuming the inadequacies of designing phase may give rise to risk occurrence in time, quality and cost of execution of the projects which accepted by the statistical society. As shown in Table 8-3, this hypothesis and hypothesis No. 10

having the average of 3.83 has been accepted more strongly by the statistical society. More emphasis made by the respondents may be attributed to the weakness resulting from the processes currently applied in the executive and technical systems of the country. In such systems the credits of civil projects are appropriated after the budget notified by the government and the government submits the budget bill with more delays and the approval of the budget bill by the Islamic Consultative Assembly postponed to the end of August or September, accordingly. On the other hand, since the real description of the project depends on this date, so the governmental organizations are practically compelled to minimize the duration of execution of designing phase to be able to launch the execution phase of the project on due date. Non-professional haste by a governmental employer will cause some of the needs of the project's beneficiaries to be forgotten or some designing mistakes to be made. This errors and inadequacies are emerged during execution phase and will cause the designing to be updated or modified.

More generally, those contractors who had participated in the bidding based on the basic designing and provided their time schedule and quotation will complain about this modification and designing and legal disputes between two parties are intensified. From contractors' point of view, any changes in the execution plans will impose new tasks on them generally followed by many risks. Since, these contractors do not assume the costs of such risks and their consultants do not assume any legal responsibility in this regard, so the consequents of such risk will be directed toward the contractors. To maintain their interest margin, the contractors try to negotiate with the employer and revive their lost interests which this case causes new legal suits to be raised.

Incompetency and the weakness of designing team (consulting engineers) and lack of use of skilled and experienced experts to translate the needs of the beneficiaries into engineering projects is regarded as another problems cause the design-related risks to be increased. Incompetency and sometimes and inattention of designing team toward the rules and technical requirements applicable in the country will give rise to many problems during execution of the projects and will cause the contractors to become entangled in many troubles during execution of the projects and funding the renovation costs and changing the conditions necessary for the execution of the new projects.

Inability of the governmental organizations to supervise the plans proposed by the consultants is regarded as another problem causes the plans not to be executed smoothly and the quality and quantity of

designing phase will not practically be supervised, accordingly. Consequently, the respective consultants will focus their concentration on simple and routine plans and the cost-effectiveness, modernity and efficiency are excluded. Clearly, such consultants will never think of exploiting skilled and experienced experts and new techniques. The wage of consulting engineers is very low comparing those who work in developed countries and this is one of the most important factors which have not to be ignored.

Hypothesis 2: Selection of an incompetent consultant may give rise to risk occurrence in time, quality and cost of execution of the projects. Similar to the first hypothesis, it is accepted with the average of 3.27 (relatively high effectiveness). This hypothesis is one of the weakest hypotheses in the current research and in spite of its acceptance; it has the lowest rank among other 13 hypotheses.

As mentioned earlier, the executive and technical system of the country plays a key role in this regard. In such a system, the consultants are evaluated based on the availability of the experts and the numbers of previous tasks and are evaluated by the planning deputy of the presidency. Unfortunately, many of such consultants submit their forged documents to this organization to obtain their ranks. Naturally, such consultants will not be able to meet the needs of the employers and projects' beneficiaries. On the other hand, given the inadequate scientific capability of the governmental employers as well as lack of proper judgment, the selection process of the consulting engineers is not performed appropriately and incompetent consulting engineers are selected accordingly. Although, it has to be mentioned that a supervision phase has been included in job description of consulting engineers in our country. This phase together with detailed designing phase will cause the pricing not to be performed exactly and consequently those contractors whose quotations are lower, will be the winners of the bids. It is worthy to note that inadequate professionalism of the governmental employers to supervise the designing phase plays a key role in this regard.

Hypothesis 3: Failure to do the feasibility studies may give rise to risk occurrence in time, quality and cost of execution of the projects.

This hypothesis with the average of 3.6 (qualitative criteria of relatively high effectiveness) has been accepted by the statistical society. This hypothesis and the first hypothesis are nearly among the tasks of consulting engineers and the weakness of this organization is completely substantial in these two hypotheses.

The difference between this hypothesis and the first one is that the governmental organizations award the execution of this phase superficially or as

determined before to the consulting engineers or they perform it themselves through governmental facilities.

Although the feasibility phase is regarded as an unimportant phase of a project in terms of cost and time, but it plays a key role to achieve the aims of a project. A principle question is answered during this phase:

“Has the project to be done? Is it possible to execute the project given the current condition? Are there any alternatives to achieve these aims?”

There are so many civil projects in the country which are in execution stage and most of them are regarded as failed ones. So, if they were studied in terms of feasibility, they may never reach the designing and execution phases and then billion dollars of the state's budget may not be detained. In administrative and technical systems of the country the government notifies the projects to the respective ministries and then the respective ministries notify them to the concerned organizations and then the initial feasibility studies are done by governmental organizations through their own expertise capacities. Naturally, due to inadequate technical expertise as well as lack of sufficient and in-depth studies of different aspects of these projects, a superficial decision is made. The suggestions made by the respective ministries were studied on the basis of special criteria such as government's Macro policies; political pressures imposed by the members of the parliament and other influential figures, bargaining of Directors General of the provinces and easy to yield projects and were submitted to Parliament as budget's bill. The parliament ratifies the projects on the basis of similar criteria and then the ratified projects are notified to the government. Land preparation studies in which upon capacities of each area, special industries are proposed are among cases which included in decisions made by the ministries and Majlis as well as 25-year plans, but the approved projects will not be able to meet the requirements of such plans.

Naturally, when the administrative organizations are required to execute the approved civil projects, since the budget has been notified already to them and they know that budget return regarded as negative score for them, they shall be obliged to perform predetermined zero phase studies (feasibility studies) to obtain the governmental permission for executing designing phase. In fact, feasibility studies are not performed during this process, but the project will be justified and the consulting engineers try to justify the plans from technical, economic, social and political points of views through manipulation of the figures and unilateral comparison of the projects.

When these projects are executed, they would not be able to achieve the goals for which they have been suggested.

Lack of formulated instructions and specified terms and conditions to accept the civil projects and the significant effect of political and taste-related pressures imposed by the directors in different levels on acceptance or rejection of civil projects are among the most important issues we have to take into account and they were mentioned in advance. Such projects which not to be launched from technical, economic or social points of views, but for any reasons they are being executed, are entangled with some severe problems or principally they were not funded properly during execution phase. These two conditions would be followed by some modifications or delays in executing the project and will cause the investment risk for the contractors to be increased. For instance, those projects which are not executable within the suggested arrangement will be passed, but during execution phase, administrative costs of the projects like these would not be able to justify the goals resulting from its execution. Sometimes, the governmental employers who observe such projects will stonewall to appropriate the credits cause the contract to be terminated by the contractors.

Hypothesis 4: Ignorance of expectations of the beneficiaries or the customer may give rise to risk occurrence in time, quality and cost of execution of the projects. This hypothesis has been rejected on the basis of inferential analysis and related statistics. Additionally, the acceptance of this hypothesis has been rejected on the strength of its descriptive analysis. The authors believed that the rejection of this hypothesis is very unlikely, because in fact withdrawal of the consulting engineers to meet the demands of the customer or to exert taste to make the changes in the designing by the members of consulting team and as a result tendency toward design changing during execution is an inevitable phenomenon which could not be rejected and apparently, the respondents of this project 36% of which were consulting engineers have not confirmed this issue as the reason of the problems. The reason of rejection may be attributed to non-tendency to highlight the errors committed by the consulting engineers during the execution of the projects or insignificance of the designing phase from contractors or employers points of views. The researchers believe that the rejection of this hypothesis demonstrates the regrettable morale prevailing at the industry and construction society of the country. According to this outlook, all the projects are viewed in execution phase and then designing phase is downgraded to drawing phase. In advanced countries, time and cost are regarded as the most critical factors of this phase, particularly feasibility phase in order to prevent the poor and low yielded projects. By concentrating on this phase, the direct as well as indirect costs of execution phase are minimized. But in

our country, given the state's planning system and more delays in notifying the budget appropriated to the civil projects, the governmental employers try to complete designing phase as soon as possible.

