Primary care physicians' barriers to initiate insulin in
Type 2 diabetes mellitus. A survey from the Eastern Province,
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From the Editor

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In this issue various papers from the region deal with important issues in primary health care.

Qasim M, A et al ; explored barriers that PHC physicians in the Eastern Province, KSA, face in initiating insulin therapy for type 2 diabetes mellitus. A self-administered questionnaire was used among PHC physicians in the Eastern Province (Dammam and Qatif) during January and February 2014. A total of 194 primary care physicians were surveyed, with an overall response rate of 84%. Half of the physicians reported that they have no experience with the initiation of insulin. This study showed that PHC physicians faced many problems in initiating insulin for type 2 diabetic patients. Organizing focused CPD sessions and implementing clear guidelines supported with insulin initiating algorithm will make insulin initiation easier. The PHC system should provide supporting staff such as chronic care nurses, dieticians, diabetic educators and pharmacists to work in a collaborative team with PHC physicians.

Helvaci, M,R et al; looked at some alarming consequences of sickle cell diseases (SCDs). The study included 434 patients (212 females) with similar ages in males and females (30.8 versus 30.3 years, respectively, p>0.05). Chronic obstructive pulmonary disease (25.2% versus 7.0%, p<0.001), ileus (7.2% versus 1.4%, p<0.001), cirrhosis (8.1% versus 1.8%, p<0.001), coronary heart disease (CHD) (18.0% versus 13.2%, p<0.05), chronic renal disease (CRD) (9.9% versus 6.1%, p<0.05), and stroke (12.1% versus 7.5%, p<0.05) were also higher in males. There were 31 mortality cases (17 males) with similar ages in males and females (30.2 versus 33.3 years, respectively, p>0.05). The authors concluded that SCDs are severe inflammatory processes on vascular endothelium at the capillary level, terminating with an accelerated atherosclerosis induced end-organ failures and a shortened survival in both genders. Leg ulcers, digital clubbing, CHD, DVT and/or varices and/or telangiectasias, cirrhosis, CRD, and BPH may be the alarming consequences of SCDs indicating an advanced disease.

Salem, M et al carried a Descriptive cross-sectional study, this study was conducted at the Primary Health Care Corporation (PHCC) in Qatar and it included all physicians from seven health centers affiliated to primary health care in Qatar. The sample size was 144 physicians from both genders male and female. With response rate 90%. The prevalence of burnout in the study sample reaches 16.08% among primary health care physicians. No significant relation between socio-demographic characters and burn out except for social problems. The authors concluded that burnout syndrome is common among primary health care physicians. It is very serious and primary reasons should be looked at and resolved. With the improvement of physician ability and capacity to cope with their work daily stresses and teaching them with skills that could change how they perceive their work environment into positive healthy life style would result into big improvement.

Ledari, F,M et al; examined the relationship between life skills with functional dysfunction and sexual satisfaction in women referred to health centers of Shahroud University of Medical Sciences. The data collection tool was four questionnaires of demographic, General Health (GHQ-28), Life Skills and Sexual Function Index (FSFI).Data were analyzed using SPSS. Mean score of sexual function was 58.07 ± 10.63 and sexual satisfaction was 4.38 ± 0.99. The average total score of life skills was 508.99±46.82, which was ranged from lowest amount in the professional skills as 10.42 ± 2.13 and the highest amount in mental health as 81.93 ± 9.10. There was a significant relationship between life skills and sexual satisfaction and functional dysfunction. (p 0.05). The findings of the study indicated a relationship between life skills and sexual satisfaction and functional dysfunction, so that an increased functional dysfunction and sexual dissatisfaction was observed in people with low life skills.

Ghaleghazi, D, M et al; Investigated the cytotoxic effect of chamomile aqueous extract on 4T1 and 47D cells and level of caspase3 protein in breast cancer cells T-47D. Breast cancer cells 4T1 and T-47D were treated by blue extract of Chamomile with various concentrations for 24 hours and then using MTT method, the rate of cytotoxic effect of Chamomile was checked on abovementioned cells. This study showed that Chamomile extract significantly reduced breast cancer cells survival concentration-dependent compared to control group. Dependent on concentration and time, the Chamomile extract also increased caspase3 protein, indicating induction of apoptosis in mentioned cells. The authors concluded that chamomile extract, dependent on concentration and time, was able to remove breast cells that can be arising from increasing the level of caspase3 protein. These results can be used in future studies on the anti-cancer effect of Chamomile extract.

Negar Razeghi, N et al;compared the sexual behavioral patterns and mental health in women and men victims of identity in the family courts of Tehran. In order to achieve this purpose, 100 cases of women and men (50 males and 50 females) were referred to courts and cluster couples who were referred to the court or to family counseling centers through ministry of justice. Data of findings showed that the difference between mean obsessive-compulsive disorder, interpersonal sensitivity, depression, and anxiety was significant in both male and female victims. According to the men's mean in obsessive-compulsive indices, anxiety was significantly higher than women, and in depression, aggression and interpersonal sensitivity in women is more than men, and also the difference in mean sexual function in two groups of women and men are not victims of betrayal.

Kerman, M, T et al; surveyed the effect of FIFA 11+ injury prevention program on on dynamic balance and knee isometric strength of female players in soccer super league. Sample of study were included 30 subjects of female players of Shahrdari Bam, super league soccer team. 11+ injury prevention training protocol should be completed within eight weeks, at least two times a week and approximately 20-25 minutes. Research finding indicates that 11+ injury prevention training program led to significant increase in flexion and extension strength of knee joint and dynamic balance in the posterior and poster-lateral directions in experimental group (p≥0/05). The authors concluded that because 11+ injury prevention program includes special soccer movements, plyometric, strength and balance trainings, it has effect on muscular strength and dynamic balance in posterior and poster-lateral directions in professional soccer players. It can also be preventive factor in lower extremity injuries because of increasing knee strength.

Dehkordi, P,K, H et al; looked at the role of opium in the management of patients with advanced COPD remains undefined. They studied two groups of patients with COPD who were attending the chest clinic of Labaffinejad hospital. Group A- consists of COPD patients with history of smoking alone and group B- patients who consume opium in addition to cigarette smoking. Results shows that there is significant difference (p = 0) between two groups for FVC and FEVl. We conclude that opium may have an beneficial effect to improve Jung function in patients with sever COPD.

Dehkordi, P,K, H et al; looked at the Diagnosis of Pulmonary Tuberculosis by measurement of ADA.CEA and PCR in Bronchoalveolar lavage. They did a cross sectional study conducted in Shahrekord Hajar hospital and then 100 patients enrolled in our study (62 female,38male). These patients admitted in hospital and we done bronchoscopy with BAL and then fluid analysed for ADA,CEA , PCR and sputum smear for TB .from 100 patient that evaluated in this study 9 patient had TB , 39 patient had pneumonia, 11 patient had primary lung malignancy, 9 patient had metastases to lung and 8 patient had bronchitis. In Patients with TB the level of ADA were not significantly elevated in BAL. ADA increased significantly in patients with pneumonia (P: 0/95). In patients with metastases to lung & primary lung cancer &combination of both group compared to other patient without malignancy there were not relationship between CEA . PCR was positive in TB and other patients, but significantly increased in TB. (p=0/021). The authors concluded that although thought that CEA may be elevated in BAL of patients with malignancy and ADA in tuberculosis we did not found correlation in these patients. this study show that ADA and CEA levels in BAL fluid do not help us in diagnosis of TB or cancer. it may be has false positive in pneumonia ,COPD ,and other disease ,but PCR for TB may by help us for TB diagnosis but not alone.

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Primary care physicians' barriers to initiate insulin in Type 2 diabetes mellitus. A survey from the Eastern Province, Saudi Arabia

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Abstract

Background: The majority of type 2 diabetic patients seek care at the primary care level. With rising prevalence, the primary health care (PHC) physicians will have a greater role which will mandate further involvement in diabetes management, including starting and monitoring insulin.

Objectives: To explore barriers that PHC physicians in the Eastern Province, KSA, face in initiating insulin therapy for type 2 diabetes mellitus.

Methods and Material: A self-administered questionnaire was used among PHC physicians in the Eastern Province (Dammam and Qatif) during January and February 2014. We used a validated tool to assess barriers related to insulin therapy centered on 4 main themes: issues with doctor's experience; explanation burden; concerns about patients' burden and regarding insulin therapy.

Results: A total of 194 primary care physicians were surveyed, with an overall response rate of 84%. The majority of the physicians (80.9 %) were doctors with no postgraduate training, and 19.1% had postgraduate qualifications. Half of the physicians reported that they have no experience with the initiation of insulin. One third of the physicians perceived their current experience as a barrier to the initiation of insulin for their patients. There were significant variations in perceived barriers among trained and untrained doctors.

Conclusions: This study showed that PHC physicians faced many problems in initiating insulin for type 2 diabetic patients. Organizing focused CPD sessions and implementing clear guidelines supported with insulin initiating algorithm will make insulin initiation easier. The PHC system should provide supporting staff such as chronic care nurses, dieticians, diabetic educators and pharmacists to work in a collaborative team with PHC physicians.

Key words: Initiation of insulin, type 2 diabetes, primary health care physicians, and barriers.

Introduction

Diabetes mellitus (DM) is one of the most common non-communicable global diseases (NCDs) (1). The International Diabetes Federation 2010, ranked Saudi Arabia as the country with the third highest prevalence of diabetes (2).

A national survey in 2004 estimated that 23.7 % of Saudi adults had Type 2 Diabetes Mellitus (T2DM), and this percentage increased to 30 % in 2011(3, 4).

Despite the widespread benefits of controlling diabetes, only one third of patients in KSA have optimum glycemic control (5). Though there are many options for controlling diabetes, insulin is the most effective pharmacological option (6).

However, treatment with insulin is very complex in comparison to oral medications (7). Therefore; it requires a knowledgeable, experienced physician and a cooperative patient (7).

In KSA, the majority of patients with diabetes seek medical care at the primary care level(2). Furthermore, the burden on the PHC physicians will be even greater as prevalence rises, compelling them to increase the scope of their involvement in diabetes management to include starting and monitoring insulin. Research indicates that the confidence doctors in primary health care possess to start insulin varies worldwide. The majority of GPs in the UK and Netherlands start and monitor their patients, whereas in Australia, less than 20% of general practitioners start insulin among diabetic patients (8, 9). Similarly, a survey of 28 PHC centers in KSA revealed that approximately 35 % of T2DM patients had been on insulin, either alone or in combination with oral hypoglycemic agents (10).

Different barriers to initiating insulin have been studied in many nations (11). These can be categorized as physician-related, system-related and patient-related factors. The determinants which hinder physicians from starting insulin therapy include: lack of knowledge, lack of diabetes-oriented educational activities, scarcity of evidence-based guideline application, fear of hypoglycemia, non-compliance of patients as well as financial and time constraints (12).

However, there is very little published evidence in KSA on physician- related barriers concerning insulin therapy. Moreover, in order to understand the cultural and contextual care in KSA, it is important to understand the barriers associated with PHC physicians so that targeted interventions can be planned. Consequently, the aim of this study was to explore the obstacles primary care physicians face concerning insulin therapy for patients with type 2 diabetes mellitus in the Eastern Province, KSA.

Methods and Material

The study was a cross-sectional study through self-administered questionnaire targeting all primary care physicians working in the eastern province of Saudi Arabia, Qatif and Dammam cities from January 2014 to February 2014.

Physicians' experience with insulin use in type 2 diabetes mellitus and their barriers to insulin initiation (dependent variables) was compared to their demographic data including age, sex, nationality, and work experience. Certification, place of graduation, number of diabetes related CME activities attended, the number of patients seen daily, the number of diabetic patients seen weekly (independent variables).

The questionnaire was adapted from the PAINT questionnaire of the Japanese DAWN study and was approved by a consultant family physician and a clinical research expert. (see Appendix A).

Reliability of the questionnaire was examined using Cronbach's alpha statistic, and the alpha Coefficient was 0.94, which was considered highly reliable.

A pilot study of 30 PHC physicians was done to assess the reliability of this questionnaire in our community. The internal consistency of the 30 responses collected was found to be good, with Cronbach alpha of 80.9%

After granted the approval of the local research committee, the regional directorate of primary care in the eastern province authenticated the start of our research. The questionnaire were distributed to all primary health care centers in Dammam and Qatif areas, Eastern Province, Saudi Arabia. In order to increase the response rate of the study, SMS messages were sent to PHC physicians prior to the distribution of the questionnaire. Thereafter, the questionnaires were handed to the physicians either personally by the primary investigator or through the department of training and development of the regional primary care administration.

In the 8 weeks of collection, 194 questionnaire out of 230 PHC physicians in both Dammam and Qatif were obtained, giving an 84% response rate.

The Statistical Package of the Social Sciences (SPSS) version 21.0 was used for the statistical analysis.

A score was calculated for the response at each one of the four dimensions of the barrier part of the questionnaire. A score of 60% or higher was considered a barrier in each dimension.

Appropriate statistical analytical techniques were performed. Frequency distribution tables were constructed with the mean and standard deviation. Significant level was set at less than 0.05 throughout the study. Independent t-test, Pearson correlation coefficient and Chi-square ($\chi2$)

were used to examine the association between each independent variable and each outcome measure.

To our knowledge, this was the first study in the Eastern Province, which focused on the barriers confronting primary care physicians in initiating insulin in type 2 diabetes.

Ethical consideration:
The cover letter of the questionnaire clarified the objectives of the study and the assurance of confidentiality.

Approval was obtained from the local research committee of the Regional Directorate of Primary Care in the Eastern Province before conducting the research. Primary investigators encouraged physicians' participation, but they were assured of their right to refuse to participate. Physicians were given the assurance that the outcome of the research would not be used as a means of appraising their performance. To maintain confidentiality, the physicians were to send their completed questionnaire directly to the principal investigator.

Results

The total number of primary care physicians working in Qatif and Dammam was 230. A total of 194 physicians completed the study questionnaire, yielding an overall response rate of 84%.

The mean age of all respondents was 33±7.7 years, with a minimum age of 24, and a maximum age of 56 years. Of those who indicated their gender, 124(64.9 %) were female while 67 (34.1%) were male. Seventy nine percent of the study participants were Saudis and 20.8% were non-Saudis. (Table 1) A majority of them were graduates from the University of Dammam (UOD).

Table 1: Sociodemographic characteristics of physicians

Table 2: Work Experience and load on physicians		
Work experience in PHC	**N**	**%**
0 - 9	151	78.6
10 - 18	27	14.1
19 - 27	14	7.3
number of patients /day		
0 - 20	43	22.5
21 - 40	93	48.7
41 - 60	43	22.5
61 and more	12	6.3
Number of Diabetic Patients /week		
0 - 20	129	69.7
21 - 40	43	23.2
41 - 60	10	5.4
61 and more	3	1.6

The mean duration of work experience as primary care physicians was 5.8±6.3 years.

The majority of the physicians (80.9 %) were general practitioners. The minority included: Saudi board qualified 15 (7.7%), graduates with diplomas 10 (5.5%), and doctors with postgraduate qualifications other than in family medicine were 12, constituting 6.2%. (Table 1)

The majority of physicians (three quarters) had attended at least one diabetes- related CME activity in the past year, while one quarter had not attended any activity.

The mean number of patients encountered per day was 35.54±1.8 patients, with a minimum of one patient/day and maximum of one hundred patients/day. As shown in Table 2, almost one half of the physicians saw 21 to 40 patients daily, whereas, 22.5% had ≤ 20 patients/day. The same percentage of physicians saw 41 to 60 patients daily.

22.5% had ≤ 20 patients/day. The same percentage of physicians saw 41 to 60 patients daily.

Of the 194 PHC physicians who participated in this study, 46.9% had started insulin with their diabetic patients, while 53.1% had never given insulin to any diabetic patient. The proportion of physicians who offered insulin to their patients was slightly higher than those who actually started their patients on insulin (56.7% vs 46.9%). Approximately, less than half (43.3) of the participants did not offer their diabetic patients insulin therapy. In respect of qualifications, the findings

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qualifications, the findings revealed that of the PHC physicians who started insulin, the rate of initiating it was noticeably higher among qualified family physicians (100% among family medicine board graduates, and 80% among family medicine diploma graduates). Only 40.8% and 33.3% of GPs and doctors with other qualifications respectively, initiated insulin therapy.

After combining the 'agree' and 'strongly agree' as well as the 'disagree' and 'strongly disagree' responses in one category as shown In Tables 3, 4 and 5, the frequency distribution of each item response is displayed for all PHC physicians, PHC physicians without postgraduate qualifications and PHC physicians with post- graduate qualifications in family medicine.

Around 28% of physicians regarded their current experience with insulin as an obstacle to initiating insulin for their patients. There were significant variations among the doctors with different qualifications (P value 0.002). The largest group was that of GPs (35.2%), followed by doctors with other qualifications (9.1%). Family medicine certified doctors, (0.00%) both those with a diploma and board graduates did not perceive this as a barrier. The biggest obstacle, which held the physicians back from using insulin, was their disquiet about insulin therapy (the issues of patient rejection and decreased compliance, insulin use in the elderly, need for hospitalization and the risk of hypoglycemia). The majority of physicians considered this an obstacle (80%).

Despite the total agreement of doctors on the previously mentioned concerns, significant variations among the doctors with different qualifications were also noticed (P value 0.007). GPs constituted 84.5% as compared to 61.5% and 70% among board and diploma certified respectively.

More than one third of the physicians (36.6%) considered burden of patients as a barrier to use insulin. There were no significant differences with regard to the different qualifications held by the doctors, P value 0.256. Board certified formed the smallest group that considered this a burden (13.3%), while doctors with other qualifications were the most concerned about patients. The weight of this burden among GPs and diploma certified was 38% and 40% respectively. Furthermore, almost half of the doctors also considered the pain and cost as the barriers to use of insulin (46.9%). However, the difference among the physicians with different qualifications was not significant (P value 0.141). Board certified doctors was the smallest group that perceived ruminator of patient burden as a barrier (3.3%) with only 20% of them considering it as a reason for not using insulin. Almost half of GPs (49.0%) regard patient burden as a barrier and 40.0% of diploma certified did so.

The associations between each barrier domain was studied with regard to the following factors: doctors' attendance at diabetes-related CME activities; total number of patients seen daily; total number of diabetics seen weekly; and doctors acknowledgment of starting or offering insulin. There was a significant negative correlation between the total perception of barriers and CME attendance (P value 0.03); number of diabetic patients seen per week; and doctors acknowledgment of starting or offering insulin (P value 0.00) (Table 6).

Table 3: Frequency distributions for Questionnaire items, all PHC physicians

Items	Response		
	Agree to strongly agree (%)	Neutral (%)	Disagree to strongly disagree(%)
Issues with the doctor's experience			
1 My reputation would suffer if I offered insulin therapy	9.6	19.3	71.1
2 I'm not familiar with insulin therapy	25.9	21.2	52.8
3 It is difficult to select the type of insulin	28	20.2	51.8
4 It is difficult to adjust the insulin dose	34	20.6	45.4
5 It is difficult to learn the methods of use of the many types of insulin injection devices (including insulin pens)	23.6	16.2	60.2
6 It is difficult to learn new methods of insulin therapy	13.1	18.8	68.1
7 My clinic is not equipped to provide insulin therapy	33.5	16.0	50.5
8 It is difficult to remember different types of insulin preparations	13.1	21.5	65.4
9 In principle, I would rather avoid diabetes patients	6.8	8.4	84.7
10 If necessary, I can refer the patient to a specialist	78.5	12.6	8.9
11 It is difficult to add insulin with oral hypoglycemic agent	16.8	19.9	63.4
Burden related to explanations			
1 It is time-consuming to explain injection methods and the use of injection devices	46.3	13.7	40
2 It is time-consuming to explain hypoglycemia and its management	30.2	10.6	59.3
3 I do not have staff (nurses, pharmacists) who can assist with explanations	39.8	13.6	46.6
4 It is time-consuming to explain self-monitoring of blood glucose	38.2	12.0	49.7
5 It is difficult to provide guidance and education on insulin injection to patients	24	23.4	52.6
6 I do not have time to persuade patients to undergo insulin therapy or provide guidance on it	22.4	20.8	56.8
7 It is difficult to educate staff (e.g. nurses) about insulin therapy	12.4	18.7	68.9
Consideration of burden on patients			
1 It is difficult to recommend insulin therapy considering the pain associated with it	22.8	17.6	59.6
2 The patient would have to pay more for treatment and monitoring	33.3	20.3	46.4
Concerns regarding insulin therapy			
1 Patients would resist insulin therapy	76.7	17.1	6.2
2 I have concerns about the use of insulin therapy in elderly patients	61.3	22.5	16.2
3 Hospitalization is necessary to start insulin	13.5	10.9	75.6
4 There is a higher risk of hypoglycemia with insulin therapy compared to other therapies	73.1	10.9	16.1
5 Compliance with insulin therapy tends to be low	42.7	26.6	30.7

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The more the doctors started and offered the use of insulin, the less they considered experience or the lack of it as a barrier (-0.320 correlation, P value 0.00), explanation (-0.166 correlation, P value 0.03) or patients' burden (-0.127 correlation, P value 0.90). Seeing more diabetic patients and frequent attendance at diabetes-related CME activities decreased most significantly the perception of doctors' experience as barriers (correlation -0.295, -0.191 with P value 0.00 and 0.01 respectively).

