Focus on Iran Part 1

Winged bull. Circa 510BC. In the palace of Darius I, ancient city of Susa

From the Editor

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This is the second issue of the journal with focus on Iran a country with rich cultural heritage and recent academic advancement in all scientific fields. The papers in this issue focus on various topics of importance to the society. Nikfarjam M et al in a cross-sectional study, 160 students were assigned to two groups. The study was conducted to compare spiritual well-being and social health between the students attending group religious rituals and those attending individual religious rituals. The spiritual well-being and social health scores of group 2 was significantly higher than those of group 1 (p=0.001 and 0.002, respectively). The authors concluded that the mean scores for spiritual well-being and social health were higher in the group who attended group religious rituals.

Jahromi AS et al in a case-control study, anti-diphtheria toxin antibody concentration and serum ferritin levels were compared. The authors concluded that , patients with beta thalassemia major had lower anti-diphtheria antibody level than healthy subjects. Thus monitoring immunization status and recommendations for vaccine are essential for increased serum anti-diphtheria antibody concentration.

Erfanian S et al in a case-control study, 100 patients with a history of premature coronary artery diseases and 100 healthy control. The authors concluded that according to the results derived from this study, it seems like the existence of the genotype carrying the mutated allele (TC+CC) in rs1927911's mononucleotide polymorphism of TLR gene is associated with an increased risk of premature myocardial infarction.

Rashnou, F et al. did a descriptive qualitative study by using the conventional content analysis approach. The authors concluded that nurses can help manage effective VAP through learning new and standard approaches to care delivery and adhering to standards of care.

Pooria, A, et al. compare postoperative bleeding in patients undergoing coronary artery bypass surgery in two groups taking aspirin and aspirin plus CLS clopidogrel. The rate of postoperative bleeding in the clopidogrel plus aspirin group was higher than the rate in the aspirin group, but this difference was not significant (PV=0.067).

Jafrasteh A et al, conducted a descriptive-analytical investigation on premature neonates with very low birth weight (less than 1500 g) and gestational age less than 32 weeks. This study showed that CRIB II index has higher value in prediction of mortality in premature neonates with very low birth weight.

Yavangi, M et al carried a randomized clinical trial on women aged 20-59 years with moderate to severe POP. The authors concluded that Pre-colporrhaphic physiotherapy can improve quality of life and sexual function in the patients' candidate for colporrhaphy.

Hashemzadeh-Chaleshtori, M et al reviewed TECTA gene function and hearing. TECTA is a modular, non-collagenous protein of the tectorial membrane that plays a more dynamic role in normal hearing. Mutations in TECTA cause dominant and recessive forms of non-syndromic hearing loss.

Ghasemi M et al used available sampling was done using 80 patients with knee osteoarthritis and samples were divided into two groups. The authors concluded that in general, it can be suggested that the use of dextrose prolotherapy is a simple, safe, inexpensive, accessible and uncomplicated method than other treatments in these patients.

Ebrahimi H.A et al did a descriptive-analytical study on evaluation of seizures in pregnant women. Among 3807 admitted pregnant women, 38 cases (1%) experienced epileptic seizures. The authors concluded that more than 6 in 1000 pregnant women suffer from epilepsy. Eclampsia is the most prevalent cause. Epileptic seizures increased in 21% of epileptic pregnant women, and declined in 21% of the cases.

Jafarpour, E did a pre-test and post-test study to evaluate the blood level of leptin hormone before and after treatment with metformin. It is concluded that, the effect of metformin during the treatment period reduced the blood glucose level of adolescents, but its effect on weight loss and HbA1c did not significantly increase due to the duration of treatment.

Dargahi, H et al, carried a cross-sectional research on 1238 non-academic employees. The required data was collected by the Quality of Work life (QWL) questionnaire. The authors concluded that in the present study no significant relationship between the quality of work life and general health, socio-economic status and quality of work life, and also general health and socio-economic status was found.

Mangeli, M et al., explored the factors that encourage early marriage and motherhood in Iranian culture. The authors concluded that various factors (personal, social, economic, cultural, spiritual and technological) encourage adolescent to early marriage and motherhood.

Soltanian, F evaluated psychological and social factors effective on emotional separation among attendants to well-fare social emergency centers. The results showed that psychological and social factors have positive correlation with emotional divorce and regression analysis showed that social factors rank first and psychological problems are next in importance when it comes to emotional divorce.

Rajabi, M et al., investigated perceived organizational justice and organizational trust and their relationship in nurses of public and private hospitals in north of Iran. According to the results, in order to improve organizational trust, it is necessary that hospital managers develop organizational justice.

Bachari, Y.H et al conducted a quasi-experimental intervention study to compare the effects of two educational methods of role play and video feedback on learning CPR. The authors concluded that the video self-feedback method in compare to the role play method is more effective in improving cognitive and psychomotor learning of nursing students in basic cardiopulmonary resuscitation. Ziapour A et al did a pre-test-post-test study. The statistical population consisted of all couples in Kermanshah City.