Hypothesis 5: According to this hypothesis, any contradictions and inconsistencies between regulations of construction by-laws (civil projects) and its effect on projects' inefficiency have been accepted by the statistical society. As shown in Table 8-3, the average of 3.7 as a descriptive statistical data has obtained from the analysis of the questionnaires. Qualitative interpretation of the average of 3.7 indicates that the great effect of contradictions between the regulations on projects' failure has been acknowledged by the statistical society. For the first time as of 1950s, the position of state's administrative and technical system has been subjected to contextual changes due to different conditions.

For instance, assessment methods of the contractors and how the projects are awarded to them have been evolved at least five times. These subsequent changes which may be attributed to tastes and the policies imposed upon then government are not harmonized with time circumstances, economic conditions and other current legal regulations of the country such as labor law; social security and commerce act and cause the threefold factors of labor to be entangled with marginal issues. On the other hand, since the time average of the execution of major and minor projects is varied from 5 to 15 years, the subsequent changes in technical systems and rules and regulations cause many problems and claims to be raised by the parties in most of the projects.

Hypothesis 6: According to this hypothesis, the economic and social issues and crises may give rise to risk occurrence in civil projects and it has been accepted with the average of 3.33. It is understood that the civil projects are among the most significant projects in terms of Rial, the volume of physical labor and multiplicity of the beneficiaries in our country. Generally, those issues and problems of the society will cause some troubles to be made in these projects. Naturally, the contractors who are in the first rank in terms of risk taking will be exposed to much damages resulting from the crises and social and economic issues. This case is of a great importance in advance countries. In these countries, the investment-related issues and problems are studied by the international economic institutions and the risk of investment in the countries is determined. The risk of investment is very high in our country, because a long-term economic management is not applied in our country and economic and strategic decisions are subjected to fundamental and significant changes from a government to next government and from a minister to the next minister. On the other hand, improper

management of foreign affairs caused economic pressures to be imposed on the country externally and consequently the problems to be increased. Economic sanctions are a typical of these pressures. In addition to economic problems, the civil projects are entangled with social problems. In addition to economic problems, the civil projects are usually entangled with social difficulties as well. The difficulties a society usually to be entangled with them could be arise from economic or political crises and sometimes they may be attributed to the lack of cultural development. Usually, the role of the economics and economic stability in social crises is highlighted by the researchers of social research.

In the present research, the contractors are usually involved in some issues such as unexpected surge of demand for construction materials by the people without any real interpretation and or participation of ordinary people in the tenders of specialized projects. These conditions are happened from time to time and due to market stagnation. Generally, such issues will cause the administrative costs of the projects to be escalated. Therefore, the duration of execution of the project will be subject to modifications and sometimes the execution of the projects is suspended temporarily due to lack of funding or change of the policies of the contractors or local pressures.

As mentioned before, improper economic management is regarded as the one of the major problems of the contractors. Also, the involvement of local organizations that play a key role in the economic sector must be included. For instance, the rigidity of some provincial banks to provide bank facilities, the governors' meddling with the method of execution of the projects and funding the projects.

The last point we are going to mention here is the inflationary and stagnancy policies of the governments as the one of important problems the contractors are involved in. In such policies, the civil budgets are usually notified very late and on the other hand, the contractors are caught in a morass of bankruptcy due to improper funding by the respective banks and the contractors are occasionally forced to resort immoral ways to guarantee the survival of their company.

Hypothesis 7: This hypothesis which has been accepted with the average of 3.7, is similar to Hypothesis No. 5. The issue of inconsistencies between the laws and regulations is debated on the strength of hypothesis No. 5, while hypothesis No. 7 will treat the frequent changes of the laws.

Here, the issue of frequent changes in government's policies, particularly economic affairs is typically emphasized. Additionally, successive changes in the rules and procedures could increase the risk of investment as the same as changes of macro

policies for the contractors and consultants. The main reason of this issue may be attributed to bad management of the rules and regulations in the country.

The issue of management of rules and regulations is among the advanced issues which advanced societies strive to eliminate the unnecessary and redundant rules and procedures and limit the legislation channels and adapt the new rules more strictly through reviewing the traditional and existing rules and conforming them to political, economic and social strategies of the countries. One of the reasons of establishment of rules management in these countries is the tendency of the members of the parliament toward passing the laws which meet the needs of a part of the society in short term. Besides, the governments insist on to apply their tastes for state's macro plans under the new rules and regulations. Unfortunately, the jurists of council of guardians who are regarded as the final gate of passing the laws and regulations would not consider the consequent effects of the laws completely and would not include the contradictions of these laws with other state's rules and regulations. On the other hand, some of the laws and regulations passed by the government in the Cabinet are notified to executive organizations without they are reviewed by the respective supervisory organizations. In such cases, the contractors may survive on these conditions. They may forecast the upcoming changes of the rules through corruption acts or defend their own rights through employing influential attorneys at law.

Another issue raised in this regard is that the frequent changes of laws and regulations will cause the appropriate decisions concerning taking part in tenders or quotation not to be taken definitely by the contractors and time and cost-related risks not to be taken by them in this way.

On the other hand, any and all changes of the rules and procedures during the execution of a project cause some unpredicted costs to be directed toward the contractors which these costs would not be compensated by the employers. In addition, the priorities of the managers may be changed and timely notification of the budget to be ignored by high ranking managers. It is worthy to note that the changing the interpretation of the laws, may in turn double the problems of the contractors which in turn results from the frequent changing the managers and or assigning the poor and inexperienced managers to handle administrative organizations.

Hypothesis 8: Disagreements and contradictions between the executors of the project and their effects on occurrence of the problems within the projects are discussed in this hypothesis and it has been accepted with the average of 3.77 by the statistical society.

In civil projects, there is usually a claim between those who are in charge of the projects, particularly the employer and contractor. The factors that play a key role in raising a claim is as follows:

The first factor is directors' more intrusion into the affairs and or execution of the project under higher supervision of the employer and exercising their own taste in the method and quality of executing the project. In most of cases, the contractor will expose its benefit to a great risk due to these modifications resulted from exercising the unnecessary tastes and in other cases, the final user would not be satisfied by the quality of the work performed under these conditions. Therefore, changing the higher supervisor or employer's representative may give rise to new troubles.

The claim between the consultant and the contractor is regarded as the second factor. Due to lack of sufficient executive experience, some projects are proposed by the consulting engineers. The significant numbers of these projects are involved in many problems due to lack of administrative facilities or a defective designing. Therefore, a contractor who has invested a great deal of money on the project will sustain project failure's risk in terms of time and cost. When a project is failed, non-payment the fee would be the only risk directed toward the consulting engineers, while the contractor has entered the project with its own credit and investment. As a result, the consulting engineers would not undertake to comply with the requirements of time, cost and quality of the project and therefore the contractors would defend against the projects suggested by the consultants and raise the claim. Because of this, the complicated and fearlessly plans suggested as the governmental projects are failed in its initial stages in our country.