Table 4: Frequency distributions for Questionnaire items for PHC doctors without post-graduate qualification

	Items	Response		
	Issues with the doctor's experience	Agree to strongly agree (%)	Neutral (%)	Disagree to strongly disagree(%)
1	My reputation would suffer if I offered insulin therapy	9.3	19.8	71
2	I'm not familiar with insulin therapy	28.6	24.4	47
3	It is difficult to select the type of insulin	32.1	22.6	45.2
4	It is difficult to adjust the insulin dose	39.1	22.5	38.5
5	It is difficult to learn the methods of use of the many types of insulin injection devices (including insulin pens)	25.9	15.7	58.4
6	It is difficult to learn new methods of insulin therapy	13.3	21.1	65.7
7	My clinic is not equipped to provide insulin therapy	37.4	16.6	46
8	It is difficult to remember different types of insulin preparations	14.5	24.1	61.4
9	In principle, I would rather avoid diabetes patients	7.3	9.7	83
10	If necessary, I can refer the patient to a specialist	83.1	10.8	6
11	It is difficult to add insulin with oral hypoglycemic agent	18.7	22.3	59
	Burden related to explanations			
1	It is time-consuming to explain injection methods and the use of injection devices	46.1	15.1	38.8
2	It is time-consuming to explain hypoglycemia and its management	30.5	11	58.5
3	I do not have staff (nurses, pharmacists) who can assist with explanations	41	13.3	45.8
4	It is time-consuming to explain self-monitoring of blood glucose	36.1	13.9	50
5	It is difficult to provide guidance and education on insulin injection to patients	24.6	25.1	50.3
6	I do not have time to persuade patients to undergo insulin therapy or provide guidance on it	24.6	21.6	53.9
7	It is difficult to educate staff (e.g., nurses) about insulin therapy	11.9	19.6	68.5
	Consideration of burden on patients			
1	It is difficult to recommend insulin therapy considering the pain associated with it	25.6	19.0	55.4
2	The patient would have to pay more for treatment and monitoring	34.1	19.8	46.1
	Concerns regarding insulin therapy			
1	Patients would resist insulin therapy	75.6	17.3	7.1
2	I have concerns about the use of insulin therapy in elderly patients	63.5	22.2	14.4
3	Hospitalization is necessary to start insulin	15.5	11.9	72.6
4	There is a higher risk of hypoglycemia with insulin therapy compared to other therapies	74.4	10.7	14.9
5	Compliance with insulin therapy tends to be low	45.8	23.8	30.4

Table 5: Frequency distributions for Questionnaire items, PHC doctors with post graduate qualification (family medicine diploma and board certified)

Items	Response		
Issues with the doctor's experience	Agree to strongly agree (%)	Neutral (%)	Disagree to strongly disagree(%)
1 My reputation would suffer if I offered insulin therapy	12.0	16.0	72.0
2 I'm not familiar with insulin therapy	8.0	0.0	92.0
3 It is difficult to select the type of insulin	0.0	4.0	96.0
4 It is difficult to adjust the insulin dose	0.0	8.0	92.0
5 It is difficult to learn the methods of use of the many types of insulin injection devices (including insulin pens)	8.0	20.0	72.0
6 It is difficult to learn new methods of insulin therapy	12.0	4.0	84.0
7 My clinic is not equipped to provide insulin therapy	8.0	12.0	80.0
8 It is difficult to remember different types of insulin preparations	4.0	4.0	92.0
9 In principle, I would rather avoid diabetes patients	4.0	0.0	96.0
10 If necessary, I can refer the patient to a specialist	48.0	24.0	28.0
11 It is difficult to add insulin with oral hypoglycemic agent	4.0	4.0	92.0
Burden related to explanations			
1 It is time-consuming to explain injection methods and the use of injection devices	48.0	8.0	44.0
2 It is time-consuming to explain hypoglycemia and its management	28.0	8.0	64.0
3 I do not have staff (nurses, pharmacists) who can assist with explanations	32.0	16.0	52.0
4 It is time-consuming to explain self-monitoring of blood glucose	52.0	0.0	48.0
5 It is difficult to provide guidance and education on insulin injection to patients	20.0	12.0	68.0
6 I do not have time to persuade patients to undergo insulin therapy or provide guidance on it	8.0	16.0	76.0
7 It is difficult to educate staff (e.g., nurses) about insulin therapy	16.0	12.0	72.0
Consideration of burden on patients			
1 It is difficult to recommend insulin therapy considering the pain associated with it	4.0	8.0	88.0
2 The patient would have to pay more for treatment and monitoring	28.0	24	48
Concerns regarding insulin therapy			
1 Patients would resist insulin therapy	84.0	16.0	0.0
2 I have concerns about the use of insulin therapy in elderly patients	45.8	25.0	29.2
3 Hospitalization is necessary to start insulin	0.0	4.0	96.0
4 There is a higher risk of hypoglycemia with insulin therapy compared to other therapies	64.0	12.0	24.0
5 Compliance with insulin therapy tends to be low	20.8	45.8	33.3

Table 6: Relationship between barriers and Qualification degree

Barrier		Postgraduate qualification					Pearson Chi-Square		
		No	FMD	FMB	others	Total	Value	df	p
Issues with the doctor's experience	N	51	0	0	1	52	15.09	3	0.002
	%	98.10%	0.00%	0.00%	1.90%	100.00%			
	% within Qualification	35.20%	0.00%	0.00%	9.10%	28.70%			
Burden related to explanations	N	57	4	2	5	68	4.05	3	0.256
	%	83.80%	5.90%	2.90%	7.40%	100.00%			
	% within Qualification	38.00%	40.00%	13.30%	45.50%	36.60%			
Consideration of burden on patients	N	76	4	3	7	90	5.46	3	0.141
	%	84.40%	4.40%	3.30%	7.80%	100.00%			
	% within Qualification	49.00%	40.00%	20.00%	58.30%	46.90%			
Concerns regarding insulin therapy	N	131	7	8	6	152	12.12	3	0.007
	%	86.20%	4.60%	5.30%	3.90%	100.00%			
	% within Qualification	84.50%	70.00%	61.50%	50.00%	80.00%			
Total	N	57	2	0	2	61	11.20	3	.011
	%	93.40%	3.30%	0.00%	3.30%	100.00%			
	% within Qualification	40.40%	20.00%	0.00%	18.20%	34.90%			

Table 7: Correlation between each dimension and attendance of DM related CME, number of patients seen daily, number of diabetic patients seen weekly, number of diabetic started insulin, number of diabetics offered insulin

Barrier		Diabetes related CME	Daily patients seen	Weekly diabetics seen	Starting insulin	Offering insulin
Issues with the doctor's experience	Pearson Correlation	-0.191	.003	-0.295	-0.320	-0.320
	p	.011	.972	.000	.000	.000
Burden related to explanations	Pearson Correlation	-.045	.138	-.061	-0.166	-0.166
	p	.551	.063	.420	.028	.028
Consideration of burden on patients	Pearson Correlation	-.123	.097	-0.154	-.127	-.127
	p	.094	.183	.037	.090	.090
Concerns regarding insulin therapy	Pearson Correlation	-.028	-.004	-0.166	.011	.011
	p	.708	.953	.026	.883	.883
Total	Pearson Correlation	-0.164	.081	-0.270	-0.298	-0.298
	p	.032	.290	.000	.000	.000

Discussion

The aim of this study was to assess the prevalence of insulin initiation for type 2 diabetic patients by PHC physicians in the Eastern Province, Saudi Arabia, and to explore physicians' perception of barriers to the initiation of insulin. The results showed that primary care physicians faced many obstacles when considering initiating insulin for type 2 diabetic patients. Only half of the participants reported experience with the initiation of insulin for at least one diabetic patient, which is considered very low compared to the Japanese study (DAWN), in which most of the participants had experience with insulin therapy (13). The majority of physicians who initiated insulin were PHC physicians with no post - graduate qualifications (62 of the 157 i.e. 40.8 %). On the other hand, initiation of insulin was higher among PHC physicians with postgraduate qualifications (family medicine). This was consistent with the Kunt and Snoek finding (14).

For less than one third of the doctors, their perceived lack of experience (knowledge and attitude) with insulin seemed to be a barrier to the initiation of insulin. This gap was much more obvious with PHC physicians with no postgraduate qualification. The focused training and exposure to diabetic patients during postgraduate education seemed to improve knowledge and helped to change attitudes (15).

The Almesned study recommended an early introduction of diabetes training in undergraduate education(16). This can equip the newly graduated physician with adequate knowledge and skills together with the appropriate attitudes to deal with diabetic patients, and the confidence to prescribe insulin when indicated.

The most important obstacles relating to giving explanation to patients were the constraints of time: having enough time to explain injection methods, hypoglycemia and self-monitoring of blood glucose. Nearly half of the physicians' concerns were with the problem of having adequate time to explain injection devices. More than half of family physicians and more than one third of PHC physicians without postgraduate qualifications regarded explanation of self-monitoring of blood glucose as time consuming.

This finding is consistent with other studies done by Haque et al, Hayes et al and al Mesned et al (2, 15, 16).

The perception of barriers to giving explanations has no relationship with postgraduate qualification, which further suggests that these barriers relate to the health care system in Saudi Arabia. Incorporating some system focused interventions can reduce the barriers to giving explanations. For example, providing patients with specially prepared explanatory materials can facilitate the process and reduce the burden of explaining (17). In addition, preparing patients for insulin and arriving at the decision to give insulin does not have to be done in a single session. There should be a number of close consultations and discussions culminating in an agreement. All primary health care centers have chronic disease nurses who

together with the care physicians are supposed to form the diabetes management team especially with regard to education. Giving chronic disease nurses the necessary education on diabetes and encouraging them to acquire certification on diabetes management will make the process of explaining much more manageable.

This study found that more PHC physicians with no postgraduate qualifications were concerned about the pain that accompanies insulin injection; however, this difference was not statistically significant when compared with postgraduate qualified doctors. The literature reveals that factors that contribute to injection pain include: the length and diameter of the needle, injection techniques and inadvertent IM injection (18). Moreover, some diabetic patients anticipate injection pain based on their previous experience, while others have a real needle phobia. There are various ways of minimising injection pain, such as giving adequate explanation, training, and introduction of new devices like the insulin pen etc. However, for a patient with injection phobia, psychological counselling would be necessary.

One third of the physicians also showed concern about increasing the financial burden of their patients. This is consistent with other studies done in Japan and South Africa. (11,13). As with many other anti-diabetes medications, different types of insulin including those administered with pens are available at the PHC centers. In addition, glucometers and strips can be provided, at no extra cost to all diabetics on insulin by Saudi MOH. Proper and timely coordination of care between physicians, pharmacists and the central pharmacy might ensure the availability and accessibility of these essential tools.

This study highlights significant concerns on insulin therapy. It seems that the majority of physicians without postgraduate qualifications perceived more barriers including: the use of insulin in the elderly; patient resistance; need for hospitalization; and lack of compliance by patients if prescribed. Most PHC physicians without PGQ perceived the initiation of insulin in the elderly as problematic. On the other hand, family physicians seemed to be less conservative and more inclined to following the guidelines that advocate individualizing the decision on initiating insulin rather than avoiding it (19). The second concern was the anticipation of patients' resistance to initiating insulin. This is also in accord with other PHC based studies in which the majority of PHC physicians agreed on the "psychogenic resistance" in their diabetic patients (20). Family physicians completely rejected the idea of admitting a diabetic patient for the sole purpose of starting insulin, though a few of the GPs held the opposite view.

The reason for this could be the smallness of the proportion of physicians who have experience with insulin.

This study showed a significant correlation between the perception of obstacles and the number of factors (Table 7) including: previous experience with insulin (initiation

or offering insulin to patients), the number of diabetes-related CME activities attended and the number of diabetic patients seen weekly. This important correlation matches the learning theory that repetitive encounters with a new concept enhances the process of learning and facilitates the conceptualization of the new learning event (21).

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Alarming consequences of the sickle cell diseases

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Abstract

Background: We tried to understand whether or not there are some alarming consequences of sickle cell diseases (SCDs).

Methods: All patients with SCDs were included.

Results: The study included 434 patients (212 females) with similar ages in males and females (30.8 versus 30.3 years, respectively, p>0.05). Smoking (23.8% versus 6.1%) and alcohol (4.9% versus 0.4%) were higher in males (p<0.001 for both). Disseminated teeth losses (5.4% versus 1.4%, p<0.001), transfused units of red blood cell (48.1 versus 28.5, p=0.000), chronic obstructive pulmonary disease (25.2% versus 7.0%, p<0.001), ileus (7.2% versus 1.4%, p<0.001), cirrhosis (8.1% versus 1.8%, p<0.001), leg ulcers (19.8% versus 7.0%, p<0.001), digital clubbing (14.8% versus 6.6%, p<0.001), coronary heart disease (CHD) (18.0% versus 13.2%, p<0.05), chronic renal disease (CRD) (9.9% versus 6.1%, p<0.05), and stroke (12.1% versus 7.5%, p<0.05) were also higher in males. There were 31 mortality cases (17 males) with similar ages in males and females (30.2 versus 33.3 years, respectively, p>0.05). Mean ages of leg ulcers (35.3 years), digital clubbing (35.4 years), CHD (35.7 years), deep venous thrombosis (DVT) and/or varices and/or telangiectasias (37.0 years), cirrhosis (37.0 years), CRD (39.4 years), and benign prostatic hyperplasia (BPH) (41.5 years) were higher in SCDs.

Conclusion: SCDs are severe inflammatory processes on vascular endothelium at the capillary level, terminating with an accelerated atherosclerosis induced end-organ failures and a shortened survival in both genders. Leg ulcers, digital clubbing, CHD, DVT and/or varices and/or telangiectasias, cirrhosis, CRD, and BPH may be the alarming consequences of SCDs indicating an advanced disease.

Key words: Sickle cell diseases, chronic endothelial damage, atherosclerosis

Introduction

Chronic endothelial damage may be the leading cause of aging-induced morbidity and mortalities by causing disseminated tissue hypoxia all over the body. Probably whole afferent vasculature including capillaries are mainly involved in the process since much higher blood pressure (BP) of the afferent vasculature may be the major underlying cause by inducing recurrent endothelial injuries. Therefore the term of venosclerosis is not as famous as atherosclerosis in the literature. Secondary to the chronic endothelial damage, inflammation, and fibrosis, vascular walls become thickened, their lumens are narrowed, and they lose their elastic natures those reduce blood flow and increase systolic BP further. Some of the well-known accelerators of the life-threatening atherosclerotic process are physical inactivity, excess weight, smoking, alcohol, and chronic inflammatory and infectious processes including sickle cell diseases (SCDs), rheumatologic disorders, tuberculosis, and cancers for the development of irreversible endpoints including obesity, hypertension (HT), diabetes mellitus (DM), peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary heart disease (CHD), cirrhosis, mesenteric ischemia, osteoporosis, and stroke, all of which terminate with early aging and premature death. They were discussed under the title of metabolic syndrome in the literature, extensively (1, 2). Although early withdrawal of the causative factors may delay terminal endpoints, the endothelial changes can not be reversed completely after the development of obesity, HT, DM, PAD, COPD, CRD, CHD, or stroke due to their fibrotic natures (3, 4). Similarly, SCDs are severe inflammatory processes on vascular endothelium at the capillary level, terminating with an accelerated atherosclerosis induced end-organ failures in early years of life. We tried to understand whether or not there are some alarming consequences of the SCDs indicating an advanced disease in such patients.

Material and methods

The study was performed in the Medical Faculty of the Mustafa Kemal University between March 2007 and June 2016. All patients with the SCDs were included into the study. The SCDs are diagnosed with the hemoglobin electrophoresis performed via high performance liquid chromatography (HPLC). Medical histories including smoking, alcohol, painful crises per year, epilepsy, deep venous thrombosis (DVT), transfused units of red blood cell (RBC) in their lives, surgical operations, leg ulcers, stroke, and priapism and benign prostatic hyperplasia (BPH) symptoms in males including urgency, weak stream, incomplete emptying, and nocturia were learnt. Due to their cumulative atherosclerotic effects together with the SCDs, patients with a history of one pack-year were accepted as smokers, and one drink-year were accepted as drinkers. A complete physical examination was performed by the Same Internist. Patients with disseminated teeth losses (<20 teeth present) were detected. Cases with acute painful crisis or any other inflammatory event were treated at first, and the laboratory tests and clinical measurements were performed on the silent phase. Check up procedures including serum iron, iron binding capacity, ferritin, creatinine, liver function tests, markers of hepatitis viruses A, B, C and human immunodeficiency virus, a posterior-anterior chest x-ray film, an electrocardiogram, a Doppler echocardiogram both to evaluate cardiac walls and valves and to measure systolic BP of pulmonary artery, an abdominal ultrasonography, a venous Doppler ultrasonography of the lower limbs, a computed tomography of brain, and a magnetic resonance imaging (MRI) of hips were performed. Other bones for avascular necrosis were scanned according to the patients' complaints. So avascular necrosis of bones was diagnosed by means of MRI (5). Associated thalassemia minors were detected with serum iron, iron binding capacity, ferritin, and hemoglobin electrophoresis performed via HPLC. Systolic BP of the pulmonary artery of 40 mmHg or higher is accepted as pulmonary hypertension (6). The criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in one second/forced vital capacity of less than 70% (7). Acute chest syndrome (ACS) is diagnosed clinically with the presence of new infiltrates on chest x-ray film, fever, cough, sputum production, dyspnea, or hypoxia (8). An x-ray film of abdomen in upright position was taken just in patients with abdominal distention or discomfort, vomiting, obstipation, or lack of bowel movement, and ileus is diagnosed with gaseous distention of isolated segments of bowel, vomiting, obstipation, cramps, and with the absence of peristaltic activity on the abdomen. CRD is diagnosed with a persistent serum creatinine level of 1.3 mg/dL or higher in males and 1.2 mg/dL or higher in females. Cirrhosis is diagnosed with physical examination findings, laboratory parameters, and ultrasonographic evaluation. Digital clubbing is diagnosed with the ratio of distal phalangeal diameter to interphalangeal diameter which is greater than 1.0, and with the presence of Schamroth's sign (9, 10). An exercise electrocardiogram is performed in cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is taken for the exercise electrocardiogram positive cases. So CHD was diagnosed either angiographically or with the Doppler echocardiographic findings as the movement disorders in the cardiac walls. Rheumatic heart disease is diagnosed with the echocardiographic findings, too. Stroke is diagnosed by the computed tomography of brain. Sickle cell retinopathy is diagnosed with ophthalmologic examination in patients with visual complaints. Eventually, prevalences of the consequences of the SCDs were detected in both genders, and compared in between. Beside that, mean ages of the consequences were detected in the SCDs. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 434 patients with the SCDs (222 males and 212 females). Mean ages of the patients were similar in males and females (30.8 versus 30.3 years, respectively, p>0.05). Prevalences of associated thalassemia minors were similar in males and females, too (72.5% versus 67.9%, respectively, p>0.05). Smoking (23.8% versus

Table 1: Characteristic features of the study patients

Variables	Male patients with SCDs*	p-value	Female patients with SCDs
Prevalence	51.1% (222)	Ns†	48.8% (212)
Mean age (year)	30.8 ± 10.0 (5-58)	Ns	30.3 ± 9.9 (8-59)
Thalassemia minors	72.5% (161)	Ns	67.9% (144)
Smoking	*23.8% (53)*	*<0.001*	*6.1% (13)*
Alcoholism	*4.9% (11)*	*<0.001*	*0.4% (1)*

*Sickle cell diseases   †Nonsignificant (p>0.05)

Table 2: Associated pathologies of the study patients according to the gender distribution

Variables	Male patients with SCDs*	p-value	Female patients with SCDs
Painful crises per year	5.0 ± 7.1 (0-36)	Ns†	4.9 ± 8.6 (0-52)
Disseminated teeth loss (< 20 teeth present)	*5.4% (12)*	*<0.001*	*1.4% (3)*
Transfused RBC‡ units	*48.1 ± 61.8 (0-434)*	*0.000*	*28.5 ± 35.8 (0-206)*
COPD§	*25.2% (56)*	*<0.001*	*7.0% (15)*
Ileus	*7.2% (16)*	*<0.001*	*1.4% (3)*
Cirrhosis	*8.1% (18)*	*<0.001*	*1.8% (4)*
Leg ulcers	*19.8% (44)*	*<0.001*	*7.0% (15)*
Digital clubbing	*14.8% (33)*	*<0.001*	*6.6% (14)*
CHD¶	*18.0% (40)*	*<0.05*	*13.2% (28)*
*CRD****	*9.9% (22)*	*<0.05*	*6.1% (13)*
Stroke	*12.1% (27)*	*<0.05*	*7.5% (16)*
Pulmonary hypertension	12.6% (28)	Ns	11.7% (25)
Autosplenectomy	50.4% (112)	Ns	53.3% (113)
Varices and/or telangiectasias	9.0% (20)	Ns	6.6% (14)
Rheumatic heart disease	6.7% (15)	Ns	5.6% (12)
Avascular necrosis of bones	24.3% (54)	Ns	25.4% (54)
Sickle cell retinopathy	0.9% (2)	Ns	0.9% (2)
Epilepsy	2.7% (6)	Ns	2.3% (5)
ACS***	2.7% (6)	Ns	3.7% (8)
Sinus arrhythmia	4.9% (11)	Ns	3.7% (8)
Mortality	7.6% (17)	Ns	6.6% (14)

*Sickle cell diseases   †Nonsignificant (p>0.05)   ‡Red blood cell   §Chronic obstructive pulmonary disease
¶Coronary heart disease   **Chronic renal disease   ***Acute chest syndrome

6.1%) and alcohol (4.9% versus 0.4%) were significantly higher in males (p<0.001 for both) (Table 1). Disseminated teeth losses (5.4% versus 1.4%, p<0.001), transfused units of RBC in their lives (48.1 versus 28.5, p=0.000), COPD (25.2% versus 7.0%, p<0.001), ileus (7.2% versus 1.4%, p<0.001), cirrhosis (8.1% versus 1.8%, p<0.001), leg ulcers (19.8% versus 7.0%, p<0.001), digital clubbing (14.8% versus 6.6%, p<0.001), CHD (18.0% versus 13.2%, p<0.05), CRD (9.9% versus 6.1%, p<0.05), and stroke (12.1% versus 7.5%, p<0.05) were all higher in males, significantly. There were 11 males (4.9%) with BPH symptoms with a mean age of 41.5 ± 10.6 (27-58) years. All of the patients could be treated with once daily 4 milligrams of doxazosin, orally. Additionally, there were 23 cases (10.3%) with priapism with a mean age of 33.4 ± 7.9

(18-51) years. There were 31 mortality cases (17 males and 14 females) during the ten-year follow up period. The mean ages of mortality were 30.2 ± 8.4 years (range 19-50) in males and 33.3 ± 9.2 years (range 19-47) in females (p>0.05) (Table 2). When we evaluated mean ages of the consequences of the SCDs, leg ulcers (35.3 years), digital clubbing (35.4 years), CHD (35.7 years), DVT and/or varices and/or telangiectasias (37.0 years), cirrhosis (37.0 years), CRD (39.4 years), and BPH (41.5 years) may be the alarming consequences indicating an advanced disease in such patients due to the significantly shortened survival of the SCDs patients in both genders (Table 3).

Table 3: Mean ages of the consequences of the sickle cell diseases

Variables	Mean ages of the patients
Sinus arrhythmia	27.2 ± 8.3 (18-50)
Ileus	29.8 ± 9.8 (18-53)
Hepatomegaly	30.2 ± 9.5 (5-59)
ACS*	30.3 ± 10.0 (5-59)
Sickle cell retinopathy	31.5 ± 10.8 (21-46)
Rheumatic heart disease	31.9 ± 8.4 (20-49)
Autosplenectomy	32.5 ± 9.5 (15-59)
Disseminated teeth loss (< 20 teeth present)	32.6 ± 12.7 (11-58)
Avascular necrosis of bones	32.8 ± 9.8 (13-58)
Epilepsy	33.2 ± 11.6 (18-54)
Priapism	33.4 ± 7.9 (18-51)
Left lobe hypertrophy of the liver	33.4 ± 10.7 (19-56)
Stroke	33.5 ± 11.9 (9-58)
COPD†	33.6 ± 9.2 (13-58)
Pulmonary hypertension	34.0 ± 10.0 (18-56)
Leg ulcers	*35.3 ± 8.8 (17-58)*
Digital clubbing	*35.4 ± 10.7 (18-56)*
CHD‡	*35.7 ± 10.8 (17-59)*
Varices and/or telangiectasias	*37.0 ± 8.4 (17-50)*
Cirrhosis	*37.0 ± 11.5 (19-56)*
CRD§	*39.4 ± 9.7 (19-59)*
BPH¶	*41.5 ± 10.6 (27-58)*

*Acute chest syndrome   †Chronic obstructive pulmonary disease   ‡Coronary heart disease   §Chronic renal disease
¶Benign prostatic hyperplasia

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Discussion

SCDs are chronic inflammatory processes on vascular endothelium terminating with accelerated atherosclerosis induced end-organ failures and a shortened survival in both genders (11, 12). Hemoglobin S (HbS) causes loss of elastic and biconcave disc shaped structures of RBCs. Probably loss of elasticity instead of shape is the main pathology since sickling is rare in peripheric blood samples of the SCDs patients with associated thalassemia minors, and human survival is not affected in hereditary spherocytosis or elliptocytosis. Loss of elasticity is present during whole lifespan, but exaggerated with inflammation, infection, and various stresses of the body. The hard RBCs induced chronic endothelial damage, inflammation, and fibrosis terminate with disseminated tissue hypoxia all over the body (13, 14). As a difference from other causes of chronic endothelial damage, the SCDs may keep vascular endothelium particularly at the capillary level (15), since the capillary system is the main distributor of the hard RBCs into the tissues. The hard cells induced chronic endothelial damage builds up an advanced atherosclerosis in younger ages of the patients. As a result, mean lifespans of the patients were 48 and 42 years in females and males in the literature, respectively (16), whereas they were 33.3 and 30.2 years in the present study. The great differences may be secondary to delayed diagnosis, delayed initiation of hydroxyurea therapy, and inadequate RBC supports during emergencies in Antakya region of Turkey (17). Actually, RBC supports must be given immediately during all medical or surgical events in which there is an evidence of clinical deterioration in the SCDs (8). RBC supports decrease sickle cell concentration in circulation and suppress bone marrow for the production of abnormal RBCs. So it decreases sickling-induced endothelial damage and inflammation all over the body.

Digital clubbing is characterized by increased normal angle of 165° between nailbed and fold, increased convexity of the nail fold, and thickening of the whole distal finger (18). The exact cause and significance is unknown but chronic tissue hypoxia is highly suspected (19). In the previous study, only 40% of clubbing cases turned out to have significant underlying diseases while 60% remained well over the subsequent years (10). But according to our experiences, digital clubbing is frequently associated with smoking and pulmonary, cardiac, and hepatic disorders those are characterized with chronic tissue hypoxia (3). As an explanation for that hypothesis, lungs, heart, and liver are closely related organs those affect their functions in a short period of time. On the other hand, digital clubbing is also common in patients with the SCDs and its prevalence was 10.8% in the present study. It probably shows chronic tissue hypoxia caused by disseminated endothelial damage, inflammation, and edema at the capillary level

in the SCDs. Beside the effects of SCDs, the higher prevalences of smoking, COPD, and clubbing in males (p<0.001 for all) may also show some additional roles of smoking, COPD, and male sex on digital clubbing.

Leg ulcers are seen in 10 to 20% of patients with the SCDs (20), and the ratio was 13.3% in the present study. Its incidence increases with age, male sex, and HbSS genotype (21). Similarly, its ratio was higher in males (19.8% versus 7.0%, p<0.001), and mean age of the patients with leg ulcers was significantly higher than the others (35.3 versus 29.8 years, p<0.000), here. The leg ulcers have an intractable nature, and around 97% of healed ulcers relapse in a period of one year (20). As an evidence of their atherosclerotic nature, the leg ulcers occur in distal areas with less collateral blood flow in the body (20). The hard RBCs induced chronic endothelial damage, inflammation, and edema at the capillary level may be the major cause in the SCDs (21). Prolonged exposure to the hard bodies due to the pooling of blood in the lower extremities may also explain the leg but not arm ulcers in the SCDs. The hard RBCs induced venous insufficiencies may also accelerate the process by pooling of causative hard bodies in the legs, and vice versa. Pooling of blood in the lower extremities may also have some effects on development of venous ulcers, diabetic ulcers, Buerger's disease, digital clubbing, and onychomycosis. Pooling of blood in the lower extremities may also have effects on the delayed wound and fracture healings in the lower extremities. Beside the hard bodies, smoking and alcohol may also have some additional effects on the leg ulcers since both of them are more common in males. Hydroxyurea is the only drug that was approved by Food and Drug Administration for the treatment of SCDs (15). It is an oral, cheap, safe, and effective drug that blocks cell division by suppressing formation of deoxyribonucleotides which are the building blocks of DNA (17). Its main action may be suppression of hyperproliferative white blood cells (WBCs) and platelets (PLTs) in the SCDs (22). Although presence of a continuous damage of hard RBCs on endothelium, severity of the destructive process is probably exaggerated by the patients' own immune systems. Similarly, lower WBC counts were associated with lower crises rates, and if a tissue infarct occurs, lower WBC counts may decrease severity of pain and tissue damage (23). According to our ten-year experiences, prolonged resolution of leg ulcers with hydroxyurea may also suggest that the leg ulcers may be secondary to increased WBC and PLT counts induced prolonged endothelial damage, inflammation, and edema at the capillary level in the SCDs.

Varices are abnormally dilated veins with tortuous courses, and they usually occur in the lower extremities. Related factors include pregnancy, obesity, menopause, aging, and heredity. In another word, varices are more common in females and metabolic syndrome. Normally, leg muscles pump veins to return blood against the gravity, and the veins have pairs of leaflets of valves to prevent blood from flowing backwards. When the leaflets are damaged, varices and/or telangiectasias develop. DVT may also cause varicose veins. Varicose veins are

the most common in superficial veins of the legs, which are subject to higher pressure when standing up, thus patient's physical examination should be performed in upright position. Although the relatively younger mean ages of the patients in the present study (30.8 and 30.3 years in males and females, respectively) and significantly lower body mass index of the SCDs cases in the literature (14), DVT and/or varices and/or telangiectasias of the lower limbs were higher among the study cases (9.0% versus 6.6% in males and females, respectively, p>0.05) indicating an additional venous endothelial involvement in the SCDs.

Both frequency and complications of cirrhosis are increasing in the world. For example, it was the 10th leading cause of death for men and the 12th for women in the United States in 2001 (4). Although the improvements of health services worldwide, the increased morbidity and mortality of cirrhosis may be explained by aging of the human being and increased prevalence of excess weight all over the world. For example, nonalcoholic fatty liver disease (NAFLD) affects up to one third of the world population, and it has become the most common cause of chronic liver disease even in children and adolescents at the moment (24, 25). NAFLD is a marker of pathological fat deposition combined with a low-grade chronic inflammation, which results with hypercoagulability, endothelial dysfunction, and an accelerated atherosclerotic process (24). Beside terminating with cirrhosis, NAFLD is associated with higher overall mortality rates as well as with increased prevalences of cardiovascular diseases (25). Authors reported independent associations between NAFLD and impaired flow-mediated vasodilation and increased mean carotid artery intima-media thickness (CIMT) (25, 26). NAFLD and cirrhosis may be considered as the hepatic consequences of the metabolic syndrome (27). Probably smoking also takes role in the endothelial inflammatory process of the liver, since the systemic inflammatory effects of smoking on endothelial cells is well-known with Buerger's disease and COPD (28). Increased oxidative stresses, inactivation of antiproteases, and release of proinflammatory mediators may terminate with a systemic atherosclerosis in smokers. The atherosclerotic effects of alcohol is much more prominent in hepatic endothelium probably due to the highest concentrations of its metabolites in the liver. Similarly, aging alone may be another cause of systemic atherosclerosis that prevents adequate tissue oxygenation. Chronic infectious and inflammatory processes may also terminate with an accelerated atherosclerosis all over the body (29). For example, chronic HCV infection raised CIMT, and normalisation of hepatic function with HCV clearance may be secondary to reversal of favourable lipids observed with the chronic infection (29). As a result, beside COPD, ileus, leg ulcers, digital clubbing, CHD, CRD, and stroke, cirrhosis may also be one of the several consequences of the metabolic syndrome and SCDs.

Nowadays, both frequency and complications of CRD are increasing all over the world, again. For example, 1.9 to 2.3 millions of people have CRD in Canada (30). The

Centers for Disease Control and Prevention in the USA found that CRD affected an estimated 16.8% of adults above the age of 20 years between 1999 and 2004 (31). Similarly, the increased frequency and complications of CRD may be explained by aging of the societies and increased prevalence of excess weight all over the world, since CRD may also be one of the terminal endpoints of the metabolic syndrome, and an eventual advanced atherosclerosis may be the underlying cause of the CRD (32). Aging, physical inactivity, excess weight, smoking, alcohol, and inflammatory and infectious processes may be the main triggering causes of the endothelial inflammation in the kidneys. The inflammatory process is enhanced by release of various chemical factors by lymphocytes to repair the damaged renal tissues, especially endothelial cells of the renal arteriols. Due to the continuous irritation of the endothelial cells in the above pathologies, prominent changes develop in the architecture of the renal tissues with advanced atherosclerosis, fibrosis, and tissue hypoxia and infarcts. Excess weight induced metabolic abnormalities such as hyperglycemia, dyslipidemia, elevated BP, and insulin resistance cause various cellular stresses those accelerate tissue inflammation and immune cell activation further (33). For example, age (p= 0.04), high-sensitivity C-reactive protein (p= 0.01), mean arterial BP (p= 0.003), and DM (p= 0.02) had significant correlations with CIMT (32). Increased renal tubular sodium reabsorption, impaired pressure natriuresis, volume expansion due to the activation of sympathetic nervous system and renin-angiotensin system, and physical compression of kidneys by visceral fat tissue may be some mechanisms of the increased BP with excess weight (34). Excess weight also causes renal vasodilation and glomerular hyperfiltration those initially serve as compensatory mechanisms to maintain sodium balance due to the increased tubular reabsorption (34). However, along with the increased BP, these changes cause a hemodynamic burden on the kidneys in long term that causes chronic endothelial damage (35). With prolonged weight excess, there are increased urinary protein excretion, lost nephron function, and exacerbated HT. With the development of dyslipidemia and DM in the overweight and obese individuals, CRD progresses much more rapidly (34). On the other hand, the systemic inflammatory effects of smoking on endothelial cells may also be important in the etiology of CRD (36). The inflammatory and eventual atherosclerotic effects of smoking are much more prominent in the respiratory endothelium due to the highest concentrations of its metabolites there. Although some authors reported that alcohol was not related with the CRD (36), it is not logical since various metabolites of alcohol circulate even in the blood vessels of the kidneys and give harm to the vascular endothelium, there. Similarly, aging alone may be another cause of the CRD by means of the systemic atherosclerotic effects. Chronic inflammatory and infectious disorders may also terminate with the accelerated atherosclerosis on the renal endothelium (29). Although CRD is mainly be an advanced atherosclerotic process of the renal vasculature, there are close relationships between CRD and other consequences of the metabolic syndrome including CHD, COPD, PAD, cirrhosis, and stroke (37). For example, the most common cause of death in the CRD is cardiovascular diseases rather than the renal failure again (38). In another definition, CRD may actually be one of the several consequences of the metabolic syndrome and SCDs, again.

BPH is the most common benign neoplasm in men. Although prostate specific antigen (PSA) may be elevated in these patients because of an increased organ volume and inflammation secondary to urinary tract infections, BPH does not lead to cancer. BPH involves hyperplasia of the stromal and epithelial cells, terminating with the formation of large, commonly discrete nodules in transition zone of the gland. When sufficiently large, the nodules apply pressure on the urethra and increase resistance to urinary flow. This is commonly felt as obstruction, although the urethral lumen is only compressed. Resistance to urinary flow requires the bladder to work stronger during voiding, possibly leading to progressive hypertrophy, instability, and atony of bladder muscle. BPH can be diagnosed by using the UWIN score (urgency, weak stream, incomplete emptying, and nocturia) (39). BPH may be caused by failure of the spermatic venous system resulting with increased hydrostatic pressure and testosterone levels, locally (40). Authors found that the one-way valves in the vertically oriented internal spermatic veins are destroyed in the BPH patients causing an elevated hydrostatic pressure up to 6-fold greater than the normal (40). The elevated pressure propagates to all interconnected vessels leading to a venous flow retrograde from higher pressure of the testicular veins to lower pressure of the prostate. The authors found that free testosterone levels in this blood are elevated up to 130-fold above the serum (40). Consequently, the prostate is exposed to both an increased venous pressure that causes hypertrophy and to an elevated free testosterone levels causing hyperplasia. On the other hand, an age-related impairment of blood supply to the gland may also have a key role in the development of BPH (41). An advanced atherosclerosis in elder men may cause chronic tissue hypoxia, and thus be a contributing factor in the pathogenesis (42). Smooth muscle proliferation may be an important and possibly androgen-dependent step in the development of atherosclerosis and BPH (43). Similarly, there was a larger prostate in men with type 2 DM (p=0.0058), HT (p=0.0317), obesity (p<0.0001), and low high density lipoprotein (HDL)-cholesterol (p=0.0132) and high insulin levels (p<0.0001) (44). The gland volume correlated positively with the systolic BP (p=0.03), obesity (p<0.0001), and fasting insulin (p<0.0001) and negatively with HDL-cholesterol levels (p=0.009) (44). Similarly, frequencies of CHD were 9% and 29% in men with PSA levels below and above 1.0 microgram/L, respectively (p<0.03) (43). These results may suggest that BPH may also be one of the several consequences of the metabolic syndrome and SCDs in the human body.

As a conclusion, SCDs are severe inflammatory processes on vascular endothelium at the capillary level, terminating with an accelerated atherosclerosis induced end-organ failures and a shortened survival in both genders. Although the presence of several consequences, leg

ulcers, digital clubbing, CHD, DVT and/or varices and/or telangiectasias, cirrhosis, CRD, and BPH may be the alarming consequences of the SCDs indicating an advanced disease in such patients.

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Prevalence and Determinants of Burnout among Primary Healthcare Physicians in Qatar

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Abstract

Background: Burnout syndrome is characterized by a loss of enthusiasm for work manifested as emotional exhaustion, feeling of cynicism or depersonalization, and a low sense of personal accomplishment. It is marked by tiredness, loss of interest, or frustration that interferes with job performance.

Methods: Descriptive cross-sectional study: this study was conducted at the Primary Health Care Corporation (PHCC) in Qatar and it included all physicians from seven health centers affiliated to primary health care in Qatar. The sample size was 144 physicians from both genders male and female, with a response rate of 90%.

Results: Results show that in socio-demographic characters among primary health care physicians males represent 64.29%, 40+ years old represent 68,55% from both genders, 65.69% of the sample size have families with 1-3 children, 61.03% have more than 10 years employment history and 72.79% have board certificates. The prevalence of burnout in the study sample reaches 16.08% among primary health care physicians. No significant relation between socio-demographic characters and burn out was found except for social problems.

Conclusion: Burnout syndrome is common among primary health care physicians reaching a prevalence of 16.08% of the total number of primary health care physicians. Burnout syndrome is very serious and primary reasons should be looked at and resolved. With the improvement of physician ability and capacity to cope with their work daily stresses and teaching them skills that could change how they perceive their work environment into positive healthy life style would result in a big improvement.

Key words: Prevalence burnout, primary health care, physician, Qatar

Background

Burnout syndrome is characterized by a loss of enthusiasm for work manifested by emotional exhaustion, feeling of cynicism or depersonalization, and a low sense of personal accomplishment. It is marked by tiredness, loss of interest, or frustration that interferes with job performance. Burnout is usually regarded as the result of prolonged stress [1]. According to the nature of primary healthcare services, family physicians are involved in the management of a wide spectrum of both physical and psychological health problems. This style of extremely busy and widely variable practice may put them at risk of burnout syndrome [2]. Burnout appears to be quite prevalent in both developing and developed countries and probably represents considerable economic, social and psychological costs to employees and employers in these countries. Out of the 230 general practitioners recruited, 183 responded, which represents a response rate of 79.5%. The prevalence of burnout reaches 12.6% [3]. Burnout is also associated with insomnia, fatigue, headaches, gastrointestinal distress, irritability, decreased concentration and medical errors [4]. It is documented that physician burnout has been associated with impaired job performance, poor health and leads to physician error. These errors can in turn contribute to additional burnout [5]. Burnout may also lead to increased alcohol or drug use, which can also impact patient care [6]. In health care settings and specialties where burnout has been analyzed, more than one-third of the professionals examined were experiencing professional burnout. [7] The effects of the syndrome reveal a real threat for the competitiveness and survival of medical specialties that appear to be losing their attractiveness for future generations on whom they depend for their professional regeneration[8]. Now health system administrators and managers are beginning to study the extent of physician burnout in their settings as a precursor to recommending meaningful organizational changes [9]. There are four hundred physicians working in the Primary Health Care Corporation. There is only one study available in Qatar on burnout in primary care but this study was before the change of primary care into Independent Corporation with accreditation. Therefore, we want to estimate the prevalence of burnout syndrome during and after accreditation, and to identify its determinants.

Methods

Study Design: Descriptive cross-sectional study.
Study Setting: This study was conducted at the PHCC in Qatar.

Study Subjects: Included all physicians from seven health centers affiliated to primary health care in Qatar.
Sampling: The sample size was 144 physicians, with response rate of 90%.
Inclusion Criteria:
Any physician working in the PHCC and who consented to participate in the study.
Exclusion Criteria:
Any physician who refused to participate in the study.
Data Collection:
1. Socio-Demographic data and some work characteristics including age, gender, marital status, number of years in practice, educational qualification, history of smoking, presence of financial or social problems, suffering from chronic diseases were enquired about. In addition, number of patients per day, practice type most of time, type of employment and hours of work per week with government was also recorded for every participant.

2. Measuring Burnout: We used the Maslach Burnout Inventory (MBI) which is the most commonly used questionnaire to measure burnout in research studies. The MBI human services survey is a self-administered, twenty two item questionnaire that was developed to measure burnout in human services workers and is regarded to be the "gold standard" in measuring burnout. The MBI items are rated on a scale from 0 to 6 (0 = never, 1 = a few times per year, 2 = once a month, 3 = a few times per month, 4 = once a week, 5 = a few times per week, and 6 = every day) .

The questionnaire is designed to assess the 3 primary dimensions of burnout, namely, loss of enthusiasm in work (emotional exhaustion (EE), Section A of MBI), having a sense that work is no longer meaningful (low personal accomplishment (PA), Section B) that consists of the second eight questions, while the third domain entails (Depersonalization (DP), Section C) and includes the third five questions.

A participant is considered to meet the study criteria for burnout if he or she scores "high" score on at least two of the three dimensions of MBI. [10]

Data Analysis: Data collected was analyzed using Epi Info and suitable tables and figures for different variables were used. Appropriate statistical tests and p-value measurements were used to assess significance. Independent sample t-tests and ANOVA tests examined associations between demographic characteristics and burnout scores.

The score on the MBI is interpreted as follows:

Level of burnout	Emotional exhaustion (EE)	Depersonalization (DP)	Low Personal accomplishment (PA)
Low	≤ 16	≤ 6	≤ 31
Moderate	17-26	7-12	32-38
High	≥27	≥ 13	≥ 39

Results

Table 1 shows socio-demographic characters among primary health care physicians which show males represent 64.29%, more than 40 years represents 68,55%, number of children from 1-3 children represents 65.69%, more than 10 years employment represents 61.03% and 72.79% have board certificates.

Table 1: Socio-demographic characteristics of primary health care physicians

Characteristic	No.	%
Gender (140)		
Male	90	64.29
Female	50	35.71
Age (124)		
< 40	39	31.45
≥ 40	85	68.55
Marital status (140)		
Ever married	134	95.71
Never married	6	4.29
Number of children (137)		
No children	12	8.76
1-3 children	90	65.69
>3 children	35	25.55
Years of employment (136)		
<10 years	53	38.97
≥10 years	83	61.03
Educational level (136)		
No board	37	27.21
Board	99	72.79
No. of patients seen per day (140)		
<20 patients	13	9.29
≥20 patients	127	90.71
Social problem (140)		
No	131	93.57
yes	9	6.43

Figure 1 shows the prevalence of burnout reaches 16.08% among primary health care physicians

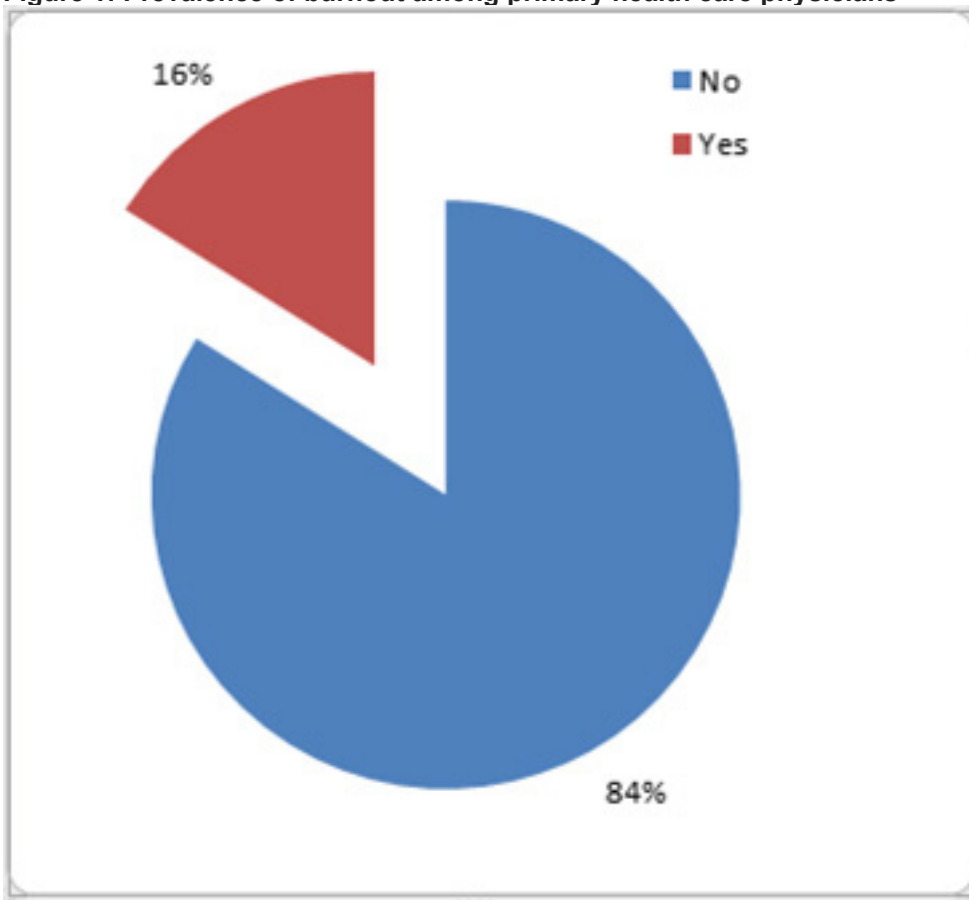**Figure 1: Prevalence of burnout among primary health care physicians**

Figure 2 shows pattern of burnout among primary health care physicians in the form of severe depersonalization symptoms in 28.87% while severe personal achievement symptoms represent 19.72% and severe emotional exhaustion represent 11.89%