The claim between the consultant and the employer is regarded as the third factor. Then, there is always a concern that the consulting engineers may have not considered the employer-related problems in their designing and the employer may be exposed to financial damages. So, this factor may cause some unrelated opinions to be expressed by the numbers of the managers of governmental organizations within first and second phases of designing. This reason of this issue may be attributed to the following scenarios:

First of all, if the taste imposed upon the consultant was accepted by him or her, his or her responsibility for proper designing will be negated and all responsibilities will be directed toward the employer. In second scenario, if the consultant refuses to accept the taste imposed upon him, the subordinate departments of governmental organization will usually implement their stonewalling during approval of the project and as a result, the duration of project execution and related costs are directed toward the

consulting engineer. Under these circumstances, the employer will try to implement its own changes through imposing pressure upon the contractor and in all such cases time, cost and consequently the quality of the project would be affected. Nowadays, application of planning and project controlling software-based systems in developed and developing countries as a critical tool for project managers has been accepted. But unfortunately the advantages and disadvantages of planning and project controlling software-based systems are still being debated in our country and such systems are not used in major projects in our country. Then when the activities of a project are not identified, the sequence of these activities could not be formulated and consequently time, resources and the cost of activities could not be estimated appropriately. Under these circumstances, supplies planning for timely provision of the materials and machineries required for the project as well as predicting the activities-related risks and preparing preventive scenarios could not be possible at all.

In minor projects, any deficiency could be coped with through experience, but in major projects in which the volume of works and numbers of involved persons are increased significantly, lack of use of a modern -computer-based and comprehensive planning system and lack of timely provision of the materials will cause the delays resulting from the risks and direct and indirect costs of the project to be increased significantly.

Hypothesis 9: On the strength of this hypothesis, the statistical society assumed that improper use of project management system will give rise to many problems during execution of the project. The issue of application of project controlling software in civil project as a question was raised and the statistical society as the respondent announced that they have used such software in most of civil projects. Of course, it is worthy to note that application of project control software in our country is only limited to time planning and consequently manpower and cost were not planned based on such software.

Hypothesis 10: it is one of the most important hypotheses of this research. The bed required for establishment of risk management in civil projects of Tehran and Zanjan provinces has been studied upon this hypothesis. This hypothesis has been presented according a single questionnaire in which the techniques and software required for implementing risk management in a civil project have been listed.

By glancing briefly down the tables and accepting the hypothesis No. 10, it is found out that the bed required for the execution of the civil projects in two mentioned provinces are sometimes to oftentimes is ready. This bed with the qualitative criterion of sometimes and oftentimes has been ready in Zanjan

and Tehran provinces, respectively. It means that, the bed required for establishment of risk management system as one of the leading techniques of project management in Zanjan province and its counterpart is not ready under any circumstances. We have to bear in mind that the data provided by the statistical society are probably optimistic values.

The issue of underdevelopment of the provinces against Tehran province is among the issues which have been mentioned in great numbers of articles and lectures. Taking into consideration of this point that the higher volume of the projects are implemented in the provinces as well as the scientific and experimental weakness of the contractors, consultants and employers who are working in the provinces, we can certainly affirm that the problem of civil projects of the country will never be solved under any circumstances and as long as the high ranking officials of the country do not include the distribution of training facilities and skilled man power in the provinces in their working policies, any chance of improvement can be expected. As mentioned in the second chapter of this research, Zanjan province is one rank above Tehran province in terms of duration of execution of the projects. It is demonstrated the statistics issued by planning management organization are not in compliance with the criteria existing in project management systems and or the criterion applied for selecting the provinces is a special one which is applicable in our country.

In the last three hypotheses of this questionnaire, the effect of the factor influencing upon strengthening the cost, time and quality-related risks of the project has been studied individually. In each of these three hypotheses, the effect of the factors mentioned in the first ten hypotheses on cost, time and quality as first, second and third priorities has been confirmed by the statistical society.

Cost-related risks of higher rank have been accepted, because in case of any problems during execution of project, the role of project's budget as a shield is usually highlighted. Generally, given the bed existing in the civil projects of the country as well as current culture among different groups of the society, the issue of costing and saving are more important than time. Delay in execution of the projects as penalty would not be directed toward the contractor. On the other hand, the politicians do not have any anxieties over time management and the people do not show any sensitivity to suspended projects. Therefore, time is of less important against the cost. In developed countries, the issues of time and sooner commissioning are more important than huge investment and the sensitivity of the parties and the people to performance of the governments in tax and revenue management. The issue of quality is sometimes ignored and in case of

budget deficit and or accelerating the completion of the projects, the quality as an item is usually ignored due to political pressures and this will cause the quality of the projects to be declined significantly and maintenance costs of the projects to be increased and life cycle of the projects to be decreased as well.

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Abuse of Selected Psychoactive Stimulants: Overview and Future Research TrendsBahaa-eldin E. A. Rahim¹, Umar Yagoub¹, M.S. Mahfouz², Yahya M.H. Solan³, Rashad Alsanosi⁴¹Medical Research Center, Jazan University, Kingdom of Saudi Arabia²Department of Community Medicine, Faculty of Medicine, Jazan University, Kingdom of Saudi Arabia³Administration of Primary Healthcare, Directorate of Jazan Health Affairs, Jazan, Kingdom of Saudi Arabia⁴Substance Abuse Research Center, Jazan University, Kingdom of Saudi Arabia
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Abstract: To date, a large and growing body of research has addressed the effect of various substances abuse from different medical, clinical and psychological perspectives. However, research on behavioral and cognitive effects of abusing particular psycho-stimulants including Khat, non-prescribed amphetamine, tobacco smoking and its rejuvenated method (waterpipe/shisha) on human subjects is not that extensive. This review aims at gathering recent scientific literature on addiction influence of selected psychoactive substances (namely Khat, tobacco and amphetamine) to human health. Considerable research studies have been done so far on prevalence of Khat chewing and effects of tobacco (mainly on cigars smoking) highlighting their addictive nature and associated health problems. On contrast, there is a substantial knowledge gap regarding the neurobehavioral effects of non-prescribed amphetamine drugs and amphetamine-type stimulant (Khat) on human neurobehavioral performance which in turn might shed the light on themes for future research trends. The literature reports that prevalence of these substances is alarmingly high among nations of Arab and African horn countries as a part of their cultural and habitual behavior. However due to the recent scattering of these nations worldwide, the issue of these substances becomes of global concern. The review attempts to extract lessons learned from previous studies and briefly summarized various aspects of the medical and psychological effects of using such stimulants on human health with much emphasis on cognitive and behavioral deficits. Chemistry, toxicity, general pharmacology of the reviewed psycho-stimulants together with the lessons learned and associated future research trends are also presented.

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1. Introduction

Substance abuse usually denotes to substances that associated with psychoactive but non-therapeutic drugs or chemical substances that lead to dependence syndrome and alter mental functioning (WHO 2011; Health Officers Council of British Columbia 2005).

The terms “drug abuse”, “drug addiction” and “drug dependence” are widely considered scientifically synonymous and been used as a technical term in the medical literature. However drug addiction has been used mainly for drug abuse to provide a more general level of information to the public. On contrast, the term “drug habit” is thought to be a psychological dependence rather than a physical dependence, and it is not thought to create the same damage to society as drug abuse (Health Officers Council of British Columbia 2005; WHO 2004; Benowitz 1999; US Department of Health and Human services 1988). Table 1 summaries the main criteria associated with substance abuse.