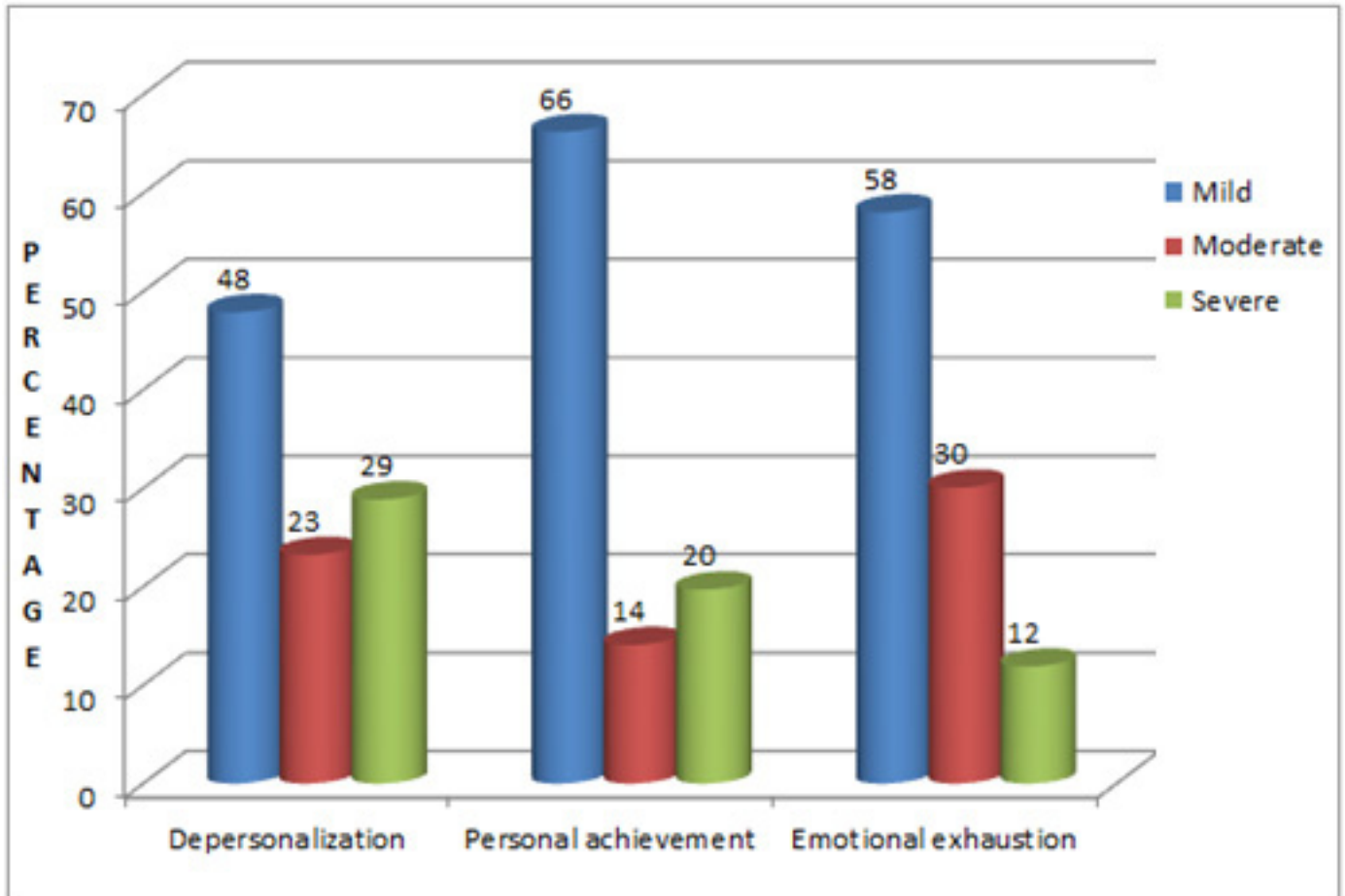**Figure 2: Pattern of burnout among primary health care physicians**

Table 2 shows that there is no significant relation between socio-demographic characteristics and burnout except for social problems

Table 2: Relationship between physician socio-demographic characteristics and Burnout

Characteristic	Burnout	No Burnout	P-value
Gender (139)			
Male	13	77	0.474
Female	10	39	
Age (123)			
< 40 years	8	30	0.446
≥ 40 years	13	72	
Marital status (139)			
Ever married	22	111	1.000
Never married	1	5	
Number of children (136)			
No children	1	11	
1-3 children	16	73	0.650
>3 children	4	31	
Years of employment (135)			
<10 years	11	42	0.340
≥10 years	11	71	
Educational level (135)			
No board	6	31	1.000
Board	16	82	
No. of patients seen per day (140)			
<20 patients	7	6	0.740
≥20 patients	16	111	
Social problem (139)			
No	19	111	0.041*
Yes	4	5	

*Significant P value <0.5

Discussion

This study showed that 16.08% of the primary health care physicians have symptoms of burnout syndrome. This level is higher than what has been reported in a previous study done in Qatar in 2011 as it was 12.6% [3]. This difference can possibly be explained by the variation in the nature of the healthcare system which changed much since that period in the form of accreditation and electronic medical record introduction; also there is variation in method of assessment used to detect burnout.

Another Danish study, showed the prevalence of burnout among general practitioners was 25% [11]. This difference can possibly be explained by culture differences or variation in the healthcare system, which includes aspects such as patients' attitude and the role of general practitioners as the first line of healthcare providers [12]. Systematic review about burnout among Arab countries revealed moderate-to-high estimates of self-reported burnout among health care practitioners that are similar to prevalence estimates in non-Arabic speaking westernized developed countries [13]. It is unclear why there were wide-ranging estimates for burnout both within and between-

countries. However, organizational (e.g., organizational climate, management/leadership styles, horizontal and vertical communication) and/or individual factors (e.g., demographic characteristics, personality characteristics, individual attitudes, maladaptive coping skills), and there was considerable methodological and statistical heterogeneity between studies, and this may account for a portion of the variability in burnout prevalence estimates. This study showed the pattern of burnout subscales in form of severe depersonalization symptoms in 28.87% while severe personal achievement symptoms represent 19.72% and severe burnout symptoms represent 11.89%. Study in Qatar on residents showed responses indicated low depersonalization, high personal accomplishment and high emotional exhaustion [14]. While studies conducted in Bahrain [15] and Jordan   [16] reported some of the lowest prevalence estimates of high EE (24.2%, 32.7%, respectively), DP (18.3%, 27.7%, respectively), and low PA (26.8%, 26.8%, respectively) across all three sub-scales. This study revealed that the most important significant determinant for burnout is social problems. This could be that work stress affects social life or social problems may bring work burnout and so the significance of social support for physicians. The most frequent stressors reported by

the residents related to workload and working conditions. The primary coping strategies were social support, such as talking with family members, and entertainment [14]. Various studies from different health care contexts have shown that social support is an important protective factor against work stress and burnout [17].

Conclusions

The study shows that the Burnout syndrome is common among primary health care physicians in Qatar. So the importance of improving physician coping skills and their work conditions are recommended especially regarding social welfare.

What is known about the topic?
The prevalence of burnout among primary health care physicians was 12.6%

What this study adds:
There is increasing prevalence of burnout among primary health care physicians reaching 16.08% and social welfare is significantly related to burnout which mandates improving social welfare with working conditions to decrease burnout

Limitations:
Our study has some limitations and strengths. Although our response rate was high, response bias is a possibility. We did not assess whether nationality impacted burnout scores due to the anonymous nature of the survey.

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Diagnosis of Pulmonary Tuberculosis by measurement of ADA, CEA and PCR in Bronchoalveolar lavage and compare with smear and culture of BK in the patient with pulmonary infiltration

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Abstract

Background: Pulmonary tuberculosis (TB) is one of the problems in diagnosis and management of patients with pneumonia and pleural effusion. Bronchoscopy and bronchoalveolar lavage (BAL) can help us in the differential diagnosis. Tumor markers are substances that are produced by cancer or other cells of the body in response to diseases. These substances can be found in the blood, urine, or body fluids, for example in bronchoalveolar lavage of some patients with pulmonary diseases. CEA is a tumor marker that can help us for diagnosis and monitoring of peripheral lung cancer. ADA has been shown to rise in the BAL of patients with TB. Because the sputum smear negative TB patients have been a diagnostic challenge for health professionals this study was designed to determine the diagnostic value of ADA & CEA & PCR in BAL fluid and then compare the relationship of these markers with sputum and clinical finding in diagnosis of pulmonary tuberculosis.

Material and Method: A cross sectional study conducted in Shahrekord Hajar hospital where 100 patients were enrolled in our study (62 females, 38 males). These patients were admitted to hospital and bronchoscopy with BAL was performed, then fluid was analysed for ADA,CEA , PCR and sputum smear for TB.

Result: From 100 patients who were evaluated in this study 9 patients had TB, 39 patients had pneumonia, 11 patients had primary lung malignancy, 9 patients had metastases to lung and 8 patients had bronchitis. In Patients with TB the level of ADA was not significantly elevated in BAL. ADA increased significantly in patients with pneumonia (P: 0/95). In patients with metastases to lung and primary lung cancer and a combination of both groups compared to other patients without malignancy there was no relationship between CEA. PCR was positive in TB and other patients, but significantly increased in TB. (p=0/021)

Discussion: Although it was thought that CEA may be elevated in BAL of patients with malignancy and ADA in tuberculosis we did not find a correlation in these patients. This study showed that ADA and CEA levels in BAL fluid does not help us in diagnosis of TB or cancer. It may have afalse positive in pneumonia, COPD and other diseases, but PCR for TB may assist in TB diagnosis but not alone.

Key words: Bronchoalveolar lavage (BAL), adenosine deaminase (ADA), polymerase chain reaction (PCR), Bronchoscopy. Carcino embryonic antigen (CEA). Tuberculosis (TB)

Introduction

CEA is a glycoprotein weight approximately 200,000 dalton. CEA is mainly found in the fetal gastrointestinal tract and in fetal serum (1,2). Secretion of CEA decreases after birth, slight to moderate CEA elevation occurs in benign situations such as in lungs, pancreas, liver disease or in malignant disease in colorectal cancer(3). Some studies have demonstrated CEA increase in BAL fluid in lung cancer, IPF COPD, and pneumonia. Applications are diagnostic but it is useful for monitoring recurrence of malignancy and prognostic factors(4).

ADA is a key enzyme in purine metabolism (5). ADA is a hydrolytic catalyzer enzyme that is irreversibly responsible for conversion of inosine to adenosine (6). ADA help in differentiation of tissues particularly height in lymphocytes in humans (7). ADA can be increased in TB effusion.

TB is the second infective etiology in mortality in the world, but there are many problems in diagnosis of TB, particularly negative smear TB.

Lung cancer is an etiology for mortality for many humans and many humans suffer from lung cancer. It has the highest mortality after prostate, breast, and colon cancer. Studies show CEA in BAL fluid is increased. We have problem in diagnosing peripheral lung cancer, because bronchoscopy can have accuracy of approximately 48%-80% in peripheral lung cancer and 79%-95% in central lung cancer.

Bronchoscopy is a method that is used to diagnose various pulmonary diseases. It enters from the mouth or nose to arrive at lung (8).

PCR is a rapid technique for replication of DNA and it is fast method for diagnosing TB but it is not cost beneficial. It used to amplify a few copies or many copies of strands of DNA across several ordersof generating thousands and millions of copies of a particular sequence of DNA(10).

A few studies have evaluated BAL fluid ADA alone for diagnosis and CEA alone for diagnosis of TB or lung malignancy, but we evaluated this markers for various pulmonary diseases. This study investigated ADA , CEA , and PCR for TB and malignancy in BAL fluid.

Material and Methods

A cross sectional study was performed then at the Hajar Shahrekord hospital in Iran between 2013-2015.

100 patients with various respiratory symptoms admitted to the hospital, who had indication for bronchoscopy and bronchalveular lavage were includes in the study; exclusion criteria were as follows (11):

1) They have contraindication such as hypoxemia, MI, recent angina, respiratory failure, incompatibility patient, tracheal obstruction

2) history of alcohol abuse, known case of malignant liver disease

Bronchoscopy and BAL was performed then samples sent to laboratory for evaluation of CEA, ADA levels and PCR in BAL fluid were compared to each other by ADA and CEA kit.

ADA investigated by ADLS2210 (ADA liquid stat) Reagent kit. CEA was evaluated by the sandwich principle and Modular analytics E170 kit.

We followed patients and did diagnostic evaluation as required (CXR,CT scan. bronchoscopy, AFB) for diagnosis of pulmonary disease, then patients were divided into six groups. The aim of this study was to investigate the relationship between ADA, CEA, and PCR in BAL and pulmonary tuberculosis and lung cancer.

SPSS16 was used for the analytical statistics of the data.

Results

From 100 patients that enrolled into the study 63 were female and 27 wer male with minimum age of 13, and maximum age of 84. Mean, median, Standard-deviation of age respectively was 57, 53, 19. For ADA the Mean, medium, and standard deviation was respectively 4, 81, 4, 1, 66 and for CEA was 11, 12, 4, 93, 16, 3. Minimum level for ADA and CEA was 3, 0/9 and maximum was 8, 56/6 .

We regarded normal cut off point for ADA as <3/5, and for CEA <5 for nonsmoking and CEA <10 for smoking patients. We divided patients into 6 groups : 1) 6 patients had TB . 2) 39 pneumonia 3) 11 primary lung cancer. 4) 9 metastases to lung. 5) 8 chronic bronchitis. 6)27 other patient with cardiac and respiratory disease

We measured level of ADA and CEA in BAL of 100 patients, then we processed the results.

The prevalence of symptoms in these patients was dyspnea (67), dry cough (31), productive cough (26), dysphonia (1), fever(11), chest pain (5) .We compared patients based on symptoms of the various pulmonary diseases that are shown in Table 1.

We used Smirnoff test because there was no normal distribution for ADA, CEA. Mann Whitney test ADA in TB group (9) and other groups (91) were not significantly different (P=0/14), primary lung malignancy(11)(P=0/19), metastases to lung (9)(P=0/16), combination two group metastases with primary cancer (20)(P=0/73),chronic bronchitis (8)(P=0/93).

We found ADA in pneumonia significantly different from the other groups, (P=0/83). It is shown that ADA can be elevated by pneumonia (infection of lung parenchyma).

Table 1: Prevalence of clinical symptoms patient separation of clinical diagnosis

	No.	DRY COUGH Yes	DRY COUGH No	DYSPNEA Yes	DYSPNEA No	PRODUCTIVE COUGH Yes	PRODUCTIVE COUGH No	HEMOMTESIA Yes	HEMOMTESIA No	FEVER Yes	FEVER No	DYSPHONIA Yes	DYSPHONIA No	CHEST PAIN Yes	CHEST PAIN No
TB	9	5 (55.6%)	4 (44.4%)	5 (55.6%)	4 (44.4%)	2 (22.2%)	7 (78.8%)	1 (11.1%)	8 (88.9%)	2 (22.2%)	7 (78.8%)	0	9 (100%)	0 (100%)	9 (%100)
Primary Lung Cancer	11	0	11 (100%)	9 (81.8%)	2 (18.2%)	1 (9.1%)	10 (90.9%)	0	11 (100%)	0	11 (100%)	0	11 (100%)	2 (18.2%)	9 (81.8%)
Metastases	9	5 (55.6%)	4 (44.4%)	6 (66.7%)	3 (33.3%)	2 (22.2%)	7 (78.8%)	0	9 (100%)	2 (22.2%)	7 (78.8%)	0	9 (100%)	1 (11.1%)	8 (81.8%)
Metastases and lung cancer	20	5 (25%)	15 (75%)	15 (75%)	5 (15%)	3 (15%)	17 (75%)	0	20 (100%)	2 (10%)	18 (90%)	0	20 (100%)	3 (15%)	17 (75%)
Bronchitis	8	1 (12.5%)	7 (87.5%)	6 (75%)	2 (25%)	4 (50%)	4 (50%)	2 (25%)	6 (75%)	0	8 (100%)	0	8 (100%)	1 (12.5%)	7 (87.5%)
Pneumonia	39	14 (35.9%)	25 (64.1%)	23 (59%)	16 (41%)	12 (30.8%)	27 (69.2%)	5 (12.8%)	34 (87.2%)	34 (87.2%)	33 (84.6%)	0	39 (100%)	1 (2.6%)	38 (97.4%)

Results showed 86 patients had negative PCR and 14 patients with positive PCR. In the TB (9) group, 4 patients had positive PCR and 5 negative PCR, in the other groups (91) 10 patients had positive PCR and 81 patients negative PCR. This finding shows a significant relationship between TB and positive PCR (P=0/021).

Positive PCR or increasing ADA more than cut of point (>3/5) was only found in 5 patients including 1 patient compared to (9) patient with a known case of TB and with this two tests 4 patient without TB. It showed there was no significant difference between TB and the other groups so we cannot use them only for diagnosis of TB.

Measurement of CEA in BAL showed there was not significant difference between patients with primary lung malignancy (P=0/78), metastases to lung (p =0/25), and combination of both (p=0/54) with other groups including TB (p=0/63), pneumonia (P=0/83),and bronchitis (P=0/45).

Our results including mean, medium, standard deviation of CEA, ADA have shown the breakdown of diagnoses.

Discussion

The finding showed a significant difference in ADA levels, in pneumonia groups compared to other groups, but there was no relationship between TB and the other groups in ADA level BAL fluid. In the study of Reechaitichikal et al, that compared ADA levels in BAL fluid of pulmonary TB, lung cancer, and other pulmonary disease they did not find significant difference among these groups (P=0/56)(7) but Banish et al's study showed ADA level as a significant difference in TB patients compared to non TB pulmonary disease and control group (12). In our result there was demonstrated positive PCR in non TB disease, but it had significant different between TB and non TB groups (P=0/021). Boonsarangsuk et al showed ADA activity of TB cases was significantly different from that of other patients with pulmonary disease (p<0/001). To differentiate TB from solid tumor the AUC was significantly higher for combination of ADA activity >3 Ana TB PCR (0/7) than for ADA alone (p<0/001) ,or for TB PCR alone (p<0/001); it showed sensitivity of 72% in combination of the two tests but alone sensitivity for ADA was 58/7% and PCR sensitivity alone was 28/1% (13).

Table 2: Median, mean, standard deviation, P. value, minimum and maximum data rate of the ADA in lung disease

		Median	Mean	Standard deviation	P. Value	Minimum	Maximum
TB	Yes	3/6	3	2	0/4	1/4	8
	No	4/86	4	4/32			
PRIMARY LUNG CANCER	Yes	4/81	4	1/66	0/19	3	8
	No	4/74	4	4/39			
METASTASES	Yes	8	4	10/9	0/16	3	37
	No	4/32	4	2/73			
METASTASES & LUNG CANCER	Yes	6/25	4	7/36	0/73	3	37
	No	4/37	4	2/85			
BRONCHITIS	Yes	4	4	1/19	0/93	2	6
	No	4/81	4	4/34			
PNEUMONIA	Yes	4/03	4	1/9	0/95	0/7	11
	No	5/21	4	5/09			

This study investigating CEA in BAL did not increase significantly in primary lung cancer, metastases to lung or both combinations. Aytemur Salak et al demonstrated CEA levels in BAL fluid do not differ between lung cancer and other groups, sensitivity, specificity of CEA in BAL was respectively 81/8%,45/1%. Diego et al investigated CEA level in serum and BAL in lung cancer patients and pneumonia and healthy patients; CEA in BAL was 5/1. It showed CEA level in BAL with respective sensitivity and specificity 77%-94% can help to us for diagnose of lung cancer (14).

However there was a high number of T-lymphocytes in BAL related to ADA, specially ADA (2) , but different studies showed different results on ADA level on BAL for diagnosing Tb. It could be due to geographic location, low and high incidence regions, or the method of measurement in different location; any way ADA cannot help to diagnose Tb.

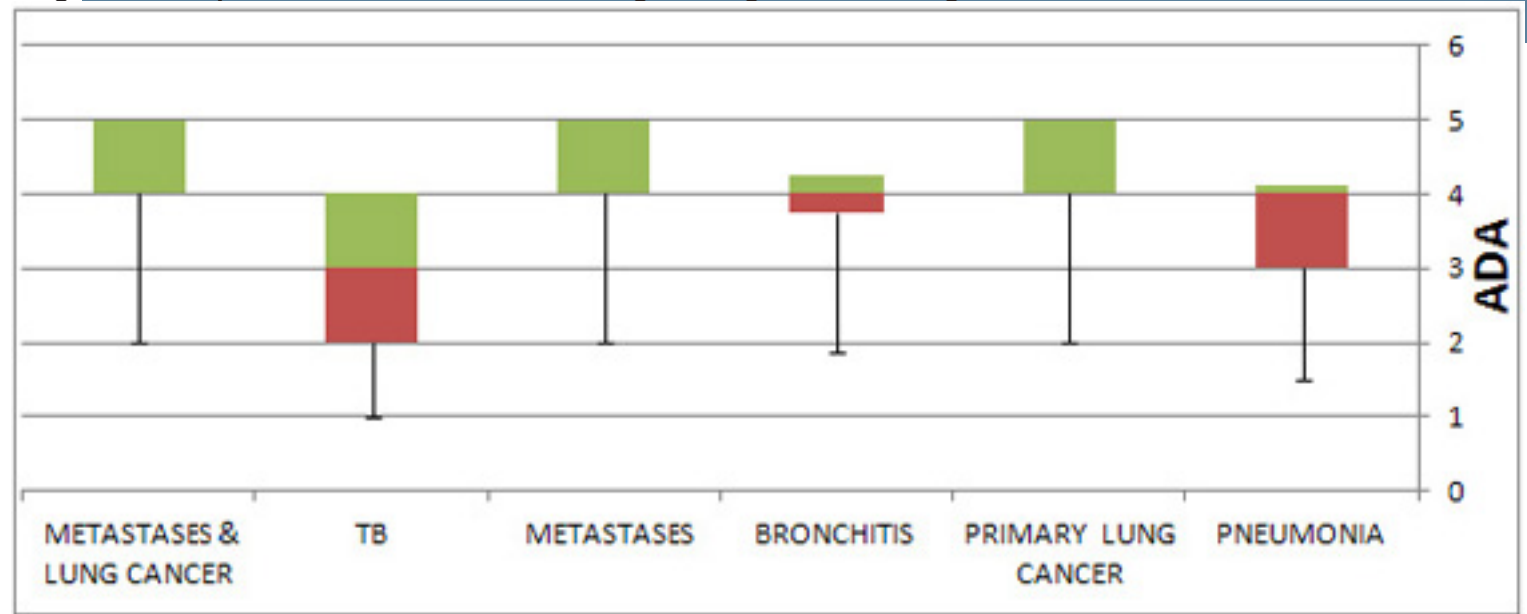**Diagram 1: Comparison of ADA's total and average of lung disease to diagnosis**

Table 3: Median, mean, standard deviation, P. Value, minimum and maximum data rate of the CEA in lung disease

		Median	Mean	Standard deviation	P. Value	Minimum	Maximum
TB	Yes	11/3	11/3	11/06	0/68	1/12	35/4
	No	11/26	11/26	1/48			
PRIMARY LUNG CANCER	Yes	11/12	11/12	16/3	0/78	0/9	56/6
	No	11/22	11/22	1/43			
METASTASES	Yes	14/51	14/51	12/6	0/25	1/26	36/9
	No	10/88	10/88	1/46			
METASTASES & LUNG CANCER	Yes	12/64	12/64	14/48	0/54	0/9	56/6
	No	10/85	10/85	1/45			
BRONCHITIS	Yes	8/18	8/18	9/05	0/52	0/5	28/16
	No	11/47	11/47	1/48			
PNEUMONIA	Yes	11/22	11/22	13/66	0/83	0/5	69/86
	No	11/2	11/2	1/5			

Diagram 2: Compare CEA's total and average of lung disease to diagnosis
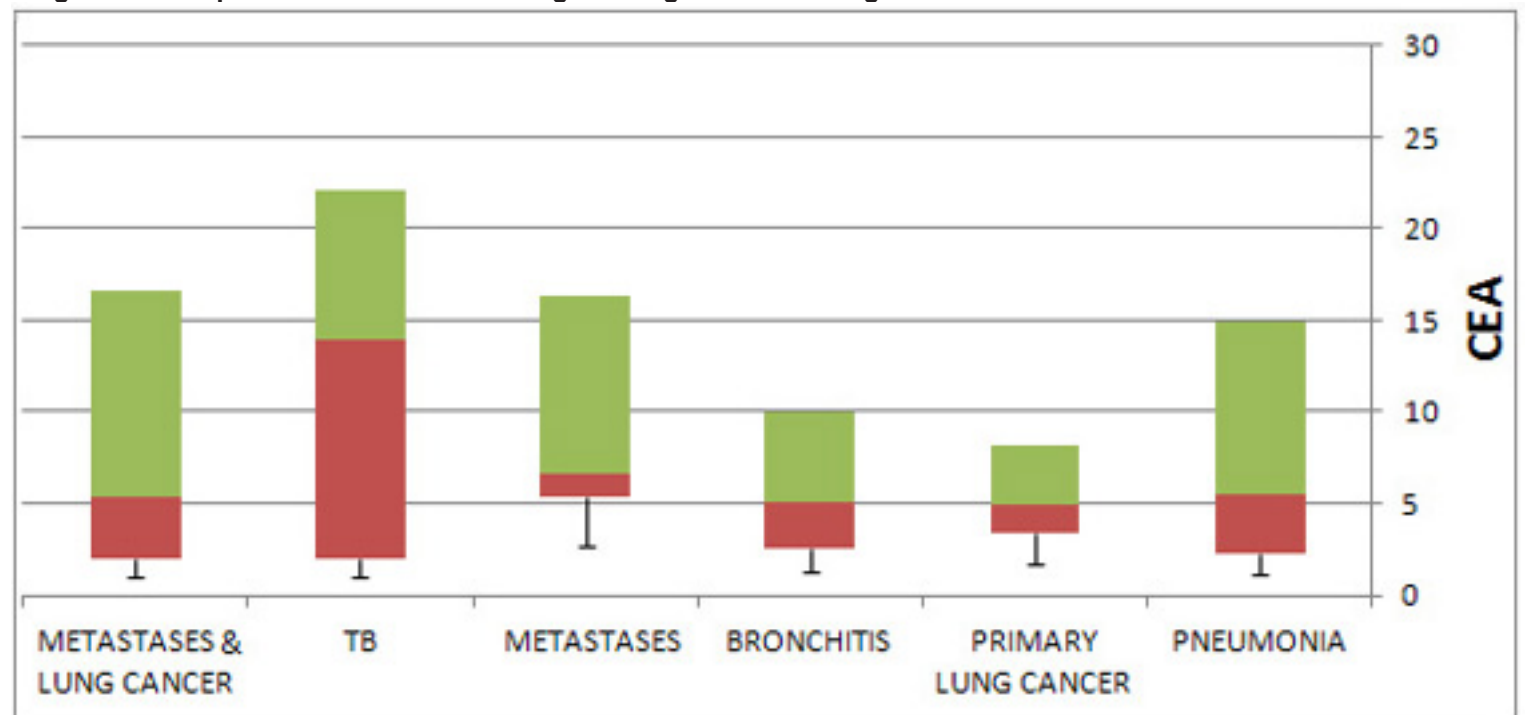
Conclusion

This study showed that ADA levels in BAL fluid do not help us in TB diagnosis. It may be that it has false positive in pneumonia, compared with other disease, but PCR for TB may help us for TB diagnosis but nt alone. CEA level in BAL cannot differentiate lung malignancy.

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The effect of opioid use on pulmonary function test in advanced COPD patients

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Abstract

Background: Opium has previously been shown to increase exercise endurance and decrease breathlessness in patients with chronic obstructive pulmonary disease, but controversy in this issue persists, therefore the role of opium in the management of patients with advanced COPD remains undefined.

Method: In order to compare the effects of opium on pulmonary function, we studied two groups of patients with COPD who were attending the chest clinic of Labaffinejad hospital. Group A- consisted of COPD patients with history of smoking alone and group B- patients who consumed opium in addition to cigarette smoking. Patients were matched for their age, and packs/year cigarette smoking habit. Individuals with history of heart disease or occupational lung disease and those with severe COPD who needed hospitalization during 6 months prior to the study were excluded. A complete history and physical examination was done and patients' chest X-ray was taken. For each patient pulmonary function was evaluated by spirometry using Fukuda, Spirometric FVC, FEV 1, FEV 1 / FVC and predicted value for each parameter was recorded, and results were compared between the two groups of patients. Statistical analysis was done by using Kolmogorov - Smirnov test and student t-test.

Results: Results shows that there is significant difference (p = 0) between the two groups for FVC and FEVI. We concluded that opium may have a beneficial effect in improving lung function in patients with severe COPD.

Key words: opioid use, pulmonary function test, COPD patients

Introduction

In patients with severe chronic obstructive pulmonary disease (COPD) quality of life is usually declined due to breathlessness and they are usually limited in their daily activities (1), despite maximum treatment including bronchodilators, corticosteroid, rehabilitation programs and long term oxygen therapy (2).

In recent years, there have been significant advances in the understanding the nature of symptoms, but as far as breathlessness is concerned, it is not quite clear what makes patients to feel shortness of breaths during daily activities (2,3).

In order to alleviate this symptom, many therapeutic modalities have been tried including dihydrocodeine (4) and morphine with conflicting and inconclusive results.

Several reports emphasize the beneficial effects of oral opiate on breathlessness and exercise tolerance.

It is important to know the effects of opiate on pulmonary function of patients with severe COPD. Therefore we have studied the pulmonary function tests in two groups of COPD patients, with history of cigarette smoking habit alone and those with history of cigarette smoking plus opium addiction.

Material and Method

From October 2000 to February 2001 a total number of 4320 patients attended Labafinejad chest clinic. Among these patients: 1230 were diagnosed as COPD.

We performed this prospective study, sequential and case control, on COPD patients. The including criteria were as follows:

1- History of cough and expectoration for 3months in two consecutive years or HRCT finding compatible with diagnosis of emphysema.
2- Shortness of breath either in rest or activity.

Excluding criteria were as follows:
1- History of CHF or any other heart disease
2- History of exposure to noxious material.
3- History of exposure to war gases.
4- History of hospitalization from 6 months prior to study.
5- Severe COPD or complications such as hemoptysis or pneumonia which needed hospitalization.

After selection of patients, they were divided in to two groups. Group A with history of cigarette smoking habit and group B with history of opium addiction 2 years as well as cigarette smoking. Patients in these two groups were matched for age.

A questionnaire was filled for each patient. Chest X-rays were taken and spirometry done for each patient using Fukuda spirometer, (FEVI, FVC, FEVI/FVC) and percent of predicted value for each parameter recorded.

Statistical analysis:

For data analysis, we first transformed the research variables with natural logarithm for the variables to be in proportion. Then we tested hypothesis normality and homogeneity of variance in two groups with use of Kolmogorov - Smirnov and Levene's test. Then we Compared mean of variables in the two groups with use of t-test. We used SPSS relies 10.5 for data analysis.

Result

From October 2000 to February 2001, 60 patients with diagnosis of COPD included in our study, 30 patients for each group, (group A: only smoker and group B: opium addicts in addition to smoking.)

All patients were male and all were smokers with ranges of 15 to 180 packs/ year with a mean 48.00+/-25.31 packs/ year (49.2+/-29. 78 packs/ year for group A, and 46.80+/-20.35 packs/ year for group B.)

Group B patients were opium addicts for a minimum of 3 years and maximum of 40 years (mean 16.23+/-8.64 years). By Kolmogorov - Smirnov test we confirmed that our two groups are completely similar (95% confidence, and P> 0.5).

The most common complaint of our patients in both groups was cough and dyspnea as well as sputum production. One patient in group A also complained of weight loss. Patients with hemoptysis were excluded because most of them require hospitalization.

The most common chest examination finding in both groups was wheezing (68%), 60% in group A and 76% in group B (page 38). Early inspiratory crackle was the next common finding in both groups.

The most common chest X-ray finding in both groups was increased vascular marking and hyperinflation.

Spirometry was done in all patients after taking history and physical examination. And by Levenes' test we compared homogeneity FEV I, FVC, and FEV I/FVC in two group and with confidence 95% and P>0.5 we confirmed this homogeneity. FEV I/FVC ranges were from 35 to 91 with a mean 62.31+/- 13.24 in our patients.

In group A, FEV I/FVC ranged from 35 to91 with a mean of 58.31 +/-12.76, and in group B, ranged from 40 to85 with a mean 66.30+/- 12.68 (P = 0.19).FVC ranged from 16 to 83 % predicted with a mean of 46.37+/-17.20 in our patients, and in group A FVC ranged from 16 to 61% predicted with a mean 37.4+/-15.3 and in group B, ranged from 27 to 83% predicted with a mean of 55.3+/-14.2 (P=O). FEV I ranged from 2 to72% predicted in our patients with a mean of 44.67 +/-18.01. In group A, FEV I ranged from 2 to 72% predicted with a mean of 35.10+/- 15.6, and in group B, ranged from 22 to 72% predicted with a mean of 54.2 +/- 15.0 (P = 0). Therefore, according to above data, and similarity of our two groups that were confirmed by statistical analysis, and results of student t-test, mean value for FEV 1 and FVC in group B is significantly higher than group A.

Table 1: Group A patients

Age	Packs/year smoking	FEV1	FVC	FEV1/FVC
52	38	72%	61%	65
70	50	35%	24%	45
75	20	55%	27%	65
75	18	50%	39%	46
65	50	40%	56%	75
69	55	43%	19%	44
73	50	49%	53%	65
67	40	56%	46%	57
75	10	49%	55%	46
76	30	43%	42%	56
36	20	36%	58%	66
68	40	20%	16%	65
53	40	43%	52%	45
75	54	20%	23%	43
59	40	44%	53%	76
61	42	30%	19%	35
60	45	43%	48%	65
60	42	33%	27%	84
49	20	22%	27%	85
60	40	23%	24%	78
57	30	60%	61%	78
59	40	56%	50%	87
84	54	46%	52%	76
49	30	36%	16%	78
65	40	35%	32%	88
65	25	35%	32%	87
51	27	44%	33%	65
67	30	42%	62%	54

	t-test	sia	Lower limit	Upper limit
FVC	-4.705	0.0000	-25.56	-10.32
FEV1	-4.533	0.0000	-27.05	-4.20

Table 2: Group B patients

Age	Packs/year smoking	Opium Addiction/ years	FEV1	FVC	FEV1/FVC
58	80	10	1.57(54%	1.84(51%)	83
51	45	20	2.22(72%'	1.62(69%)	84
67	100	8	1.29(50%'	1.85(56%)	69
69	30	3	1.68(62%'	2.15(61%)	63
69	40	30	1.61(56%	2.52(68%)	66
62	30	20	1.12(43%'	1.58(48%)	63
70	50	10	2.43(71%"	2.85(80%)	85
47	20	10	2.08(62%'	2.54(67%)	81
63	15	10	1.07(37%'	1.86(34%)	56
69	40	10	0.98(41%'	1.38(45%)	58
72	100	20	1.12(40%'	1.33(36%)	84
64	30	20	0.79(25%'	1.73(46%)	46
80	60	40	1.10(55%'	1.31(48%)	83
54	30	20	2.22(70%'	3.09(83%)	72
63	40	10	34%	37%	55
65	45	15	65%	67%	70
78	50	10	71%	80%	50
57	30	10	50%	45%	56
58	30	10	29%	27%	43
54	30	20	42%	39%	73
64	503	36	72%	69%	53
50	70	34	54%	51%	62
52	40	10	72%	61%	77
72	60	20	22%	42%	40
74	50	20	57%	54%	64
58	55	30	64%	60%	70
49	54	20	68%	59%	66
53	50	20	55%	53%	70
47	30	20	64%	59%	77
60	50	30	70%	65%	70

Discussion

Breathlessness and dyspnea are commonly experienced by patients with advanced lung disease. Some past studies have shown that the use of morphine increased exercise endurance and pulmonary function in this group of patients (7). Woodcock et al (4) demonstrated l 8% increase in treadmill walking distance and a 20% decrease in breathlessness at equivalent workload 45 minutes after administration of 15 mg of oral dihydrocodeine. Light et al (31) showed that the administration of 0.8 mg/kg morphine orally resulted in a 20% increase in the exercise tolerance of patients with COPD. However, the administration of opiates to patients has led to mental cloudiness in some studies (8). Another study reported that low doses of aerosolized morphine (<2mg) increased the endurance time by 35% in patients with lung disease. It is of interest that such a low dose of aerosolized morphine would lead to this degree of improvement since a higher dose of oral morphine (30mg) has not elicited significant improvement. This raises the possibility that aerosolized morphine acts directly on lung afferent nerves to reduce dyspnea. However, the mechanism responsible for the improved breathlessness and exercise tolerance is unknown. It has been suggested that the primary factor responsible for the increase tolerance is a decreased metabolic requirement at a given workload.

Our results also show that opium significantly improves spirometric value in patients with COPD, despite that our two groups had no significant difference in other parameters, such as occupation, other diseases that may adversely effects on lung function, and etc.

Our patients were selected randomly from those with a diagnosis of COPD visited in out¬patient clinic of Labafinejad hospital, and those needed admission into the hospital were excluded.

The pathophysiological basis of the sensation of breathlessness remain incompletely understood. Despite some advances in the knowledge of the perception and genesis of breathlessness, those have little impact on therapy (2). In clinical practice this often is a distressing symptom and demands relief. The treatment of breathlessness is most effective when the primary cause can be identified and modified, but in those conditions, in which treatment currently has little to offer, it is intuitively attractive to attempt to manipulate the symptom of breathlessness itself.

Over the years many attempts have been made in this regard and although there have been some claims of success, none have achieved more than an alteration of the underlying mechanical events which subserves the symptom of breathlessness, for example, ventilatory drive, the pattern of breathing, etc (6).

Opiates have long been popular treatment for the alleviation of breathlessness in patients with respiratory disease (2). However they have not achieved widespread usage largely because of potential side effects, such as respiratory depression and addiction. There are a number of possible mechanism by which morphine may alleviate the sensation of breathlessness in a short time after use. (2). Firstly morphine may reduce the degree of anxiety experienced by a particular subject and hence the degree of breathlessness. Secondly, perceptual responses to the incoming neural traffic or its central interpretation may be blunted and finally, morphine may alleviate the sensation of breathlessness for a short time after use by direct local action on peripheral neural receptors in the small airway and probably by this mechanism may improve spirometric values (2). If opiates work at the level of the bronchial mucosa, it is possible that lower doses administered via nebulization might be effective. Opiate-peptide like activity has been detected in bronchial mucosa, and thus morphine may be in a position to modify the perception of breathlessness in the same way as it alters the perception of pain.

Light et al, used oral morphine (0.8 mg/kg) in patients with severe COPD and showed that exercise capacity was increased and breathlessness, assessed by using a modified Borge scale, waas significantly decreased. The reduction in breathlessness in this study was achieved at the expense of an increase in Pa CO2, a reduction in ventilatory derive, and was thought by the authors to be due to a combination of lower ventilatory requirement for a given workload and also to altered perception. Dihydrocodeine administered orally before exercise has also been shown to reduce dyspnea by 20% (assessed using a visual analogue scale) in a similar group of patients. Minute ventilation and oxygen consumption were reduced in this study despite an increase in exercise capacity.
Also naloxan restored blunted ventilatory responses in patients with chronic airflow
obstruction.

Conclusion

Opium may be useful in improving pulmonary function and relieve of dyspnea in patients with COPD unresponsive to other medication. Because the risk of adverse effects such as respiratory depression is high, use of such drugs could be limited to advanced and end stage disease. Further studies for confirmation of result of this study should be done in a larger group of patients.

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Relationship between life skills with functional impairment and sexual satisfaction in women

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Abstract

Background: Sexual dysfunction in women is a progressive and prevalent age-related problem which affects quality of life, quality of sexual relations and interpersonal relationships.

Objective: This study aimed to examine the relationship between life skills with functional dysfunction and sexual satisfaction in women referred to health centers of Shahroud University of Medical Sciences.

Materials and methods: This cross-sectional study was conducted on 478 eligible women referred to eight health centers of Shahroud University of Medical Sciences in 2016-2017. The data collection tool was four questionnaires of demographic, General Health (GHQ-28), Life Skills and Sexual Function Index (FSFI). Data were analyzed using SPSS.

Results: Mean score of sexual function was 58.07 ± 10.63 and sexual satisfaction was 4.38 ± 0.99. The average total score of life skills was 508.99±46.82, which ranged from the lowest amount in the professional skills as 10.42 ± 2.13 and the highest amount in mental health as 81.93 ± 9.10. There was a significant relationship between life skills and sexual satisfaction and functional dysfunction. (p≤0.05)

Conclusion: The findings of the study indicated a relationship between life skills and sexual satisfaction and functional dysfunction, so that increased functional dysfunction and sexual dissatisfaction was observed in people with low life skills.

Key words: sexual satisfaction, functional dysfunction, life skill

Introduction

Sexual function is part of human life and behavior, and according to the World Sexology Association, it is so mixed with personality that it is impossible to consider it as an independent phenomenon (1-3). It is also a multidimensional phenomenon affected by many biological, psychological and social factors. Importance of sexuality is a realistic fact, because sexual problems may have multiple effects on other aspects of individual and social life, so that it may cause mental disturbances, incompatibilities, and failures in marital life (4, 5). Sexual function involves desire, stimulation or motivation, orgasm and suppression (6, 7). Sexual dysfunction is a chain of sexual-psychiatric disorders that is defined as a disorder in desire, stimulation, orgasm and sexual pain (8-10).

These disorders are common in women and various demographic studies estimate its range between 25-50%, Female sexual dysfunction (FSD) is one of the most common problems and affects approximately 40% of women (11, 12) . Based on the Sexual Dysfunction Index questionnaire, 31.5% of Iranian women have at least one sexual dysfunction: 35% with lack of sexual desire, 30% lack of stimulation, 33.7% lubrication disorder, 37% orgasm disorders, 26.7% the pain disorders, and 31.5% were dissatisfied (13-15). Important issues such as mental health, sexual relationship, sexual function of partner, personality, infertility, medications, chronic diseases, pelvic surgery, gynecology and malignant diseases, diabetes, pregnancy, and postpartum period are involved factors in sexual dysfunction (16).

Sexual dysfunction exists in all societies and affects the quality of sexual relations of married people(13). It is also known as a factor influencing the quality of life of individuals (9, 15, 17) (9, 15, 16) which can cause severe personal inconvenience and affect personal relationships (18)(17). Currently, physical, psychological, and sexually transmitted infections are evaluated in women to treat these disorders(16) (15). Medication and surgical and mechanical therapies are also used to treat certain types of sexual dysfunction. Some medicines may initially improve sexual performance, but they may impair sexual function after prolonged use. It is hard to show the effectiveness of traditional psychotherapy for sexual problems(19) (18). People with sexual dysfunction usually hide their problem, and lack of proper treatment can cause chronic symptoms, anxiety, introversion and feelings of guilt (20). Several studies have pointed to the role of communication skills and life skills in solving couples' sexual problems and increasing their satisfaction and performance (21-26) (20-25). Life skills can affect the quality of relationships, play a major role in promoting mental health and general health, in reducing family stress and increasing social acceptance (27-30).

It seems important to recognize the family as the most essential social element. Marital satisfaction is a general assessment of the status of marital relationship or the current romantic relationship of an individual. Marital satisfaction can be a reflection of the level of happiness of individuals from their marital relationships or a combination of pleasure due to many factors specific to a marital relationship. Marital satisfaction can be considered as a psychological situation that is very unstable and at greatest risk in the early years (31, 32). Sexual dysfunction, occurring due to any reason, leads to a decrease in quality of life and dissatisfaction with relationships with others. Sexual dysfunction may lead to problems such as depression or divorce and separation between the husband and wife (32, 33). According to negative effects of sexual dysfunction in women and its complications on the family and society, and given the importance of the family bond, it is necessary to identify the factors related to marital satisfaction, which is the basis for strengthening the family relationship. Considering the factors affecting marital satisfaction, it can be expected that many psychological, emotional and social problems of families and the whole society will decrease by increasing marital satisfaction.

Besides, the higher level of marital satisfaction makes people more relaxed in performing their social, cultural and economic services and duties, and also families will benefit from this advancement. Evidence suggests that women often lack information and have poor sexual skills, while these are behaviors that enable individuals to adapt and effectively deal with the demands and challenges of life. Considering the fact that no specific research has been conducted on the relationship between life skills and sexual performance so far, this study aimed to determine the life skills, with Sexual function and satisfaction in women referred to health centers of Shahrood during 2016-2017.

Material and Methods

This cross-sectional (descriptive-analytical) study was conducted on 478 women referred to health centers of Shahroud for periodic examinations or other services. The samples were selected by multistage random sampling method. The number of samples in this study was estimated to be 450 in the 10% prevalence of self-esteem (extracted from Ramezani's study in Tehran), which practically reached 478 cases (34). In the first stage, 2 centers of 8 centers and 1 base from 5 urban bases (clusters) were randomly selected and then based on the number of visits using available method. The inclusion criteria was the age between 15-49 years old, have reading and writing skills, nationality of Iran, married and living with the husband, at least one year of marriage, no recent abortion or delivery, no physical and psychological disorders, no gynecologic diseases. Exclusion criteria were those who scored more than 23 for their health assessment using the General Health questionnaire (with psychological problems). For data collection, four questionnaires containing demographic questionnaire (age, education, occupation, prevention method and number of children) were used. The validity of the demographic questionnaire and its content validity were evaluated using the revision comments of 10 university professors; its reliability was

also measured using the Re-test method. The General Health Questionnaire (GHQ-28) has 28 questions in four scales (physical symptoms, anxiety and sleep disorders, impaired social function and severe depression) and each scale has 7 questions. Options range from zero to three scores. Those who obtained the score of 24 or higher were suspected of being ill or having a disorder and were excluded from the study. Those who obtained the score of 23 or less were identified as healthy persons. The general health questionnaire was validated in the study of Nourbala et al. because they assessed the reliability of this questionnaire using the Symptom Checklist-90-Revised SCL-90-R test. Both questionnaires were highly validated and re-test method was used to determine their scientific reliability. The third questionnaire is life skills and includes 142, 5-options questions in 17 areas, including questions 1-11 about self-awareness training, 12-21 about having a goal in life, 22-32 questions about human communication skills, 33-44 about interpersonal relationships, 45-52 about decision making, 53-75 about hygiene and mental health, 76-81 about problem solving skills, 82-89 about participation and collaboration skills, 90-95 about creative thinking skills, 96-109 about critical thinking, 110-114 about understanding Principles of Freedom, justice and equality, 115-120 about participation in beneficial activities, 121-125 about showing social behaviors, 126-130 about the citizenship of globalization, 131-133 about professional skills, 134-137 about skills on the observance and use of safety tips, 138-142 about how to collect information. Samples expressed their life skills based on a very Low scale of 1 and a very high score of 5. The minimum total score was 3 and maximum score was 170. For each life skill separately, the average amount was calculated. Test retest method was used to determine the reliability. For this purpose, the questionnaire was completed by 15 women referred to the health center who had the same characteristics similar to the research samples. Then, the questionnaire was completed again by the same individuals and the correlation coefficient was obtained as 0.78. The face and content validity was approved by completing the questionnaire by 10 faculty members and approved after necessary corrections. The final part of the questionnaire was the Persian version of the FSFI, which evaluated sexual satisfaction and function, and included 17, 5-options questions, in which the questions 1-2 were about sexual desire, 3-5 about stimulation, 6-8 about lubrication, 9-11 about orgasm, 12-13 about sexual satisfaction, 14th question was about family life satisfaction and 15-17 about sexual pain, in order to evaluate the sexual desire, orgasm, sexual pain, vaginal moistness, and sexual satisfaction. Each question had 5 points (from zero to four), multiplied by the factor of that area, and the final score was obtained by adding all six scores. The minimum score was 2.40 and the maximum score was 32.20 with the average 22.57. Scores higher than 22 were considered without sexual dysfunction and score less than 22 was classified as sexual dysfunction. For each of the sexual stages, the average score was calculated separately. The average sexual desire score was 3.91, with minimum score of 1.20 and maximum score of 6.00; the mean score less than 3.6 was considered as having a sexual desire disorder.