The use or abuse of addictive substances, namely Khat (*Catha edulis*, *Celastraceae*), tobacco (cigars and waterpipe), and recently amphetamine is

the major socio-medical issue that threatens the community peace worldwide. This phenomenon becomes a tradition to region of the Middle East, African Horn nations and some parts of central Asia. Cigarette smoking is a serious health problem and most important avoidable causes of death in world (Council of The European Union 2011; UNODC 2010; Ali 2007; Carrier 2007; Tesfaye et al 2006; Gelaw and Haile-Amlak, 2004; Drake, 1988; Kennedy 1987). During a Khat session, other psychoactive and addictive substances including Arabic coffee, light tea and tobacco (water pipe or cigarettes) are provided. Smoking has been strongly implicated as a risk factor for chronic obstructive pulmonary disease, cancer and atherosclerosis, etc. (Khan and Malhotra 2011; Pasupathi et al 2009). Khat plant (Figure 1) grows wild in countries bordering the Red Sea and along the east coast of Africa. It's an evergreen shrub, which is cultivated as a bush or small tree. The leaves have an aromatic odor.

The taste is astringent and slightly sweet. The plant is seedless and hardy, growing in a variety of climates and soils. Khat can be grown in droughts

where other crops have failed and also at high altitudes (Glenice and Hagen 2003). Khat chewing (also pronounced "Takhzeen") is a common deep-rooted socio-cultural traditional habit among nations of African Horn and southwest of Arabia Peninsular. Such habit aims at attaining a state of euphoria and stimulation.

Table 1. Criteria for Drug Abuse/Dependency

<p>Primary criteria</p> <ul style="list-style-type: none"> ▪ Highly controlled or compulsive use ▪ Psychoactive effects ▪ Drug-reinforced behaviour <p>Additional criteria</p> <ul style="list-style-type: none"> ▪ Addictive behaviour often involves: <ul style="list-style-type: none"> ○ Stereotypic patterns of use ○ Use despite harmful effects ○ Relapse following abstinence ○ Recurrent drug cravings <p>Dependence-producing drugs often produce:</p> <ul style="list-style-type: none"> ▪ Tolerance ▪ Physical dependence ▪ Pleasant (euphoriant) effects

Source: US Department of Health and Human services 1988

The habit involves picking tender leaves of Khat, inserting them into one side of the mouth, chewing them for a while and storing them in the same side of the mouth. Khat is a green leafy shrub that acts as a mild stimulant when chewed. The Khat tree grows abundantly in Yemen, where Khat is legal. It is commonly consumed by Yemeni expatriates in Saudi Arabia, being smuggled from Yemen. Many Saudis also visit Yemen with the purpose of consuming Khat. Yet, Khat is cultivated as well in the Saudi Arabian part of the Yemeni border (Jazan), where locals consider it as a part of their daily lives and culture. Hence, the authorities have been implementing a different approach for controlling the use of Khat based more on persuasion and information campaigns rather than prosecution (Council of The European Union 2011). Yemenis also use Khat for sociologic and anthropologic reasons described in detail in early works (Chaouachi 2007). One of the major findings of these studies in the field of social sciences shows that the use of the mada'a is a chief element of the ritual Khat parties that take place during the long afternoons in Yemen.

Cigarette smoking is powerfully addictive, and caused 100 million deaths in the 20th century. In the 21st century, if smoking trends persist as expected, one billion people will die from smoking tobacco (Royal College Physicians 2007). The World Health Organisation Study Group on Tobacco Product Regulation (TobReg) has issued in 2005 an



Figure 1. Abundle of Khat (*Catha edulis*) (after Al-Motareb et al 2010)

"Advisory Note" entitled: "Waterpipe Tobacco Smoking: Health Effects, Research Needs and Recommended Actions by Regulators". "Waterpipe" smoking is now considered a global public health threat and the corresponding artefact is actually known in the world under three main terms: hookah, narghile and shisha (Chaouachi 2006). Figure 2 illustrates a cross-sectional view of a water-pipe device.

Fenethylamine, commonly known by the trademark name 'captagon', is one of the most popular drugs of abuse among the young affluent communities of the Middle East (Mahmoud, 2005). The most common drugs in Saudi Arabia are hashish and amphetamines. Hashish comes mainly from Afghanistan, Pakistan, UAE and Yemen. The amphetamines are mostly produced in Turkey, Syria and Jordan and usually come in the form of Captagon pills. Captagon was the brand name of fenethylamine, a synthetic stimulant used as a milder alternative to amphetamines before being banned in 1986 (Council of The European Union 2011). Captagon is very common among students, especially before exams, because it is considered to enhance performance. For the same reason it is used by people employed in strenuous jobs, such as drivers, workers, etc. Captagon, being a member of the Amphetamine family, is trafficked into Turkey from eastern European countries; and shipped to Middle East and Arabic countries transiting Turkey. Captagon is not widely used in Turkey (TMCDDA 2008).

The main literature searches for this review were conducted during December 2011 using a number of search terms and bibliographic data sources including PubMed, Medical Database, sciencedirect.com, Taylor & Francis, Wiley-Online Library and published technical reports. In drawing together the evidence for this review we aimed to:

- i. understand the nature and extent of the problem for the selected addictive substances.
- ii. extract lessons from previous studies.

- iii. identify areas for future research studies with much emphasis on psychosis and neuropsychological effects of nicotine, amphetamine and amphetamine-type stimulants (ATS) on human health.

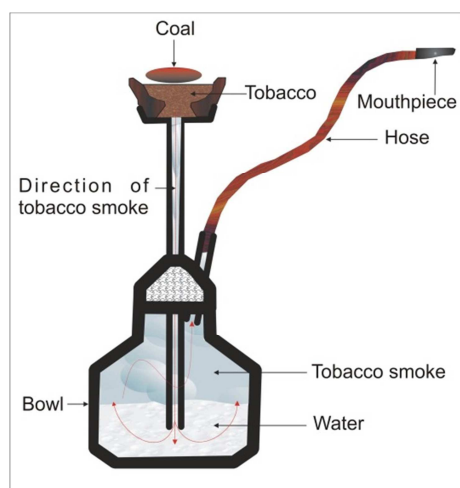


Figure 2. Water-pipe cross-sectional view

2. Prevalence

Khat is a psychostimulant plant used by over 10 million people daily, mainly in eastern Africa and the Middle East particularly southern of the Arab Peninsula where leaves of the Khat bush are widely used as a stimulant (Rashad et al 2011; Al-Motarreb et al 2010; Lukandu et al 2008a; Date 2004; Brenneisen et al 1990). The major cultivation and production areas of Khat are in Ethiopia, particularly in Harar district, and in Yemen (Al-Hebshi and Skaug 2005). Global seizures of Khat were estimated at 106.9, 97.5 and 101.4 tons in 2004, 2005 and 2006,

respectively (Griffiths et al 2010). The habit of chewing Khat has prevailed for centuries among populations in the regions where it is grown, and its use is gradually spreading to other parts of the world including Europe (Table 2; Figure 3) and North America due to global migration (Griffiths et al 2010; Lamina 2010; El-Wajeh and Thornhill 2009; Lukandu et al 2009; Al-Hebshi and Skaug 2005; Mion, et al 1998).