The mean stimulation disorder was 2.92 with minimum score of 0.00, and the maximum score of 4.50; the mean score less than 3 had a sexual stimulation disorder. The average lubrication score was 3.07 with minimum score of 0.00 and the maximum score of 4.50; the mean score less than 3 was considered as sexual dysfunction. The mean score of sexual orgasm was 4.10 with minimum score of 0.00 and a maximum score of 6.00; the mean score less than 4 had sexual orgasm dysfunction. The average score of sexual satisfaction was 4.37 with minimum score of 0.00 and the maximum score of 6.00; the mean score less than 4 had sexual satisfaction disorder. The mean score of sexual pain was 4.17 with minimum score of 1.20 and maximum score of 6.00; the mean score less than 4 had sexual dysfunction.

Validity and reliability of the questionnaire were confirmed by Hasani et al. in the Iranian population in 2006 (35). Data were analyzed by SPSS software version 22 and Chi-square, Fisher's exact test, independent t-test and Mann-Whitney test; 0.05 was considered as significant level. The obtained information was presented in absolute and relative abundance distribution tables. All information obtained in this study was completely confidential and anonymous. In addition, the present study was approved by the Ethics Committee of Shahroud University of Medical Sciences under IR.SHMU.REC.1395.36 code dated 28/02/1395.

Results

The mean age of the participants was 30.72 ± 8.82 years. The level of education in most of the samples (39.7%) was high school and 80% were housekeepers. The most commonly used contraceptive method (32.8%) was condom. The average number of children was 1.7± 0.99. The mean score of life skill test was 508.99±46.82; the lowest life skill score was 337.00 and the highest score was 789.00. The lowest mean was observed in professional skills as 10.40 ± 2.09, and the highest mean in mental health as 82.30 ± 8.86. The sexual performance score varied from a minimum of 2.00 to a maximum of 87.00 with the mean sexual performance score of 58.07±10.63. The score of sexual satisfaction varied from the minimum of 00 to the maximum of 6.00 with the mean score of sexual satisfaction of 4.37±0.98. Most of the items related to life skills, had a correlation with sexual function and satisfaction, which means improved level of life skills can increase the sexual function and satisfaction. The level of life skills, different aspects of sexual function, sexual dysfunction and sexual satisfaction are shown separately in Tables 1, 2, and 3. The mean score of life skill in both groups, with and without sexual dysfunction and mean scores of life skills in both groups with and without sexual satisfaction are also shown in Tables 4 and 5.

Table 1: Simple correlation coefficient of sexual function, sexual satisfaction and life skills

	sexual function	sexual satisfaction	life skills
sexual function	1		
sexual satisfaction	0.548** 0.000	1	
life skills	0.113* .014	0.142** 0.002	1

(Two-tailed test): P<0.05*، p<0.01**

Table 2: Frequency distribution of life skills and distribution of sexual satisfaction in women referred to health centers of Shahroud

Rate	life skills	The number (percentage)	Sexual satisfaction	The number (percentage)
	Yes	245(51.3)	Yes	190(39.7)
	No	233 (48.7)	No	288(60.3)
	Total	478(100)	Total	478(100)

Table 3: Frequency distribution of sexual dysfunction in terms of components of sexual function in women referred to health centers in Shahroud

Sexual dysfunction	Components of Sexual Function	Sexual desire The number (percentage)	Arousal The number (percentage)	Lubrication The number (percentage)	Orgasm The number (percentage)	Pain The number (percentage)
Yes	232(48.5)	111(23.2)	54(11.3)	244(51.0)	244(51.0)	238(49.8)
No	246(51.5)	367(76.8)	424(88.7)	234(49.0)	234(49.0)	240(50.2)
Total	478(100)	478(100)	478(100)	478(100)	478(100)	478(100)

Table 4: Comparison of mean scores of life skills components in study subjects with sexual function in women referred to Health Centers in Shahroud

sexual dysfunction / life skill	p value	T test value	No	Yes
Self-awareness	.027	-2.223	39.6545	38.7069
Having a Goal in Life	.234	-1.193	36.1016	35.5560
Human communication skills	.063	-1.860	40.1992	39.2328
Interpersonal Relations	.851	-.189	44.2561	44.1552
decision	.339	-.957	29.0244	28.6940
Mental health	.000	-3.594	83.7033	80.8233
Skills in problem-solving	0.151	-1.438	22.0691	21.6422
. Collaboration skills	.027	-2.225	28.3211	27.4655
Creative thinking skills (creativity)	.000	-3.750	22.0772	20.9698
Critical Thinking	.001	-3.491	51.3252	49.3405
Understanding the principles of freedom, justice and equality	.05	-1.928	18.8537	18.3448
Participate in activities that improve the interests	.007	-2.686	21.8089	21.0043
Showing social behaviors	.013	-2.505	18.5650	17.9310
Citizen of globalization	.102	-1.637	18.1016	17.6767
Professional skills	.174	-1.361	10.5325	10.2716
Skills related to compliance and application Safety Tips	.993	-.009	14.1138	14.1078
How to collect information	.028	-2.209	16.8862	16.0690
Total life skill	.001	-3.362	533.2368	**506.8977**

P value<0.05

Table 5: Comparison of Mean Scores of the Life Skills components in study subjects with Sexual Satisfaction in Women Referred to Health Centers in Shahroud

Sexual Satisfaction / life skill	p value	T test value	No	es
Self-awareness	.002	-3.105	38.3842	39.7292
Having a Goal in Life	.140	-1.478	35.4211	36.1111
Human communication skills	.025	-2.254	39.0105	40.2049
Interpersonal Relations	.004	-2.760	43.3053	44.8021
Decision	.027	-2.168	28.4053	29.1667
Mental health	.001	-3.499	80.5789	83.4444
Skills in problem-solving	.003	-2.952	21.3263	22.2153
. Collaboration skills	.080	-1.757	27.4895	28.1806
Creative thinking skills (creativity)	.001	-3.426	20.9158	21.9514
Critical Thinking	.005	-2.798	49.3789	51.0104
Understanding the principles of freedom, justice and equality	.085	-1.726	18.3263	18.7917
Participate in activities that improve the interests	.008	-2.669	20.9263	21.7431
Showing social behaviors	.000	-3.639	17.6947	18.6285
Citizen of globalization	.796	.259	17.9368	17.8681
Professional skills	.347	-.941	10.2947	10.4792
Skills related to compliance and application Safety Tips	.558	.586	14.3632	13.9444
How to collect information	.280	-1.083	16.2421	16.6528
Life skills in all gamuts	.001	-3.448	500.0000	514.9236

Discussion and Conclusion

Sexual dysfunction is a common and serious problem among women , which has an important impact on marital and interpersonal relationships, and their quality of life. The aim of this study was to determine the relationship between life skills and the sexual function and sexual satisfaction of women. Life skills increase the person's adaptability to the environment and problems, and help the person to effectively deal with the marital life issues. Self-awareness and self-expression skills can help the person to know themselves and their sexual and non-sexual needs and how to express their feelings properly. On the other hand, empathy skills can prepare them to understand the needs of their partner more compassionate in terms of emotional and psychological and interpersonal needs, and to have a more honest, respectful, and intimate relationship. Decision-making and problem-solving skills counselling can help them to precisely define the problems encountered in marital life and to identify and review existing solutions to find most appropriate solutions. These skills can avoid stress and anxiety in critical situations and not to use unsafe ways to solve marital problems(25).

In the present study, frequency of sexual satisfaction was 39.7 and the frequency of sexual dysfunction in the studied population was 48.5%, and for each separate component was: 49.8% sexual pain, 51% orgasmic disorder, 51.0% lubrication disorder, 23.2% sexual desire disorder, and 11.3% stimulation disorder, respectively. The results of a structured review and meta-analysis of Ranjbaran in Iran showed that there was 21.6% sexual satisfaction, prevalence of sexual dysfunction was 43.9%, with 42.7% lack of sexual desire, 38.5% of stimulation disorder, 30.6% of lubrication disorder, 29.2% of orgasm disorders, and 40.1% sexual pain(36).

According to the findings of present study, it can be concluded that the level of life skills is effective in improving sexual dysfunction and marital satisfaction in married women. It should be mentioned that professional life skills s a person to know herself better, to understand her husband, develop an effective relationships with him, identify and control her own negative emotions and daily stresses, remain well and meet the needs and challenges of everyday life and to solve the problems in a proper way, and adopt the most appropriate decisions. Also, life skills may cause the person to not think of the stereotype and not accept the information without processing (37) and can empower a woman to effectively find and activate her knowledge, attitudes and values, and to motivate and behave in a healthy way. The present study concludes that the level of life skills has a positive relationship with sexual satisfaction, which is consistent with the studies if Azizi and Pourheidari (25, 30)

The findings of this study indicated the relationship between life skills with sexual satisfaction and sexual dysfunction, so that an improvement was observed in terms of functional disorder and sexual dissatisfaction in people with low life skills. Therefore, it is recommended to health centers and midwifery and women's clinics to employ counselors or psychologists on sexual education in order to improve the life skills among young girls and women.

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The effect of FIFA 11+ injury prevention program on dynamic balance and knee Isometric Strength of Female players in soccer super league

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Abstract

Aim: The aim of this study is to survey the effect of FIFA 11+ injury prevention program on dynamic balance and knee isometric strength of female players in soccer super league.

Method: Sample of study included 30 subjects of female players of Shahrdari Bam, super league soccer team. 11+ injury prevention training protocol should be completed within eight weeks, at least two times a week and approximately 20-25 minutes. Lower extremity strength is assessed by using dynamometer device and dynamic balance test was evaluated (in the pre-test and post-test) by star test (SEBT). For data analysis, descriptive statistics of paired t and independent t test at significant level of p<0/05 were used.

Result: Research finding indicates that 11+ injury prevention training program led to a significant increase in flexion and extension strength of knee joint and dynamic balance in the posterior and postero-lateral directions in the experimental group (p≥0/05). There was a non-significant increase in the other directions and the control group P≥ 0.05. Also there was a significant difference between the experimental and control groups in posterior and postero-lateral posterior (p =0/001). But there was no difference in the control and experimental groups in other directions. Also a prominent difference was observed between experimental and control group in flexion and extension strength of knee (0/001).

Conclusion: Because the 11+ injury prevention program includes special soccer movements, plyometric, strength and balance training, it has an effect on muscular strength and dynamic balance in posterior and postero-lateral directions in professional soccer players. It can also be a preventive factor in lower extremity injuries because of increasing knee strength.

Key words: 11+ training, strength, balance, soccer, female

Introduction

We live in an era when sport penetrates the life of people. Among all sports, soccer is one of the most popular sports around the world and has more than 265 million participants of which 21 million are female soccer players, and in near future, soccer will turn into the main female sport all over the world. Because of this increasing popularity of soccer, physicians will encounter more injured females (1). Most of these soccer-related injuries occur in lower limbs (2). Most sport injuries are avoidable, however, if no consideration was taken into account, the occurrence of such injuries would increase and lead to loss of athletes' health and in some cases cause the athletes to permanently quit sport (3,4).

Injury is one of the main concerns of coaches and athletes reducing physical performance, with the main factor a waste of time and it imposes enormous treatment costs on athletes (5). Eggar states that the cost of sports injuries is approximately one billion dollars a year in Australia alone (6).

Damage may occur due to a simple accident or a complex interaction of risk internal factors. Risk of internal factors is an inherent characteristic of an individual that can lead to injury or increase the risk of injury. Lack of enough muscle strength is one of the most important internal risk factors of injury (7).

Many soccer skills such as successful landing after jumping (heading and catching ball in the space), tackling, kicking, and kicking strength require muscle strength to protect against joint injuries. It is possible that a large percentage of the ankle and knee injuries result from strength disabilities. Therefore, the muscle power that can be achieved through strength training is valuable for soccer players. In order to jump, spin and change direction, Quadriceps and hamstring muscle groups should produce much power. Ability of muscles is important to continue strong contraction in balance and body control. Since almost 76% of soccer-related injuries occur in lower limbs, the amount of muscle strength according to the ratio of hamstring to Quadriceps muscle is very important in knee stability and reducing the risk of injuries. Quadriceps femur muscle has a critical role in performance of knee joint. This muscle is effective in all motion and stable performances of knee and also has a key role in absorbing the incoming forces to knee. Quadriceps femur muscle cooperates with PCL in maintenance of knee anteroposterior stability.

The risk of injury in women footballers is high and more than 80% of injuries occur in the lower limbs (8,9). Various internal and external factors cause injury in athletes and one of these cases is the ability to maintain balance. Balance is an integral part of daily activities and it is the determining index in the study of functional ability of athletes (10,11) and it is known as an important factor in many athletic skills such as gymnastics, basketball, volleyball and football and its weakness is related with a number of injuries such as ankle and knee instability or

pain, severe osteoarthritis of the knee and ankle sprains. Dynamic balance is defined and measured as a person's ability to maintain balance from dynamic to static state. In various sports such as football and basketball, which need quick reactions, an inherent protection against injury is provided. The results show that the lower limbs are more vulnerable than the other parts of body in football in all positions. Due to the prevalence of ankle and knee injuries because of the shear jumping movements and the role of muscles of the lower limbs to bring the body skeletal status to a balanced state, an effective training program to improve the dynamic balance has major importance (12,13). Grancher et al concluded that the four-week balanced exercise program significantly improves dynamic balance and controls fluctuations in stature (14). Kimberly et al studied the effect of the five-week central stabilization training on the balance dynamic of tennis athletes. The results showed that these exercises improve dynamic balance of athletes (15). Buchner et al did a survey on the effect of strength and endurance training on balance, walking and risk of falling in retired older people and concluded that the exercise program had no effect on balance (16).

Therefore strength and balance are important factors for a successful soccer player (14,17,18) which results in better performance of technical and tactical skills in this sport (19). Reduction of injuries prevents early retirement, provides a safe environment for players and minimizes expenses. Hence, the implementation of prevention programs is highly recommended to coaches (20). In 2006, FIFA medical committee provided an injury prevention program called 11+ that aimed at reducing injuries among male and female soccer players. Soligard et al reported that 11+ training program reduces injuries of the lower extremity of amateur female soccer players (21). The finding of Berito et al showed that 11+ training program enhances the strength of Quadriceps femur and hamstring muscles (22). That research has not examined the effect of FIFA 11+ injury prevention program on professional female players and different exercises achieved different results on dynamic balance and there is no survey about +11 injury preventing exercise program of FIFA on the dynamic balance of professional female footballers so the purpose of this study is to survey the effect of FIFA 11+ injury prevention program on balance and knee isometric strength of female players in soccer super league.

Methodology

In this study pretest – posttest were used. The sample of study consisted of 30 players from Shahrdari Bam team in the super league. Then they were randomly assigned into control (N= 15) and experimental (N= 15) groups. Table 1 demonstrates the descriptive characteristics of participants.

The participants had no serious injuries in their lower limbs. To make sure, the participants were chosen by team physician confirmation and by reviewing their medical records.

FIFA injury training program 11+

The training program with body warm up structure was designed by FIFA medical center of research and evaluation in collaboration with Oslo sport injuries research center and Santa Monica sport medicine center and called +11. This program was designed to prevent injuries in soccer players' lower limbs. The required time to perform this program is 20-25 minutes. This program consists of three parts. The first part includes 8 minutes jogging. The second part contains six types of strength training, balance exercise and jumping exercises with time duration of 15 minutes at three elementary, intermediate and advanced levels. The final section includes speed running combined by bounding, planting and cutting movements (speed running with sudden change of direction). This section lasts 2 minutes (23). This program was done 3 times a week for two months in the morning.

Measurement of static or isometric strength:

Maximal isometric strength of the knee extensor and flexor muscles at 90 degrees were measured by using a dynamometer (Model 300kED made in Japan, with credits ICC = 0/92 (24). Subjects sat on a table or bench so that their feet were dangling. Dynamometer was fastened to the top of the ankle and subjects were asked to perform as much maximum contraction as they could do in flexion and extension without using their hands and hold for 5 seconds. After each move, the subjects were given 5 seconds rest (25).

The ability of the dynamic balance of samples was determined by access distance record in eight directions of anterior, internal anterior, internal, internal posterior, posterior, external and external anterior. In this test, eight directions are drawn on the ground like a star with an angle of 45 degrees to each other. Before the start of the test, preferred foot of the subjects is determined and if the right foot is superior, the test is done in the opposite of clockwise direction but if the left foot is superior, the test is done clockwise. Subjects are placed in the center of the star on the superior foot and perform access operation with the other foot in eight directions without errors (errors: The movement of foot from the star Centre, stay on the other foot at the point of contact and person falling). The distance between the contact place of the free foot and the center of the star, is access distance. Each subject does each of them three times and finally the average is calcuated, divided by the foot height in cm, and then multiplied by 100 in order to obtain access distance in terms of a percentage of the length of the foot (26). The star test for 8 weeks training protocol was applied to the experimental group while the control group only began to work normally.

In the present study, descriptive statistics were used to calculate mean and standard deviation of tests. In inferential statistics paired t and independent t tests were used to compare intra- and inter-group changes respectively. The data was analyzed through SPSS software version 19, and the level of significance was considered P≤ 0.05.

Results

Demographic features of 30 players divided into two 15 players groups can be seen in Table 1.

Table 1: Descriptive characteristics of subjects

Experimental group X ± SD	Control group X ± SD	
24.53 ±1.68	24.33±1.44	(year) age
57.10±6.62	52.4±5.74	(kg) weight
161.27±6.96	161.53±5.42	(cm) height

Table 3 shows the results from paired t and independent t test to compare the means of flexion and extension strength of knee joint between experimental and control group. In experimental group there is significant difference in flexion and extension strength of knee joint P≤ 05/0 .

Also prominent difference was observed between experimental and control group in flexion and extension strength of knee 0/001.

In the dynamic balance experimental group, there was a significant increase from pre-test to post-test in the posterior and poster-lateral posterior P≤ 0.05 and a non-significant increase in the other directions and the control group P≥ 0.05. Also there was a significant difference between the experimental and control groups in posterior and postero-lateral posterior (p =0/001). But there is none in the control and experimental groups in other directions.

Table 2: Dependent and independent t-test to compare means of dynamic balance in both experimental and control groups

value P independent	P value paired	X±SD after program	X±SD before program	Direction	Group
0.992	0.152	76.24±10.36	74.56±10.79	frontal	control
	0.092	93.75±12.82	92.08±14.68		experimental
0.560	0.114	78.99±14.17	77.30±12.48	Frontal-interior	control
	0.234	91.65±14.45	90.70±15.52		experimental
0.347	0.826	73.06±11.76	73.20±12.46	interior	control
	0.306	85.63±16.44	84.89±15.27		experimental
0.207	0.061	83.44±13.79	81.27±12.73	Postero-interior	control
	0.345	107.60±11.67	107.2±12.22		experimental
0.001	0.090	87765±12.28	85.51±11.37	posterior	control
	0.001	112.14±15.99	83.58±13.91		experimental
0.001	0.150	91±12.47	89.54±12.08	Postero-lateral	control
	0.001	109.75±13.83	82.78±14.46		experimental
0.835	0.085	91.33±11.19	90±11.20	lateral	control
	0.197	95.49±17.15	94.40±17.68		experimental
0.574	0.106	80.99±11.41	80.15±10.65	Frontal-lateral	control
	0.181	91.49±13.88	89.99±14.40		experimental

Table 3: Result of paired and independent sample t-test

P value independent	P value paired	X±SD after training program	X±SD before training program		
0.001	0.535	7.13±2.53	6.87±2.97	control	Flexion strength of knee
	*0.001	12.07±4.71	7.47±3.42	experimental	
0.001	0.872	7.73±2.05	7.67±2.69	control	Extension strength of knee
	*0.001	14.93±4.43	7.87±3.09	experimental	

P≤ 0.05 *

Discussion

The present study investigated the effect of FIFA 11+ injury prevention program on dynamic balance and knee isometric strength of female players in soccer super league. The results indicated that there is a significant difference in flexion and extension strength of knee joint between experimental and control groups. Moreover, the training program had a significant increase on dynamic balance from the pre-test to post-test only in the posterior and lateral-posterior directions only in the experimental group but in the other directions, they had a non-significant effect in the experimental and control group. There is a significant difference between the mean differences of pre-test and post-test in posterior and lateral-posterior directions in experimental and control groups. But in other directions, there is no significant difference in the control group and the experimental group.

Strength

Results of the present study are in line with Berito et al findings (22). The consistency of the results may be due to the fact that strength is one of the important factors in prevention injury program and the program is structured based on the body warm up. So this factor might be one of the reasons for the positive effects of exercise on strength increase .11+ training program, includes training exercises such as single leg squat, jumping and landing, bounding, plant and cut movements that strengthen the quadriceps muscles (24,27). Therefore, exercises to increase balance, strength and attention to the correct landing could be possible reasons for the effects of +11 training program on strength of knee muscles (22,24,27). Soligard et al reported a preventive effect of the 11+ among female youth soccer players. They reported a reduction in the incidence of knee injuries (21). Also Kirkendall et al noted comprehensive warm-up program is the best type of training for injury prevention (28). A study by Steffen et al, which included female youth soccer players, reported no effects of the 11 training program on strength of knee

joint. They suggested that low compliance with the program explained the lack of effects and this was one of the most important reasons to introduce a modified program (8). The11+ includes a greater diversity of exercises, changing both the type and the intensity during the soccer season. 11+ is a modified program of 11 training program. 11 training program consisted of ten exercises of 15 minutes based on body warm up. 11+ in comparison with 11 is more useful and more effective for improving isometric quadriceps and hamstring strength (23). Performing the FIFA 11+ warm up for an average of 2 months led to enhanced knee strength ratios, as well as agility skills and superior static/dynamic balance in Asian male players (29–31). Stabilization exercises (SE) are one of the aspects FIFA 11+ is following. Previous studies showed poor trunk stability and strength are associated with a higher risk of lower extremity injury (32,33). The warm up programs with SE included, which FIFA 11+ is one such program, have significant effect on the incidence of lower extremity injuries reduction (21,34).

Balance
The results of the present study are consistent with Leavey et al. (2010) (35), Filipa et al (2010) (36), Mattacola et al (37), Kimberly and Samson (2005) (15), Granchar et al (14). Leavey et al (2010) concluded that six weeks of proprioception and strengthening training, middle sciatic exercises or a combination of these two can improve the performance in the star test in healthy subjects (35). Filipa et al (2010) reported the improvement in performance of female soccer players in the star test after eight weeks of training focused on neuromuscular control of the trunk and leg muscle strength (36). Mattacola and Lloyd (1997) concluded that the program of strength training and proprioception improves the ability to maintain balance (37). Kimberly et al (2005) studied the effect of a five-week stabilization dynamic training on the balance of tennis athletes. The results showed that these exercises improve dynamic balance in athletes (15). Granacher et al (2010) in a study also concluded that the four-week exercise program significantly improved dynamic balance and controlled the height fluctuations (14). Because the +11 injury prevention program is a set of strength, balance, plyometric training and also focuses on strengthening core stabilization muscles, neuromuscular control, and maintains the correct direction of the knee and hip joints, (21,24,27) it can represent its consistency with this study. From the possible reasons of the increase in +11 exercises of dynamic balance, proprioceptive receptors, the preparation of motor neurons in a group of muscles and muscle tone can be stated. The program consists of training in eccentric and concentric contraction and coordination of these exercises can also show the improvement of balance (21). Bouchner et al (1997) surveyed the effect of strength and endurance training on balance, walk and risk of falling in older retired people, and concluded that the balance training program is unaffected (16). The discrepancy could be due to differences in the type of exercise, exercise intensity, duration of exercise and type of subjects. Depending on the fact that this test is used to assess the dynamic balance of star test, the following are necessary to be mentioned. During doing the posterior, lateral posterior and external directions, biceps femoral are active and the person must have trunk flexion to do this in order to be able to open the foot backward and

in these cases, eccentric hamstring should be contracted to resist hip flexion moment. Surrounding and functional muscle strength on the joints and the contraction to stabilize lower limb joints, deep receptor activity and neuromuscular control in order to achieve balance while performing the star test and get the most distance is of particular importance (38). Another possible reason for the increase in dynamic balance after +11 FIFA program is increasing muscle strength. Strength training, such as squat and Launch, in this program can help to improve the strength of the muscles around the hip, knee and ankle. Brito et al reported that +11 exercises increase strength of the muscles around the knee (22). On the other hand, Hirosmus states that increasing the power of the lower limbs can cause an increase in dynamic balance of athletes (39).

According to the studies, the players who undertook the FIFA 11+ during the season improved their functional balance (34). Neuromuscular control is one of the crucial factors so as to have functional balance efficiency which can be averred. There are studies that showed FIFA 11+ provokes core and hip musculature, and therefore improves neuromuscular control (40). Considering these results of studies, FIFA 11+ can trigger core muscles activation and with that effect, it may improve core stability in individuals. This program can also improve performance with better hamstring/quadriceps strength ratios, jumping and agility skills (41). Bizzini et al stated that physiological responses, performance, and static and dynamic balance were improved immediately after the FIFA 11+ program (42).

So it can be said that the+11 exercises (strength, balance and plyometric) due to the variety it provides for athletes, can cause a significant increase in dynamic balance of athletes.

Conclusion

Finally it can be concluded that the training program 11+ including balance, strength, plyometric, and soccer specific exercises can be effective in increasing the strength of knee joint of professional players. Considering the special muscle strength that athletes require in sport skills and also as an important factor in prevention of sport injuries, these kinds of exercises are recommended as a part of athletes' preparation program at the beginning of each season. In addition, the training program can be effective in increasing the dynamic balance of professional players. Thus, according to the special needs of athletes for dynamic balance in athletic skills as well as an important factor in the prevention of sports injuries, this kind of exercise is considered as a part of the preparation of the athletes at the beginning of the season.

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Comparison of Sexual Behavioral Patterns and Mental Health in male and female Victims of Betrayal in Family courts of Tehran city

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Abstract

In this paper, we compared the sexual behavioral patterns and mental health in female and male victims of identity in the family courts of Tehran. In order to achieve this purpose, 100 cases of women and men (50 males and 50 females) who were referred to courts and cluster couples who were referred to the court or to family counseling centers through ministry of justice were studied. Targeted achievement sampling was selected, and SCL-90 questionnaires and sexual performance of Farajnia and Shahidi were evaluated for assessing mental health and sexual function. Finally, the data obtained from the questionnaires were analyzed by using independent t-test and multiple variance analysis variables. Data of findings showed that the difference between mean obsessive-compulsive disorder, interpersonal sensitivity, depression, and anxiety was significant in both male and female victims. According to the men's mean in obsessive-compulsive indices, anxiety was significantly higher than women, and in depression, aggression and interpersonal sensitivity in women, was more than men, and also the difference in mean sexual function in the two groups of women and men who were not victims of betrayal.

Key words: Sexual behavior patterns, mental health, betrayal, sexual performance

Introduction

From the point of view of the biological, psychological, social, health model, it is something that a person takes through the consideration of biological, psychological and social needs. Pegler et al. (2013) [1] studied the differences in the patterns of high-risk sexual behavior among young girls . The results of this study categorized different patterns of sexual behavior based on race / ethnicity in black and Spanish, and young women , and concluded that risky sexual behavior patterns have a direct relationship with infectious diseases. And in this case, it has given serious warning to youth and teenagers. Braver and Abel (2015) examine the relationship between machoism o and sexual behavior: motivation, deception and betrayal. The results showed that those with high levels of Machismoavellianism were more likely to interact in sexual behavior for physical reasons, achievement, and insecurity. In particular, stress reduction, the search for experience, resources, social status, revenge, practical reasons, increased self-esteem, duty / pressure and motivation for the sexual behavior of the spouse were confirmed in Machiavellianism of male and female. Marital infidelity can cause severe emotional outcomes in couples. Psychotherapists report that spouses who have been betrayed themselves often experience feelings such as anger, low self-esteem, tiredness, depression and inability. The traitor spouse also deals with feelings like shame, guilt, hesitation, fatigue and despair (Glass and Wright, 2001, quoted by Fathi et al., 2013). Extreme emotional distress is often associated with cognitive disturbance after the disclosure of marital infidelity. One

of the important disturbances experienced by a spouse who is a victim is a severe obsession with the event, which can be so severe and uncontrollable as to disturb the daily performance and concentration of the person (Glass and Wright, 1997). In this study, the comparison of sexual behavior patterns and mental health in male and female victims of betrayal in family courts of Tehran is studied and investigated. Researchers believe that satisfactory sexual behavior patterns play a significant role in obtaining a sustainable culture. Therefore, any disorder that results in inconsistent sexual dissatisfaction may result in sexual disorder. A healthy sexual behavior and proper marital relationship are the basic elements of a stable and intimate relationship, and are one of the important factors in the physical and mental health of couples, and the continuity of the family depends on these relationships.

Statement of the problem

The three factors, marital, social and familial, are factors that cause men to be disloyal. In this study, some of the underlying cause of men's disloyalty are: sexual and emotional problems in marital relationships, diversity and excitement, proof of masculinity and youthful feelings, harmlessness of knowing marital relationships for marital relationships, experiences provides relationships with the opposite gender, abusing of the possibility of multiple wives and temporary marriages for men, community attention and attitudes about men's insecurity, the influence of friends and the satellite and pornographic films, and the role of facilitating the use of the internet and mobile phones to create opportunities for engagement with the opposite gender. Modarresi, Zahedian and Hashemi Mohammad Abad (2014) also introduced the issue of marital infidelity as a growing concern. By studying the degree of marital adjustment and the quality of love, divorce applicants with a history of marital infidelity and lack of marital infidelity found that between divorced applicants with and without marital infidelity, in terms of intimacy, passion, commitment and decision were in relation with each other. Investigating the quality of love in individuals with a history of marital infidelity revealed the difference in all of Sternberg's love triangle in relation to the husband and marital relationship. Bravow and Lepkin (2010) in a model for explaining marital betrayals, state one of the most important factors in the occurrence of this phenomenon is the lack of securement of needs and deficiencies in response and fatigue. Here, the possible factors of betrayal in marital affairs will be investigated. One of the variables that is related to betrayal is patterns of sexual behavior. In fact, it has now become apparent that the cause of many mental disorders, moral slurs, betrayals, failures of marital life, incompatibilities, insults, offenses, and even crimes, is due to the lack of attention to sexual affairs, or factors which are related to it. Many families whose warm and sincere conditions and atmosphere have become a distant environment due to the lack of familiarity with sexual affairs, and romantic expression is replaced with **unpleasant** words and maybe marriage leads to divorce. As a result, aside from the diversion of many men and women, innocent infants have also been neglected and thus indirectly contributed to the corruption of society. Failure to have appropriate sexual

behavior patterns can be a factor in affecting the mental health of victimized women and men. The lack of attention to sexual issues affects people's lives to a large extent, according to the experience of betraying the spouse, mental health of these people can also be under scrutiny and investigation. According to the World Health Organization, health is a complete physical, mental, social state of affairs, and does not refer to the absence of a disease or disability. The condition of human health is fundamental to the achievement of peace and security, which depends on the highest level of cooperation between people and governments.

Research method

Statistical population
A group of individuals or subjects that have at least a common feature, is a statistical society. Usually in each research, the community under investigation is a statistical society that the researcher wants to study regarding the adjectives or variables of their units (Saeed Abbas Zadeh, 1380). The statistical population includes male and female victims of betrayal referring to the family courts in Tehran city.

Estimation of sample size and sampling method
A targeted sampling method was used (because betrayal in our country is taboo and there is no specific reference for classified access to traitors). Sample size according to the research method, which is comparative, for each group, of 50 people was considered, and a total of 100 completed questionnaires were entered into statistical analysis. Measurement tools were characteristics of questionnaires. The present research in the first stage related to gathering related scientific materials, a type of library research and the stage of distribution and completion of questionnaires was the field study.

Questionnaire of sexual behavior
This scale has 60 items which are categorized into seven components of sexual participation, sexual expression, emotional and sexual feelings, sexual orientation, sexual fulfillment, and sexual awareness. The answering method in this questionnaire was Likert scoring, and the score for the responses were as well a 5-point-Likert scale ranging from completely agree, to totally disagree. Questions 47, 46, 45, 44, 43, 42, 40, 39, 38, 31, 28, 26, 25, 22, 21, 18, 17, 13, 10, 2, 1 are scored in reverse order. In this scale, in addition to the 7 component-related scores, a total score of at least 60 and a maximum of 300 for each subject was calculated. Since the components and questions related to each of them were already identified and reviewed by the experts, a confirmatory factor analysis was used to determine the validity of the components. In doing this kind of analysis, the basic assumption of the researcher is that each factor is associated with a certain subset of the variables, and at least the necessary condition is that the researcher has a certain default on the number of model factors before the research (Human, 2009). The results of this analysis showed that all components are well fitted and each of them is considered appropriate for the purpose, thus they are capable of proper measurement.

SCL-90 Psychological Disorders Checklist

Introducing of questionnaire

This short answer personality test, in addition to the diagnosis of mental illness among alcohol and drug addicts, sexual disorder, patients with cancer, patients with severe physical illnesses, and those who need counseling or screening (especially in recruitment) has been successfully used. The initial and preliminary form of this questionnaire (SCL-90) was designed by Draughts, Lipmann and Curie (1973) to illustrate the psychological aspects of physical and mental patients. In 1984, Dragothis et al. revised the questionnaire and published the final form of the Psychosocial Reinstated List (SCL-90-R). This short answer list contains 90 five-choice questions (no = 0, little = 1, partially = 2, high = 3, very high = 4). The content of this test measures nine different dimensions as follows:

1. Physical Complaint (So): A person experiencing and understanding the function of his body.
2. Compulsory obsession: The individual focuses on thoughts, impulses, and actions that are unwanted.
3. Sensitivity to interpersonal relationships (Is): A person feels inadequate, self-conscious, and uncomfortable with others.
4. Depression (DP): A person feels helpless and frustrated, is disinterested in the pleasure of life and has a depressed mood.
5. Anxiety (An): An individual has a lot of anxiety.
6. Aggression: An individual with thoughts, actions and **feelings of anger.**
7. Phobia (PH): A person with acute fear is irrational to a particular stimulus.
8. Paranoid Thoughts (Pa): One is suspicious of others.
9. Psychosis (PS): A person with psychotic disabilities (weak to severe).

In addition, 7 questions were scattered to shield the subject's knowledge from the nature of the test to the questionnaire, which is given as other dimensions of the score.

Scoring and commentary method

The 90-item questionnaire is a 5-point Likert scale (0 = no, 1 = partially, 2 = somewhat, 3 = high, 4 = very high). In scoring, the first step is to provide a key to calculating the total scores of each dimension. For this purpose, ten keys are provided to calculate 9 after the symptoms and additional questions of the questionnaire. In the second stage, the volunteer scores were transmitted to the table for recording the scores of subjects in a questionnaire. In order to get the total scores for each dimension, all numbers other than those for each dimension were aggregated. In the third step, in order to obtain the mean of symptoms in each dimension, the scores of subjects in the dimensions of the questionnaire (with the exception of additional questions) were divided into the number of questions in each dimension and the mean of the symptoms of each dimension in the summary table of each subject, is determined. In the next step, the GSI was calculated. In other words, the total score that each subject received after symptoms of anxiety and extra questions were combined was divided by 90 (the total number of test questions) in order to calculate the overall symptom score. In the next step, the number of questions that the subject had scored zero was determined, and we deduced from the total number of questions, i.e., the number 90, to calculate the (PST). In the next step, to obtain the PSID, we divided the total GSI by the total PSI to obtain the PSDI index.

Reliability and Validity

Salzmann, and Shedder used the SCL-90-R questionnaire as a tool for studying the relationship between marijuana and aggression. According to them, this questionnaire

Table 1 shows SCL-90-R test dimensions and questions for each dimension

Number of related questions in test	Related questions	Dimension	Row
58-56-53-52-49-48-42-40-27-12-4-1	12	Physical complaints	1
3-9-10-28-38-45-46-51-55-65	10	Physically and mentally obsessive	2
73-69-61-41-37-34-21-6	9	Interpersonal sensitivity	3
79-71-54-32-31-30-29-26-22-20-14-5	13	Depression	4
86-80-78-72-57-39-33-23-17-2	10	Anxiety	5
81-74-67-63-24-11	6	Aggression	6
82-75-70-50-47-25-13	7	Phobia anxiety	7
83-76-68-43-18-8	6	Paranoia	8
90-88-87-85-84-77-62-35-16-7	10	Psychosis	9
89-66-64-60-59-44-19	7	Other questions	10

was able to show the difference between addicted and non-addicted drug groups and aggressive groups for which they had been prescribed medication (Mohammad 2001, quoted by Cloche et al, 2010). To determine the internal consistency of the questionnaire, which was conducted on 219 volunteers in the United States, they used Alpha coefficients and Richardson coefficients 20 and the results of the number of coefficients obtained for 9 dimensions were completely satisfactory. The test-retest reliability, which measures the stability of the questionnaire over time, was calculated on 94 mentally ill- patients and one week after the initial evaluation. The results showed that in most cases, most of the correlation coefficients were (from 0.78 to 0.91) (Sharif, 1997, quoted by Cloche et al., 2010).

Method of Data analysis
Statistical analysis was done in two sections. In the descriptive section, frequency, percentage, mean, and standard deviation were investigated and inferential analysis was used for analyzing the method (t) for independent groups and multivariate analysis of variance (MANOVA).

Results

Descriptive statistics

Table 2: Demographic report

Frequency	Gender
50	male
50	female
100	total

Frequency

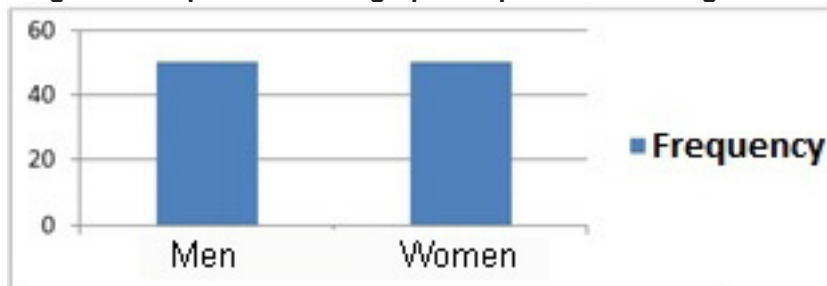**Diagram 1: Population demographic report in terms of gender variable**

Table 3 describes the indexes of the research. The average, standard deviation, skewness, elongation, minimum and maximum amounts of mental health indicators are reported. Also, the table above shows that the indexes of skewness and elongation of any of the agents did not pass the 2-foot boundary. It is necessary to explain that skidding should be at least between -2 and +2 in order to distribute data at a level of 0/05 (Klein, 2005). Therefore, it can be said that the distribution of data for each of the variables is normal. Table 4 describes sample individuals in terms of sexual performance indicators.

Table 4 describes the research indicators. mean, standard deviation, skewness, elongation, lowest value and maximum value of 7 factors and the overall score of sexual function are reported. Also, the table above shows that the indexes of slip and elongation of any of the agents did not pass over the ± 2 boundary. Therefore, it can be said that the distribution of data for each of the variables is normal.

Inferential statistics
Question 1: Is mental health different in the male and female victim of betrayal in the family court of Tehran city? In order to test the first question, multivariate analysis of variance (MANOVA) was used. The evaluation of the homogeneity assumption of variance of covariance by the "M box" statistics showed that the equivalence assumption of the observed variance-covariance matrices does not depend on the data of the two groups (Box's M, = 0> P, 017/2 = F). Despite the lack of homogeneity assumptions for variance of covariance, it is not expected that this issue will invalidate the results of the study, because Tabachinck and Fidel (2007) believe that if the sample size is comparable in the groups, the analysis of variance and analysis of covariance will be resistant to non-delivery of assumptions. The results of the Bartlett St test with a degree of freedom of 36 were obtained at a significant level of 0.001 and equal to 150.819. This result shows

Table 3: Describes sample individuals in terms of mental health indicators

Maximum value	Minimum value	Elongation	skewed	Standard deviation	Mean	Gender	Indicator
17	4	-0.231	0.296	2.31	11.76	female	Physical complaint
				2.71	11.56	male	
39	8	2.461	0.585	3.81	20.60	female	Physically and mentally obsessive
				4.67	24.44	male	
30	4	-0.845	-0.107	5.66	18.42	female	Interpersonal sensitivity
				6.39	15.08	male	
48	1	-0.493	0.180	11.21	27.58	female	Depression
				11.63	19.44	male	
33	4	-0.437	-0.019	61.15	16.88	female	Anxiety
				5.33	21.22	male	
22	15	-0.506	-0.006	1.64	18.90	female	Aggression
				1.66	18.18	male	
28	15	0.489	-0.061	2.50	21.36	female	Phobia
				2.80	21.78	male	
24	2	0.108	0.325	4.36	11.52	female	Paranoia
				4.28	12.68	male	
36	8	1.473	0.253	3.94	21.72	female	Psychosis
				4.90	22.94	male	

Table 4

Maximum value	Minimum value	Elongation	Skewness	Standard deviation	Mean	Gender	Indicator
189	156	-0.770	0.069	7.63	170.52	female	Sexual performance

Table 5: Analysis of One-Way Variances in Comparison of Mental Illness among Men and Women

η^2	Significance level	F	Squares of error	Squares of mean	Variables
0/040	0/693	0/157	6/362	623/44	Physical complaints
0/414	0/001	20/269	18/187	1782/32	Physical and mental obsession
0/269	0/007	7/643	36/488	3575/86	Interpersonal sensitivity
0/339	0/001	12/692	130/515	12790/50	Depression
0/356	0/001	14/209	141/33	3247/860	Anxiety
0/215	0/032	4/741	2/733	167/880	Aggression
0/061	0/549	0/362	7/065	692/40	Phobia
0/134	0/183	1/800	18/687	1831/36	Paranoia
0/137	0/174	1/875	19/846	1944/90	Psychosis

with a degree of freedom of 36 were obtained at a significant level of 0.001 and equal to 150.819. This result shows that an acceptable level of correlation exists between dependent variables. Therefore, multivariate analysis of variance is a suitable method for comparing mental disorders in men and women. Analysis of variance of multi-variable was performed and the results showed that F value (0.003 = 0) = Wilkes Lambda, 2 = 438 = 2 partial ⁊, P = 0.001, 0.891 89 = (90 and 9) F) at the significance level of 0.05. For this purpose, one-way analysis of variance was performed to determine which psychiatric disorders were statistically different between the two sample groups. Tables 4-5 show the results of one-way ANOVA in comparing mental illness among men and women.

Tip 1: In the analysis of variance, there was one line between degrees of freedom between groups 1 and degree of error 98. It should be explained that Table 3 shows the eta squared (2η) for each variable. The eta squared means that several percent of the variance of the variable depends on the variable of the group. For example, the number of physical complaints is 0.040, which means that approximately 4% of the variance in physical complaints is explained by being in the group. Further, considering that the group variable in the present study consists of two classes, therefore, in order to evaluate the difference, a follow-up test is not required. According to the significance level and the means, it can be determined that the difference belongs to which group. Thus, the first question of the research test is as follows (Is the mental health in the victim of betrayal women and men different in Tehran family courts?), It was concluded that men with obsessive disorder are significantly more anxious than women. And depression, aggression and interpersonal sensitivity in women is seen more than in men. There was no difference in physical complaints, phobic anxiety, paranoid thoughts, and psychosis in the two groups of male and female. The regnant equations were solved by the Simplified algorithm. Reynolds number, Hartmann's number, Baffle length, Baffle height, Richardson number and volume fraction of nanoparticles were changed.

Conclusion

In this paper, the comparison of sexual behavior patterns and mental health in male and female victims of betrayal in family courts in Tehran was investigated. The first hypothesis examined the difference between the mental health of male and female victims of betrayal referred to family courts. Findings show that physical and mental obsession, anxiety in men is more than women and depression, aggression and interpersonal sensitivity in women is more than in men. There was no difference in the indicators of physical complaints, paranoid thoughts and psychosis among men and women. There is no difference in the context of comparing mental health of male and female victims of betrayal research. But Peelers et al. (2013), and Brewer and Abel (2015) also found increased levels of psychiatric illness in betrayal women and men . Glass and Wright (1997) also pointed out that woman have more mental disturbances than men. This obsession is so acute, intensive and uncontrollable that it interferes with daily performance and concentration of the individual. And this is confirmed by the findings of the present study, which showed depression in women more than men. Karimi et al. (1393) also referred to disturbances such as anxiety and depression in women. In explaining the findings of this study, it can be said that since women are more likely to be depressed than men, and behave more socially than men, Therefore, it seems logical that emotional failure would show symptoms of more interpersonal sensitivity. Also, the appearance of psychological stress caused by treason in men is in the form of anxiety and it seems to be normal. But that these stresses go beyond the bounds of physical and mental obsession thought, perhaps because of the culture of our country and the people's view about the betrayal of women and man who face a lot of challenges, and it emerges in the form of obsessive disorder. The second hypothesis of the study examines the differences between sexual behavior patterns in male and female victims of betrayal, which revealed no difference between men and women. Also, there was no research about patterns of sexual performance in males and females of Iran. And this issue shows need for innovation of research. But research findings suggest that the overall difference between women and men in sexual behavior is largely determined by the role of gender and the cultural variables (Bam, 1983). For example, women in our culture have accepted that they talk less about their sexual performance in marriage and express their dissatisfaction less. They face this stereotype that "a good woman never talks about her sexual behavior." Therefore, by considering that sexual behavior is always in a state of ambiguity, there is not enough awareness in this regard before serious disturbances in sexual performance . In the whole of the same research for comparing male and female sexual responses, it has been shown that all women and men show similar responses to movies when they watch film with sexual subject . Hayman's study also showed that women and men are similar in their responses to sexual stimuli, but women are sometimes unaware of their sexual arousal (Hayman, 2011). In terms of the information processing theory, any sexual stimulation can lead to arousal , and thus result in pleasant feelings, but the meanings of the stimulus are acquired through positive experiences (love) and negative experiences (betrayal) and gender role schemas of the strengths provided in the brain. Whenever sexual attention is given, sexual response takes place. This answer is initially at the unconscious level. But retaining attention to sexual stimulus leads to higher levels of sexual arousal. And when this state is above the perceptual threshold, arousal is also experienced at the conscious level. The processing of sexual stimuli leads to the preparation of sexual activity. It seems that women in this area face many difficulties because of the mental schemas and cultural stereotypes which are intrusive in this area . Excitement is an indication and reaction to an external event which can be measured with a number of indices of central nervous system activity, such as protuberance of reproductive organs. The motor preparation experience is probably related to the expectations of reinforcements and can be felt as something pleasant. Here, cultural stereotypes based on mental scheme form negative expectations. At the same time, during life and in the context of the relationship between the partners, the power of sexual stimuli can be reduced.