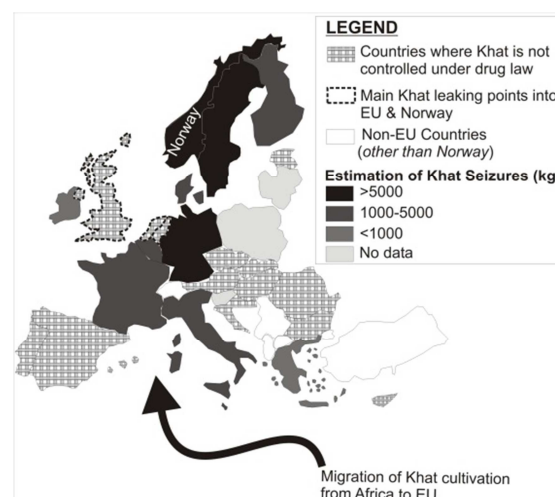


Figure 3. Countries among EU Member States and Norway not specifically controlling Khat under drugs laws, and estimates of Khat seizures. (Modified after Griffiths et al 2010)

Among other addictive substances, tobacco use, especially in form of cigarette smoking, remains highly prevalent all over the world (Royal College Physicians 2007; United Nations 2005). The literature nowadays reports that the use or misuse of addictive substances, such as cigarettes, and Khat is

Table 2. Prevalence estimates of Khat chewing among nationals and communities of Khat producing States

Author, year, State of study	Study Design	Male #	Female #	Sample Size	Data Collection	Age (years)	Prevalence (%)		
							Overall	Male	Female
Elmi (1983), Somalia	Hargesia and Mogadishu towns and neighborhoods	4526	2959	7485	Face to Face interview	16-78	59	-	-
Mwenesi (1996), Kenya	22 districts	-	-	2301	-ditto-	6-90	4.1	-	-
Selassie and Gebre (1996), Ethiopia	24 Towns	-	-	3200	-ditto-	>15	30.5	-	-
Alem et al (1999), Ethiopia	Rural community households Butijira	4397	6071	10468	-ditto-	15+	50	70	35
Belew et al (2000), Ethiopia	Rural and urban households	626	402	1028	-ditto-	>15	31.7	40	18.2
Ayana et al (2002), Ethiopia	Jimma Town	519	481	1000	-ditto-	>16	30.6	61.13	23.9
Gelaw and Haile-Amlak (2004), Ethiopia	Population of technical staff of Jimma hospital and the academic staff of Jimma University	330	142	442	-ditto-	18+	30.75	27.25	3.5
Numan (2004), Yemen	3 urban and 3 rural areas households	510	282	792	-ditto-	15-76	67.9	81.6	43.3
World Bank (2004), Yemen	7 governorates	2220	1807	4027	-ditto-	12+	54.6	72	32.6

Table 2. (Cont'd)

Odenwald et al (2005), Somalia	Hargesia households	2449	2405	4854	- ditto-	>12	10.2	-	-
Aden et al (2006), Kenya	Inhabitants of Ijara District	-	-	50	- ditto-	15-34	88	-	-
Khawaja et al (2007), Yemen	Data from Yemen Demographic and Maternal and Health Survey	-	7343	7343	- ditto-	15-49	40.7	-	40.7
Odenwald et al (2007), Somalia	Military personnel of 7 regions	7238	886	8124	- ditto-	Average 37.3	36.4	-	-
Tesfye et al (2008), Ethiopia	Population of Addis Ababa	1648	2353	4001	- ditto-	25-64	8.7	18.3	1.9
Laswar & Darwish (2009), Yemen	Population of medical students of Aden University in Yemen	100	-	100	- ditto-	Average 31.8	90	90	-
Getahun et al (2010), Ethiopia	Population of villages of Butajira District in Ethiopia	348	316	664	- ditto-	35-65	50.3	53	47
Rashad et al (2011), Saudi Arabia	Population of college and secondary school students in Jazan region ⁴	4639	4326	8965	- ditto-	15-25	21.4	37.70	3.60
Reda et al (2012), Ethiopia	Population of high school students in Harar, eastern Ethiopia	856	851	1707	- ditto-	15-25	24.2	28.5	71.5

increasingly prevalent worldwide among male and females from different backgrounds in the Khat-origin countries (Rashad et al 2011; Ageeli 2009; World Bank 2007; Tesfaye et al 2006; Schoenmaker et al 2005; Patel et al 2005; Gelaw and Haile-Amlak 2004; Rani et al 2003; Kalil 2002; Tariq and Naseem 2000; Griffiths 1998).

Today waterpipe tobacco smoking is alertly emerging worldwide specially the Arabian Peninsula, Turkey, India and Pakistan (Abdullah and Naseem 2011; Attia et al 2010; Cobb et al 2010; Knishkowsy and Amitai 2005). Narghile smoke contains toxicant inhalation at even greater levels than with cigarette does (Eissenberg et al 2008). Water-pipe smoking recently has become the favorite form of tobacco use by youth globally specially the Eastern Mediterranean region (Akl et al 2011; Sutfin et al 2011; Dar-Odeh et al 2010; Eissenberg et al 2008; WHO 2005). While very few national surveys have been conducted, the prevalence of waterpipe smoking appears to be alarmingly high among school students and university students in Middle Eastern countries and among groups of Middle Eastern descent in Western countries. There is growing evidence that smoking tobacco through a waterpipe by youth and young adults is on that smoking tobacco through a waterpipe by youth and young adults is on the rise worldwide (Maziak 2011; Roskin and Aveyard 2009; Eissenberg et al 2008; WHO 2005). Figures 4 and 5 illustrate the prevalence of waterpipe usage across the world corresponding to different age.

Marijuana, heroin, morphine or cocaine are the substances which come to mind first when the use or illegal trade of narcotics or stimulatory substances are thought. However, there are also some other active drug components such as amphetamine-type stimulants (ATS) possess psychoactive effects, are known to be used outside of their medical prescriptions (Ascioglu et al 2010).

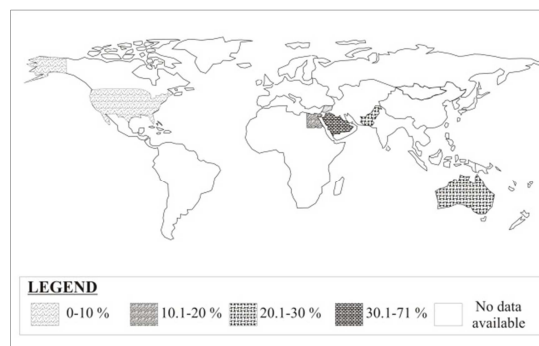


Figure 4. Waterpipe use among school students across the world (Modified after Akl et al 2011)

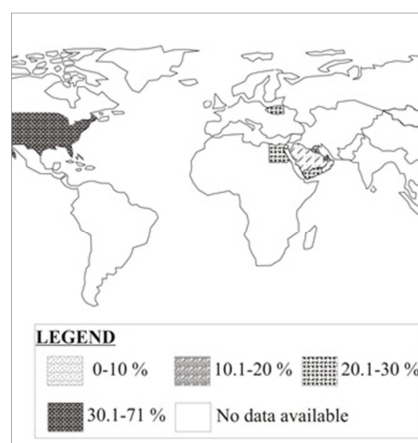


Figure 5. Waterpipe use among adult across the world (Modified after Akl et al 2011)

Global seizures of amphetamine reached a record level of 23.7 tons in 2007, and essentially sustained this level in 2008, amounting to 22.9 tons. Amphetamine seizures remained concentrated in the Near and Middle East States and West and Central Europe (Table 3), which together accounted for 96 per cent of global seizures in 2008 in which Saudi Arabia is accounted for approximately 30% of all global

Table 3. Global and regional drug seizures and seizure trends, 2007-2009

Stimulant ¹	2007		2008		Trend in NME	
	NME ² (Kg)	Global (Kg)	NME (Kg)	Global (Kg)	2007 - 2009 (%)	2007 - 2009 (%)
Amphetamine	15,065	23,750	14,203	22,944	-6%	*
Methamphetamine	38	18,211	1,473	20,656	3775%	Increased
Non-defined Amphetamine	233	1,802	57	3,829	-75%	*
Ecstasy	119	7,937	104	3,860	-12%	Decreased

¹Amphetamine-type stimulants are seized in various forms, including liquid and tablet form, and may be reported by mass, volume, number of tablets or other units.