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Investigating the cytotoxic effect of chamomile aqueous extract on 4T1 and 47D cells and level of caspase3 protein in breast cancer cells T-47D

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Abstract

Introduction: Breast cancer is one of the most common cancers of women in the world. Many methods have been devised to treat breast cancer, such as radiation therapy, surgery and chemotherapy. Clinical effectiveness of chemotherapy has been limited due to side effects, toxicity and drug resistance. The studies have shown that some medicinal herbs have anti-cancer effects which do not cause side effects of chemotherapy. One of these herbs is Chamomile, the anti-cancer effect of which is being studied by researchers. The effect of Chamomile aqueous extract on cellular survival of breast cancer cells T-47D,4T1 and protein level of caspase3 in breast cancer cells T-47D has been investigated in this study.

Methodology: Breast cancer cells 4T1 and T-47D were treated by blue extract of Chamomile with various concentrations, for 24 hours and then using MTT method, the rate of cytotoxic effect of Chamomile was checked on the above mentioned cells and following that the apoptotic effect of Chamomile extract on treated cells was investigated using ELISA method for determining the amount of caspase3 protein.

Results: This study showed that Chamomile extract significantly reduced breast cancer cells survival, concentration-dependent, compared to the control group. Dependent on concentration and time, the Chamomile extract also increased caspase3 protein, indicating induction of apoptosis in the mentioned cells.

Conclusion: Chamomile extract, dependent on concentration and time, was able to kill tumour cells that can arise from increasing the level of caspase3 protein. These results can be used in future studies on the anti-cancer effect of Chamomile extract.

Key words: breast cancer, Chamomile extract, caspase3, cell lines of 4T1 and T-47D

Introduction

Cancer is nowadays considered as one of the most important health problems around the world. According to the statistics of World Health Organization, after cardiovascular diseases, cancer is the second highest cause of death in the world. According to the report of the Iran Cancer Statistics Center, more than 51,000 new cases of cancer, are annually identified and 35,000 deaths occur each year because of cancer in the country (1).

Among female cancers, breast cancer is the most important health issue. Breast cancer is the most common cancer in women and the second highest cause of death in women after lung cancer (2-6). The prevalence of breast cancer is different in various countries. The highest prevalence is in the USA and North Europe and the least prevalence has been reported in Asia (3). Breast cancer is rare in women younger than 20 years old and uncommon in women younger than 30 years old. The incidence rapidly increases up to 50 years old. Average age of cancer incidence is 62 years old. 94% of breast cancers occur in women older than 40 and only 6% has been reported in women younger than 40 (5). The most important symptom of breast cancer is a breast lump. If a lump is diagnosed in examination or mammography, breast cancer diagnosis should be proven or rejected through biopsy (6). In spite of affluent developments in controlling and treating cancer, much research has been conducted to recognize the mechanisms, involved in its growth and production of effective drugs. Moreover, a wide range of these studies have been allocated to medicinal herbs.

Using various medicinal herbs, such as garlic, Echium, Althaea officinalis, mulberry tree leaves and Rosmarinus officinalis is common in traditional medicine of Iran for different reasons (7). The relation of Terpenoids in herbs with strong anti-inflammatory effects has been proven (8). Chamomile has active compounds such as Terpenoids and Flavonoids. Among these five herbs, Chamomile, in addition to evident antioxidant properties, contains the most anti-inflammatory effects. Because of its anti-inflammatory property, this herb is widely used for treating skin abnormalities as well as different types of cosmetic products (9). Apoptosis is cellular physiologic death which has an effective role on controlling body pathologic conditions. The diseases with infinite power of proliferation, such as cancer, are created as the result of a changing genome. The studies show that several pathologic changes lead to the growth of malignant cells. These changes include self-sufficiency in cell proliferation, resistance to cell inhibitory signals, Angiogenesis, escaping from apoptosis, lack of limitation in proliferation of cell and attack on other tissues. One of these changes is escaping from apoptosis so that resistance to apoptosis is one of the potential symptoms of cancer. Reducing the sensitivity to apoptosis leads to increase of treatment threshold for classical cases such as radiotherapy and chemotherapy. Therefore, one of goals in treating cancer is activation of apoptosis paths (caspases) in cancer cells. In this study, two cell lines of breast cancer including 4T1 and T-47D were used. 4T1 is a mouse breast carcinoma cell which has tumorous and offensive properties and can metastasize from the primary lump to other points of the body such as lymph, blood, liver, lung and brain. The mentioned property makes it a proper experimental model for breast cancer. T-47D cells are also extracted from breast duct carcinoma of a 54-year-old woman. This line of cell contains epithelium morphology and steroid receptors such as estrogen and progesterone. T-47D lacks epidermal Growth Factor Type 2 (her2). A few studies have investigated the role of Chamomile aqueous extract in preventing meiosis as well as apoptosis induction dependently on dosage and time (10). Hence in the current study, the effect of treatment with Chamomile aqueous on properties of cytotoxic, apoptotic and also effectiveness on caspase3 protein in cell lines of breast cancer are investigated.

Materials and Methods

1- Extraction manner
In the current experimental study, the flowering head branches of Matricaria chamomila herb were extracted in flowering season (early March). The herb was collected in Khuzestan Province (Dezful) in an area with geographical coordinates of 48 degrees and 24 minutes north and 32 degrees and 22 minuteseast. Flowering head branches were dried in shade and at room temperature. To provide aqueous extract, chamomile dry flower was turned to powder by mill and mixed and boiled with distilled water. Then the contents inside the container were filtered using Whatman filter paper and the obtained extract was concentrated using a rotary machine. The concentrated solution was kept in a freezer at -80˚C until testing.

Different concentrations of chamomile aqueous extract were treated in culture environments including 2600-1300-650-325 micrograms per milliliter concentrations. Selection of concentrations was conducted based on previous studies (11).

2- Cell culture
Cell lines 4T1 and T-47D were prepared from Tehran Institute Pasteur cell bank and cultured in culture environment of RPMI 1640, enriched with Fat Bovine Serum (FBS) of 10% and penicillin antibiotic 5%. After reaching proper coating level in 96-cell plates, 10,000 cells were cultured in each well and were incubated for 24 hours in 37˚C and 5% carbon dioxide and 95% of incubator moisture. The different concentrations of extract including 2600-1300-650 and 325 micrograms per milliliter were added to the cell and they were treated for 24 hours.

3- Testing the effect of chamomile aqueous on the rate of cell survival
The rate of cells survival was determined using MTT test, as it was explained before (12-13). Based on the activity of succinate dehydrogenase enzyme in mitochondria of living cells, this method turns MTT yellow solution to insoluble purple formazan crystals that can be evaluated by ELISA Reader machine after dissolving in dimethyl sulfoxide. The rate of 10,000 cells were transferred to a 96-cell plate.

They were incubated at 37°C for 24 hours. Then they were treated by different concentration of chamomile extract (2600-1300-650 and 325 micrograms per milliliter) and finally, the volume of wells reached to 100 microliters.

The plates, containing cell and extract, were incubated in the equal conditions for 24 hours. After the considered time, 96-cell plates were taken out of the incubator and 10 microliters of MTT solution was added to each well and they were put in incubator for 3 hours. Then 100 microliters of DMSO was replaced with incubated environment with MTT and they were kept in the dark for half an hour.

After being dissolved in DMSO, Formazan crystals create a purple solution the rate of which indicates the biological potential of treated cells. Optical absorption of plates was evaluated in wavelength of 570 nanometers (14).

To investigate the toxicity effect of chamomile aqueous extract on treated cancer cells, the following formula was used.
1-ODexp/ODcont×100= the rate of cells mortality

4- Investigating caspase3 activity through ELISA method
To evaluate caspase3 activity, CASP3 (human) Cell-Based ELISA Kit was used and implemented according to the following protocol:

1. 200 microliters of culture area containing 20,000 T-47D cells were cultured for a night at 37°C and with 5% of carbon dioxide.
2. The chamomile aqueous was added to the cells with different concentrations (1300, 2600 micrograms).
3. 100 microliters of fixing solution was added and incubated in room temperature for 20 minutes.
4. 100 microliters of quenching buffer was added and incubated in room temperature for 20 minutes.
5. 200 microliters of blocking buffer was added and incubated in room temperature for 1 hour.
6. 50 microliters of initial anti-body (anti-caspase3 or anti-GAPDH) was added and incubated one night at 4°C.
7. The secondary antibody (HRP-conjugated) was added and incubated at room temperature for 1 and a half hours.
8. 50 microliters of reaction substrate was added and incubated at room temperature for half an hour.
9. 50 microliters of stop solution was added and samples absorption was read at a wavelength of 450 nanometers.

Statistical analysis
On average experiments were calculated three times. The collected data were analyzed using SPSS16 software and two-way ANOVA test and the diagrams were drawn using EXCEL software.

Findings

The effect of chamomile aqueous extract on stopping cell proliferation:
The effect of different concentrations of chamomile aqueous extract was evaluated on the rate of cell mortality in cell lines. As shown in Diagrams 1 and 2, in both cell lines, 2,600 micrograms per milliliter concentration of extract in 24 hours after treatment prevented cell proliferation significantly in comparison with the control group (P<0.05). Chamomile extract lacked significant effect in cell cytotoxicity at concentrations of 162 and 325 micrograms per milliliters so these concentrations were eliminated as follows.

The effect of chamomile aqueous extract on caspase3 activity
The Caspase enzyme family is of main apoptosis intermediates and their activity increases within apoptosis procedure. The results of investigating caspase3 activity showed that the value of caspase3 protein at 1 and 3 hours, affected by 2600 and 1300 micrograms per milliliters of chamomile aqueous extract, significantly increased in comparison with control group (Diagram 4). Therefore, chamomile aqueous extract can be said to lead to cell mortality in breast cancer cells through caspase3 activity compared to control group. GAPDH has been also shown as an interior standard in the diagram (P<0.05).

Discussion and Conclusion

In spite of important developments in diagnosing and treating cancer, breast cancer is still one of the common problems of women. One of the goals in treating cancer is returning the apoptosis mechanism in cancer cells. New medicines have always been required and researchers all around the world have made a wide range of efforts to identify new, natural or synthesized compounds with anti-cancer properties. The studies have shown that herbal medicines are more important in preventing cancer due to their lesser side effects (15). The chamomile aqueous extract through MTT method in breast cancer cells was investigated in this study and the obtained results of cytotoxicity indicated that the extract significantly and concentration-dependently increases breast cancer cells mortality in 4T1 and T-47D cell lines.

Dependent on concentration and time, the Chamomile extract also increased caspase3 protein, indicating induction of apoptosis in mentioned cells.

In this field, Janmejai, K. et al conducted a study, the results of which showed a significant decrease in cancer cells liveability after Chamomile treatment. The apoptotic anti-proliferative effects of chamomile extract on cancer cells was also observed in this study (16). As mentioned before, chamomile has strong anti-cancer effects. In a study by Asgari et al, it was observed that the rate of antioxidant markers activity in liver cells of rats, faced with oxidant composition after chamomile extract, significantly increased (17).

Sedighara concluded in a study that chamomile has antioxidant and anti-inflammatory effects. In this investigation, the rate of herbs' antioxidant power and copper ion survival and their anti-inflammatory power were tested through tests for preventing serum protein denaturation (18). Given that apoptosis is an important

Diagram 1- The comparison of cytotoxicity percentage of T-47D cells, treated with concentrations of 2600, 650 and 1300 of chamomile aqueous extract with MTT test
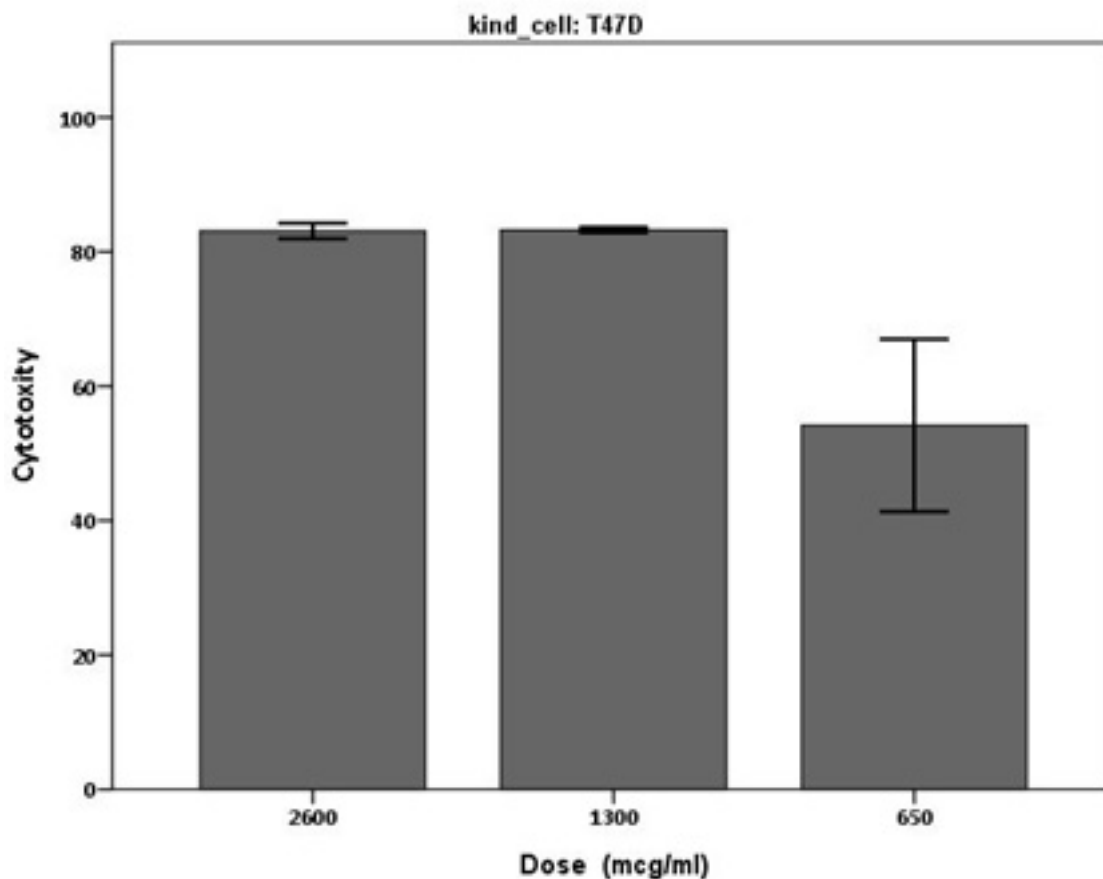

Diagram 2- The comparison of cytotoxicity percentage of 4T1 cells, treated with concentrations of 2600, 650 and 1300 of chamomile aqueous extract with MTT test
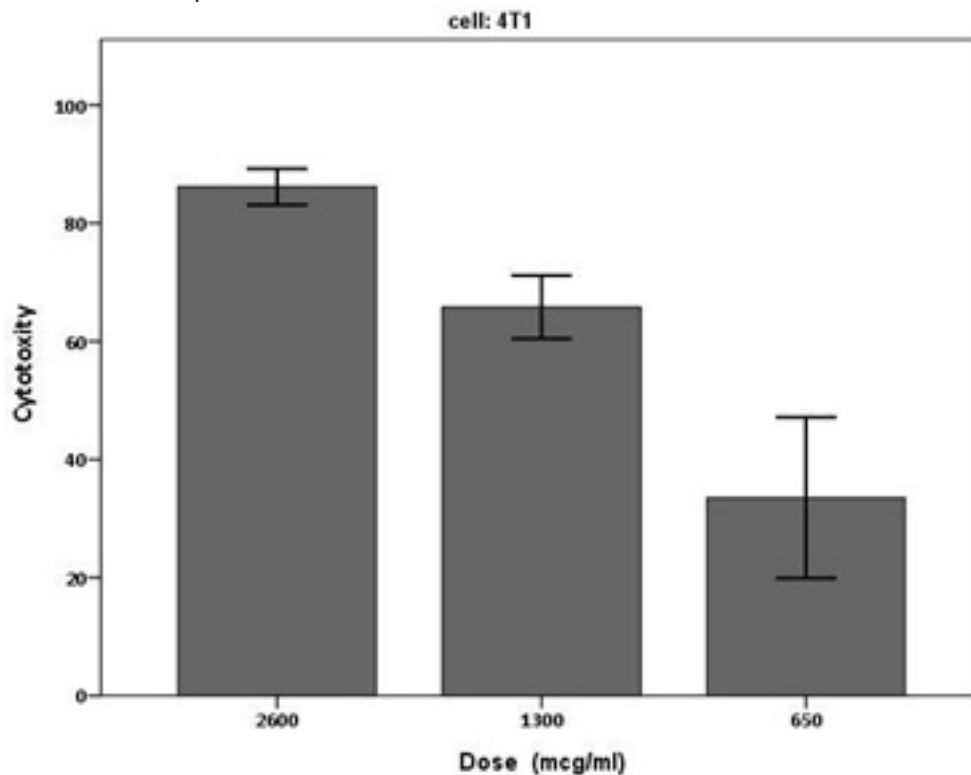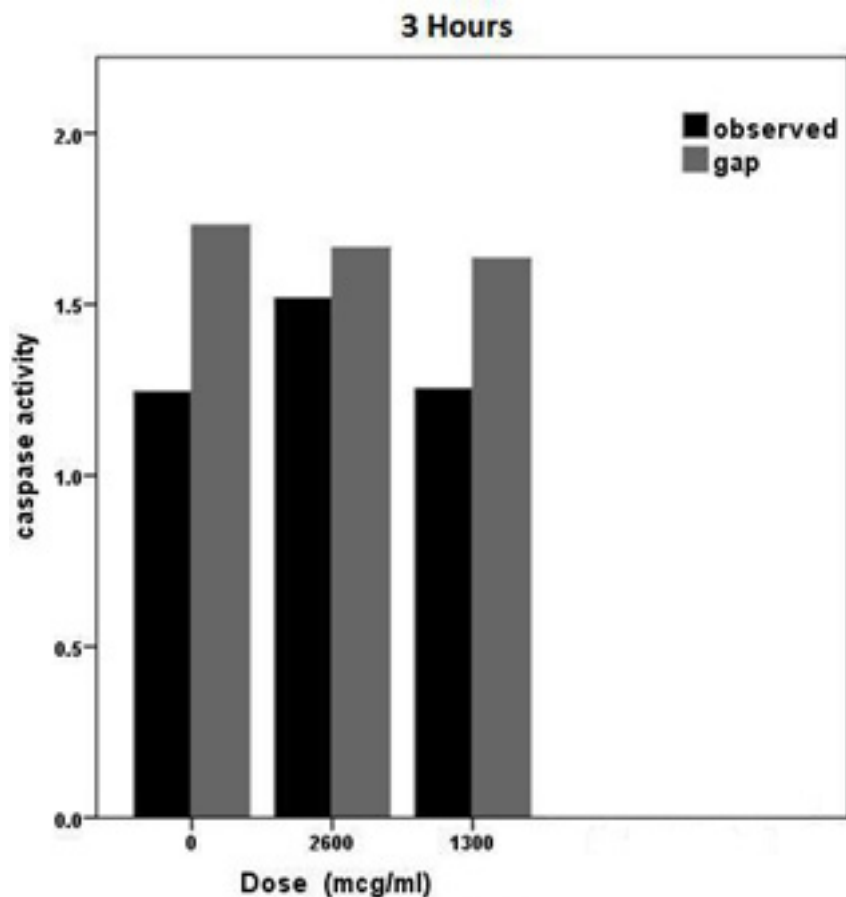
Diagram 3- The changes of caspase3 gene, affected by concentrations of 2600, 650 micrograms per milliliters of chamomile aqueous extract three hours after treatment
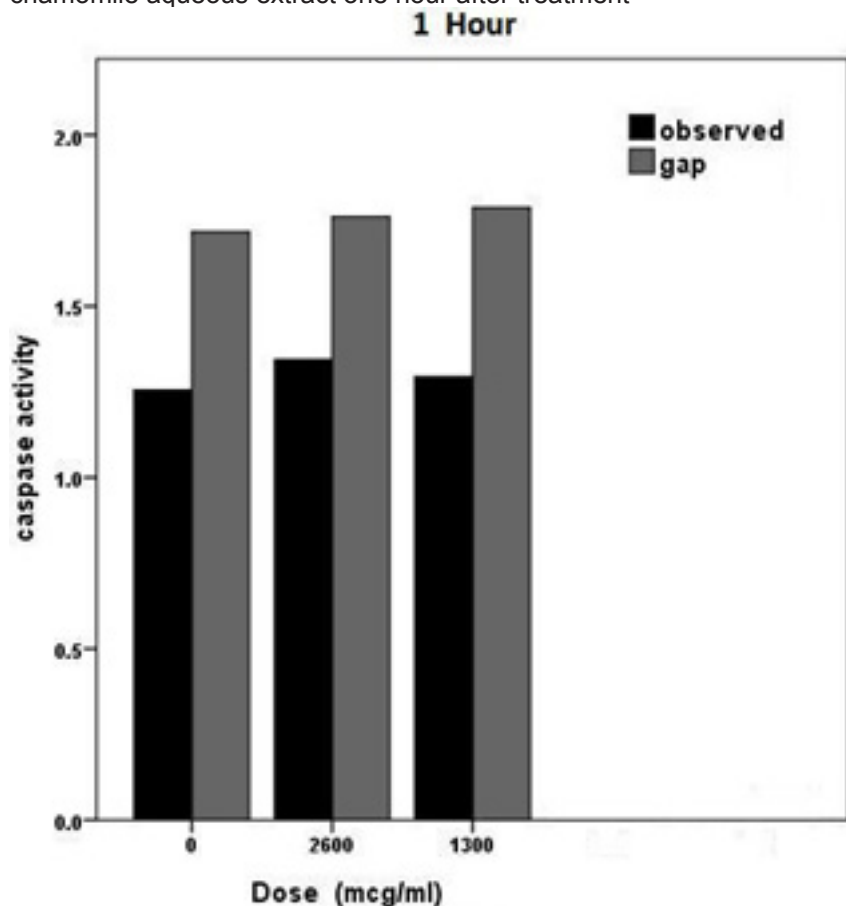

Diagram 4- The changes of caspase3 gene, affected by concentrations of 2600, 650 micrograms per milliliters of chamomile aqueous extract one hour after treatment

process to control cells proliferation and remove cancer cells (19), as the next step, the capability of apoptosis creation in breast cancer cells was investigated. Caspases are of pivotal intermediates in apoptosis mechanism. During cell death process, capase3 activity first begins being influenced by apoptosis stimulus. By proteolytic failures, this caspase then causes caspase 8 and 9 activation which are of great importance in the process of beginning apoptosis. It was shown in this study that treating T-47D cells with chamomile extract increases caspase3 activity. The apoptotic effects of chamomile through flow cytometry method was investigated in the past studies but its accurate mechanism is unknown.

In this study, the obtained results of morphologic investigation and cells survival test through MTT method showed that inhibitory effect of chamomile aqueous extract began from the low concentration (325 micrograms per milliliter) to 2600 micrograms per milliliter from the initial hours and after 24 hours of treatment, inhibitory effect increased on cancer cells. The obtained results show that in different times, by increasing the concentration, the rate of cancer cells survival decreases, that is probably because of extract effect on apoptosis path. Cytotoxic effect of chamomile aqueous extract can be applied through increasing the rate of caspase3 gene expression. The results of this study generally showed that time and concentration-dependent chamomile aqueous increased proliferation inhibition in breast cancer cells (caspase-dependent path).

In addition, to confirm previous findings, these data have proposed some evidence based on the effect of chamomile as an effective Chemo-preventive factor with apoptotic effect. The commentary studies in cell levels are recommended to find the mechanism of chamomile (Flavonoids) in molecular dimensions and also clinical studies for confirming the effectiveness of this compound on treating cancer.

Acknowledgement

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