²NME: Near and middle east region

*: Since data for 2009 were incomplete at the time of preparation of the present report, totals for 2009 are not presented in the table. The trend between 2008 and 2009 was assessed by comparing totals over 15 members of the NME states for which amphetamine-type stimulants' data were available for both 2008 and 2009, for 90 % or more of the total for 2008.

Source: UNODC (2010)

amphetamine seizures (Council of The European Union 2011). While drug seizures vary dramatically from year to year, clear increases in the amount of amphetamine seized began around 2000, with large increases reported in 2005. These increases are due, in large part, to interceptions of a fake pharmaceutical marketed as captagon (amphetamine) in the Near and Middle East which in turn, enhanced the ATS market to rejuvenate in these areas (Figure 6).

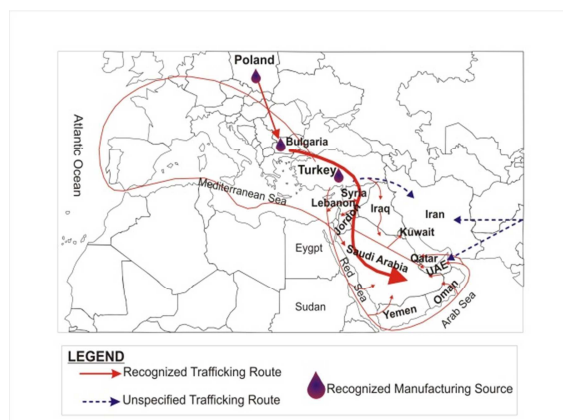


Figure 6. Road map of amphetamine manufacturing and trafficking. (Modified after UNODC 2009)

3. Chemistry

The chemistry of Khat is much dependent on climatological conditions. There are some 44 different types of Khat plant cultivated in different geographic areas across Yemen (Lamina 2010; Al Motarreb 2002; Geissshusler and Brenneisen 1987).

Among many different chemical compounds found within the manufactured cigarette, the main source of tobacco addiction is nicotine. Nicotine is a weak base with a pKa (index of ionic dissociation) of 8.0 which means that at pH 8.0, 50% of nicotine is ionized and 50% is non-ionized. Nicotine absorption

across biological membranes depends on its pH (Benowitz 1988; US Department of Health and Human services 1988). The pH of smoke from flue-cured tobaccos found in most cigarettes is acidic (pH 5.5 to 6.0). At this range of pH, the nicotine is almost completely ionized, which means that the nicotine is barely absorbed when the smoke is held in the mouth. However, when tobacco smoke reaches the lung, nicotine is rapidly absorbed because of the huge surface of the alveoli in the lung and the higher pH of the fluid in the lung (approximately 7.4) compared with the mouth (Benowitz 1999; US Department of Health and Human services 1988; Gori et al 1986).

Amphetamines include Δ -amphetamine, L-amphetamine, ephedrine, methamphetamine, methylphenidate, and pemoline. Another member of this group is cathinone, the active ingredient in freshly gathered leaves of the Khat shrub (*Catha edulis*), whose actions are very similar to that of amphetamine. On the other hand, synthetic cathinones abuse (i.e. cathinone-based drugs) is considered somehow a growing proportion of the new psychoactive substances identified in Europe which in turn may suggest its significant potential for future diffusion (WHO 2004; Jaffe 1990).

There are many different compounds found in Khat including alkaloids, terpenoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins and minerals (Aiman 2009; El-Wajeh and Thornhill, 2009; Cox and Rampes 2003; Mion et al 1998; Kalix et al 1990; WHO 2004). The phenylalkylamines and the cathedulins are the major alkaloids. The Khat phenylalkylamines comprise cathinone [S(-)-cathinone], and the two diastereoisomers cathine [1S,2S-(+)-norpseudoephedrine or (+)-norpseudoephedrine] and norephedrine [1R,2S(-)-norephedrine]. These compounds are structurally related to amphetamine and noradrenaline (Coppola and Mondola 2012; ACMD 2010; EDCC 2006).

3.1. Chemical formulae:Cathinone: C₉H₁₁NOCathine and norephedrine: C₉H₁₃NO**Relative molecular mass (*M_r*):**

Cathinone: 149.2

Cathine and norephedrine: 151.2

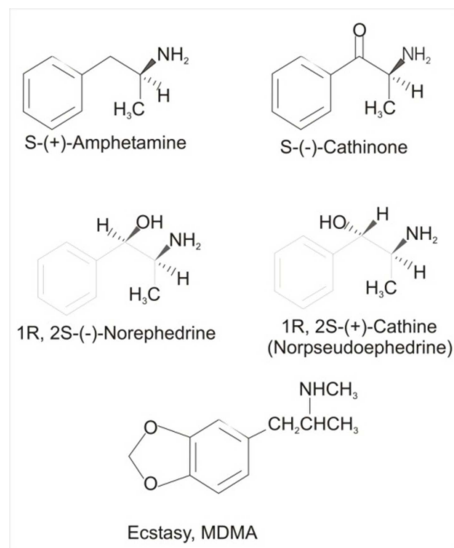


Figure 7. Chemical structures of amphetamine, cathine and cathinone

4. General Pharmacology

Khat contains more than 40 alkaloids, glycosides, tannins, amino acids, vitamins and minerals. Most of the effect of chewing Khat is thought to come from two phenylalkylamines – cathinone and cathine – which are structurally related to amphetamine (Cox and Rampes 2003). The main psychoactive compounds in Khat leaves are cathine and cathinone, which are some 2- to 10-fold less active than amphetamine (Pennings et al 2008). The pleasure derived from Khat chewing is attributed to the euphoric actions of its content of (-)-S-cathinone, a sympathomimetic amine with properties described as similar to those of amphetamine (Kalix and Braenden 1985; Kalix 1988; Kalix 1992). Khat may severely influence the effectiveness of immune surveillance and anti-microbial capacity of PBMCs (Murdoch et al 2011).

5. Toxicity

Several cigarette brands are marketed as less harmful products and are erroneously advertised as “addiction-free cigarettes.” Examples of such products are “clove cigarettes” and the “American

Spirit.” Smokers are being encouraged to switch to such products. Increasingly, these products are popular among young smokers, but may be as dangerous as regular cigarettes (Tobacco.org. 2011). Health professionals must be aware of such industry tactics to correctly inform smokers of the nicotine content in these cigarettes and the addictive properties of the products. For example, clove cigarettes manufactured in Indonesia are believed to be safer than regular cigarettes (Malson et al 2003). In fact this is not true because clove cigarettes are composed of a mixture of tobacco (60% to 80%) and ground clove buds (20% to 40%) and thus still possess certain amounts of nicotine. Some literature demonstrates that 28 smoke yields from standardized machine-smoking analysis indicated clove cigarette products delivered more nicotine, carbon monoxide (CO), and tar than conventional cigarettes (Tobacco.org. 2011; Malson et al 2003; Sohn et al 2003). Nicotine acts presynaptically to facilitate the release of neurotransmitters such as acetylcholine, norepinephrine, dopamine, beta endorphin, and serotonin-causing behavioral arousal and sympathetic neural activation (Sohn et al 2003; Benowitz 1996; Benowitz 1992). Nicotine’s effect on these neurotransmitters, which can mimic the pharmacologic effects of many antidepressants, have been implicated as a major component in the reinforcing effects of cigarette smoking, and the subsequent development of nicotine addiction. The neurotransmitters released by nicotine and their associated behavioral effects are presented in Table 4.

Table 4. Effects of Neurotransmitters enhanced by nicotine

Neurotransmitters	Effect
Dopamine	- pressure - Appetite suppression
Norepinephrine	- Arousal - Appetite suppression
Acetylcholine	- Arousal - Cognitive enhancement
Vasopressin	- memory improvement
Serotonin	- Mood modulation - Appetite suppression
Beta-Endorphin	- Reduction of anxiety and tension

Source: Benowitz 1999

Khat is genotoxic to cells within the oral mucosa, and several studies have suggested an association between Khat use and oral lesions like

hyperkeratosis and oral cancer (Lukandu et al 2008b). Cathine and cathinone are responsible for the desired psychogenic (suppression of hunger, mind stimulation, euphoria) and sympathicomimetic effects (Mion et al 1998). Chronic toxicity of Khat is modest when used in low amounts, whereas at high levels, Khat use is associated with adverse effects, like hypertension, heart rhythm disorders, insomnia and loss of appetite. In addition, Khat users show a higher prevalence of cancers in the digestive tract (Coppola and Mondola 2012; Al-Motarreb et al 2010; Pennings et al 2008). Khat is cytotoxic to peripheral blood mononuclear cells in a dose- and time-dependent manner and cell death was mediated by apoptosis (Murdoch et al 2011).

6. Medical and Psychological Effects on Human Performance

There is nowadays a handful of literature to suggest the harm impacts of addictive substances (Table 5) on different aspects of human health (Murdoch et al 2011; Köseoğlu et al 2006; Verdejo-Garcia et al 2004; Baker et al 2003; Rogers and Robbins 2003; Tariq and Naseem 2000). Khat use by untreated hypertensive patients who react strongly to vasoconstrictive effects can lead to hypertension and resulting cardiovascular complications (Mion et al 1998; Hassan et al 2000; Tesfaye 2006; Ali 2007; Shatoor et al 2011). Due to its serve impacts on human life, tobacco researches have been expended to understand the health consequences of cigarette smoking, both to the smoker and to nearby nonsmokers (Reno et al 2011; Sharma and Vijayaraghavan 2008; Jha et al 2008; Royal College of Physicians 2007; Gupta et al 1997; Church and Pryor 1985). Harm ranking of the major psychoactive substance is presented in Figure 8.

6.1. Cognitive and behavioral deficits

There is a possible complex connection between the impact of tobacco use and influence of amphetamine-like of Khat use. Despite both nicotine and amphetamine are dopamine agonists, there are noticeable differences in their influence on behavioral measures. Observational and single-case studies are the most available researches investigated cognitive and behavioral impacts associated with Khat chewing in human. Obviously Khat chronic chewing habit associated with various mental and cognitive problems (Ersche et al 2006; Ersche and Sahikian 2007; Odenwald 2007; Odenwald et al

2007; Balint et al 2009; Odenwald et al 2009). Amphetamine has been associated with performance improvement on cognitive processes e.g. attention and psychomotor functioning. In contrast, it appears to impair performance in other areas of cognitive functioning, particularly those requiring ability to sieving out irrelevant information and/or visual scanning (Hoffman and Al'bsi 2010; Silber et al 2006).

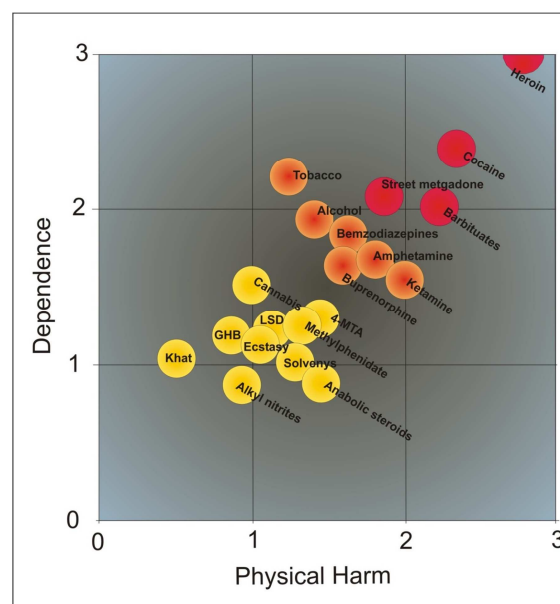


Figure 8. Rational scale to assess the harm of five drugs (Source: Nutt David et al 2007)

6.2. Oral consequences

The association between Khat chewing and cigarette or water-pipe smoking may increase the risk of epithelial dysplasia (Tefsaye 2006; Ali 2007). Oral diseases reportedly associated with Khat chewing include periodontitis, oral leukoplakia and oral cancer (Lukandu et al 2010; Rastam et al 2010; El-Wajeh and Thornhill 2009; Fasanmada and Newman 2007). In recent a study (Faleh et al 2007) the association of Khat chewing with the occurrence of oral cancer, the frequency of oral cancer among whole body cancers and the patients' histories of tobacco consumption and Khat chewing were examined in Yemen. the high relative frequency of oral SCC may be related to the habits of chewing tobacco and Khat. The association between tobacco smoke and

Table 5. Characteristics of the selected psychoactive stimulants

Stimulant	Primary Mechanism Action	Behavioral Effect	Tolerance	Withdrawal	Prolonged use Effects
Nicotine	<ul style="list-style-type: none"> - Nicotinic cholinergic receptor agonist. - Increases sodium inflow through the channels, - Causing depolarization 	<ul style="list-style-type: none"> - Arousal, - Increased attention, concentration and memory - Decreased anxiety and appetite. - Stimulant-like effects 	<ul style="list-style-type: none"> - Tolerance develops through metabolic factors, as well as receptor changes. 	<ul style="list-style-type: none"> - Irritability, hostility, anxiety, dysphoria, depressed mood, decreased heart rate, increased appetite. 	<ul style="list-style-type: none"> - Health effects due to smoking well-documented. - Difficult to dissociate effects of nicotine from other tobacco components.
Amphetamines	<ul style="list-style-type: none"> - Increased release of dopamine from nerve terminals via dopamine transporter. - Not dependent upon action potentials. - Inhibits monoamine oxidase (MAO) 	<ul style="list-style-type: none"> - Increased alertness arousal, energy, motor activity, speech, self-confidence, concentration, feelings of well-being - Decreased hunger. - Increased heart rate. - Increased respiration, euphoria 	<ul style="list-style-type: none"> - Develops rapidly to behavioral and physiological effects 	<ul style="list-style-type: none"> - Fatigue - Increased appetite, irritability, emotional depression anxiety 	<ul style="list-style-type: none"> - Sleep disturbances - Anxiety - Decreased appetite - Increased blood pressure. - Decreased brain dopamine, precursors, metabolites and receptors

Source: WHO 2004

periodontal diseases has been studied in a plethora of clinical and epidemiological investigations and many carcinogens such N-nitrosamines, aromatic amines, and polycyclic aromatic hydrocarbons are found in tobacco smoke (Smith et al 2000; Smith et al 1997; Bartsch et al 2000). However it has been estimated that smoking accounts for half of all periodontal diseases (Tomar and Asma 2000). Tobacco in its many forms is a risk factor for oral cancer, periodontal disease, gingival recession, coronal, and root caries and oral mucosal lesions (in the case of smokeless tobacco).

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tobacco smoke (Smith et al 2000; Smith et al 1997; Bartsch et al 2000). However it has been estimated that smoking accounts for half of all periodontal diseases (Tomar and Asma 2000).

Tobacco in its many forms is a risk factor for oral cancer, periodontal disease, gingival recession, coronal, and root caries and oral mucosal lesions (in the case of smokeless tobacco). Moreover, tobacco adversely affects healing after periodontal treatment (Reno et al 2011; Tariq and Naseem 2000). While cigarette smoking is recognized as an important risk factor in human oral cancers (Reno et al 2011; Royal College of Physicians 2007; Sohn et al 2003; Tariq and Naseem 2000; Carl et al 1995), the effect of water pipe smoking (WPS) on these cancers is not known (Khan and Malhotra 2011; Rastam et al 2010). It is possible that the co-morbidity of Khat and tobacco use poses higher risk than use of Khat alone on emotion regulation and cognitive functions.

Most of previous researches focused on the effects of addictive behaviors related to the co-morbidity of tobacco and other psychoactive substances use e.g. alcohol (John et al 2003; Hurt and Patten 2003) and marijuana use (Humfleet and Haas 2004; Lai et al 2000; Burns et al 2000). Substance abuse behavior can be perceptively addressed in emergency departments via screening and delivery of brief intervention. Nonetheless, level of patients' readiness to change is not taken into account, and then such substance abuse interventions may not be efficient (Fraustoand Bazargan-Hejazi 2009). Cigarette, waterpipe, Khat and amphetamine

are psychoactive stimulants with the capacity to alter mood, cognition and behavior. Literature shows that students and workers like long distance drivers chew Khat to get the stimulant effect that improves performance, keeping them alert and increasing work capacity (Halbach 1972; Kalix and Braenden 1985; Zein 1988; Toennes et al 2003; Al-Habori 2005). Khat chewing associated with various neurobehavioral impairments such as anorexia, weak stream of micturition, post-chewing urethral discharge and insomnia (delayed bedtime), which in turn result in late wake-up the following day, besides low work performance (Nageeb et al 2002; Tesfaye et al 2006). These effects are believed to be caused by the central and peripheral actions of cathinone and cathine in the Khat leaves (Smith-Simone et al 2008). While psycho-social indicators of cigarette smoking (i.e. socio-demographic level, risk assessment, social norms, and pluralistic ignorance) were considered essential determinants of understanding smoking behavior, mainly among youth (DHHS 1994; Flay et al 1999; Tariq and Naseem 2000; Kobus 2003; Tyas and Pederson 1998), surprisingly, a few researches have investigated these factors in young adults, particularly those that are using alternative forms of tobacco such as waterpipe (Attia et al 2010; Eissenberg et al 2008; Smith 2006; Smith-Simone et al 2008). Nicotine is a potent and powerful agonist of several subpopulations of nicotinic receptors of the cholinergic nervous system and depends on dopamine for the behavioral effects that are most relevant for its reinforcing properties. This is likely to be the basis of the addictively-producing ability of tobacco. However, other neuronal systems related to substance dependence, such as opioid, glutamate, serotonin and glucocorticoid systems may also be modulated by nicotine and may be of importance to specific aspects of substance dependence (Dani and De Biasi 2001; Kenny and Markou 2001; Malin 2001). Nicotine results in some dose-related psychoactive effects in humans that are similar to those of addictive substances, and it elevates scores on comparatively standardized tests for liking and euphoria that are depended upon by WHO for evaluating addiction potential (Henningfield et al 1996; Vidal 1996; Paterson and Nordberg 2000; WHO 2004).

Dependence to some psychoactive drugs such as methamphetamine causes slow performance in executive functions related to frontal lobe (Han et al 2008) and weakened performance on the tests associated with ability of information manipulation, abstract thinking and perceptual speed (Simon et al 2002). Patients are considered comorbid whenever reported any use of any synthetic substances

including cocaine, opiates (illicit or illicitly obtained), marijuana, or (meth)amphetamine in the 30 days prior to admission or if their examined urine-positive for one of these synthetic drugs at admission. Major psychiatric diagnoses associated with (meth)amphetamine includes major depression, bipolar, other mood, schizoaffective, schizophrenia (Magura et al 2009). Galloway et al (2008) hypothesize that subsequent methamphetamine use will decrease only when interventions relatively reduce the associated craving. Cognitive-behavioral therapy has a capable efficaciousness in elevating patients' confidence to resist craving to methamphetamine misuse (Hekmat et al 2011; Yen et al 2004).

7. Lessons Learned

In order to design effective substance abuse control policy, it is essential to understand the abuse prevalence and its associated risk predictors. In the majority of cases, people use psychoactive substances because they expect to benefit from their use, whether through the experience of pleasure or the avoidance of pain. Reviewed literature has covered wide range of research topics associated mainly with neuro-cognitive deficit of chronic users of psychoactive substances including amphetamines and methamphetamines.

Careful screening of previous research studies addressed various addictive substances indicates an alarmingly increasing prevalence of nicotine addiction in the form waterpipe smoking in Arabic Peninsular and among Arab communities across the world. Despite the lethal ailments associated to waterpipe (shisha) smoking, a little attention been paid to address its disastrous consequences. This underestimation to the health risks of shisha smoking attributed mainly to the common misconceptions developed by users who considered shisha smoking to be less deleterious to human health than cigarettes. Reviewed literature indicates that waterpipe tobacco smoking involves toxicant inhalation at even greater levels than with cigarette smoking, nonetheless is notably increasing in prevalence which represents a growing public health issue. Due to lack or absence of public health awareness, youth particularly in Arabic countries and among Arab communities worldwide, have fallen back on shallow experiences to form views that waterpipe smoking is less harmful than other forms of smoking and it currently becomes much more common and acceptable in students communities than other forms of addictive substances. This situation is even made worse by the fact that Near- and Middle-east regions account for > 90% of global amphetamine seizures in which Saudi Arabia alone

accounts for approximately 30% of all global amphetamine seizures. In bringing all these issues together, a roadmap is drawn for future substance abuse research studies pertaining to psychosis and neuropsychological effects of nicotine, amphetamine and amphetamine-type stimulants (ATS) and psychiatric comorbidity on, emphatically, Arab populations worldwide.

A vast body of evidence has proved that there is an adverse impairment in memory remarkably associated with chronic amphetamine and methamphetamine abuse. Pharmacologically, there is some correspondence between the active constituents (e.g. cathinone and cathine) of Khat and amphetamines; future studies therefore, should also vigilantly pay attention to examining the cognitive functioning (with much emphasis on the domains of learning, memory, and executive functions) in chronic Khat users and abstinent Khat users. In light of some common psychoactive characteristics of the reviewed substances, effects of addictive pleasurable combination of these psychoactive substances should be taken in account when extracting hypotheses for future studies tackling the neurobehavioral effects of Khat.

Care should be taken in future research studies dealing with psychoactive substances to account for the co-morbidity or polystimulant use factor. Furthermore, more attention should be given to the perplexed factors of inadequate sample size and distribution as well as inappropriate variables of inclusion/exclusion criteria.

Knowledge gained from this literature should lead to greater understanding on the timing, duration, and extent to which specific risk and protective factors influence the outcomes of psychoactive substance use. In turn, findings from these studies bring to light the scientific need for future substance abuse studies pertaining to treatment and prevention.

Health decision-makers together with healthcare providers, campus supervisors, health instructors, religious guiders and educators, need not only to pay attention to conventional forms of tobacco smoking such as cigars but also to rejuvenated technique of tobacco smoking such as waterpipe in order to establish more informed prevention, treatment, and policy strategies for tobacco control.

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