At the theoretical level, the results of this research can confirm the results of previous research. At the practical level, the findings of this study can be used to develop educational and therapeutic programs.

Barekati1, S et al., carried out using a pretest-posttest semi-experimental design with control group and random assignment. The findings of this research can be considered as a confirmation of the basic assumption of the cognitive-existential approach about the effect of correcting cognitive distortions that activate non-authentic responses to the existential anxieties.

Elmi, R et al., did a cross–sectional study on 87 cadavers to compare morphine in urine and other body fluids, including cerebrospinal fluid (CSF), bile, pericardial fluid (PCF), and vitreous humor to determine the most reliable fluid for detection of postmortem morphine. The moderate agreement between urine TLC and bile TLC reveals bile sample as the most reliable fluid for morphine detection, when a urine sample is not accessible.

Farzaneh Norouzi, F et al., carried out a cross-sectional study, 204 nursing and midwifery students. The authors concluded that the presence of high spiritual motivation in nursing and midwifery students compared to other types of motivation is regarded as a strong point in the education of students.

Fakheri T et al., attempted to compare the LUS (lower uterine segment) thickness among nulliparous pregnant women without uterine scar and pregnant women with previous cesarean section using trans-abdominal ultrasound in the third trimester. The authors concluded that LUS thickness was significantly lower in pregnant mother with previous CS and this led to dehiscence in such patients. In case of LUS thickness of < 1.7 mm, the risk of dehiscence and rupture increases.

Jafarkhani, F et al., examined the effectiveness of the blended approach in learning English through the mobile social networks to enhance the level of listening and speaking skills of primary school students. The findings of the study bear some significant implications for curriculum designers, teachers and students and highlight the crucial role of using the technological devices and applications in promoting the learners' capabilities in listening/speaking.

Haghanifar, S et al., attempt to determine the course of MC, anterior branch and its relation to mandibular teeth. In cross-sectional view, the MC diameter, the distance from root apex to MC.
So, any procedures in mandibular posterior area should be performed with sufficient knowledge of the nervous canal.

Shateri, L et al., evaluated the extent to which the association between chronic pain and obesity are mediated by anxiety and moderated by coping strategies. In summary, chronic pain predicted obesity directly, and specific coping strategies (emotional coping strategies) did not moderate the relationship between chronic pain, obesity and anxiety, but anxiety mediates this relationship.

Shekarbaghani, A tried to interpret the Commercial situation of astronomy, religious culture and curriculum. The author concluded that the creation of the preparing the needed science for the compilation of astronomy affect daily life with the other curriculum.

Taheri, S et al., conducted a clinical trial with the aim to determine the effect of environmental and behavioral interventions on physiological and behavioral responses of preterm infants during intravenous catheterization. It was found that dimming light and noise, nursing manipulations, and fetal positioning during intravenous catheterization effectively reduce neonatal pain.

We have two papers that dealt with obesity. Molaei, K. conducted a semi-experimental to evaluate the effect of 8 weeks aerobic exercise on the amount of resistin and body mass index (BMI) of overweight women. Data analysis indicated that the 8-week exercise program had a significant effect on BMI (P=0/001), body weight (P=0/000), and resistin (P=0/001). In the second paper data analysis showed that 8-weekly sport exercises had a significant effect on BMI (P = 0.001), body weight (P = 0.000), and leptin (P = 0.001).

Ban, M et al., carried a descriptive-analytic study on 202 nurses. Results of this study showed that nurses should firstly recognize the dimensions and ethical issues in their profession for the ethical performance of professional nursing; therefore, it is recommended to maximize the efficiency and quality of health care by educating the medical staff and raising their awareness of professional ethics.

Javadi, M.S et al., carried a retrospective descriptive cross-sectional study on 148 cases of admitted children due to febrile convulsion. This study showed that the prevalence of febrile convulsion in children younger than 2 years old is more common in males and prevalence of simple seizure is more common compared to complex one. Also, the history of seizure, seizure duration, child's age, and duration of fever onset to seizure occurrence are effective in seizure incidence.

Raezian M provides a brief report on the components of national strategies for suicide prevention suggested by the World Health Organization. Based on this report a well-designed national strategy for suicide prevention should have at the very least twelve components.

Sani, M.S et al did a causal comparative study, all fertile and infertile women referred to Arash Hospital and Mirza Kuchak Khan Hospital in Tehran. The results showed that the level of quality of life, self-efficacy and resiliency in infertile women is less. Based on these results, it can be said that considering the importance of psychological factors in exacerbating the physical and mental damages associated with infertility, psychological interventions focused on quality of life, self-efficacy and resiliency with the aim of improving the mental health of the infertile people, is necessary.

Aliza V et al did a reassessment of factor structure of the Short Form Health Survey (SF-36) where four theoretical and experimental factor structures of the SF-36 were tested and compared here to establish a best-fitting model for Iranian older people. A sample of 391 participants (60 -89 years) years completed the Farsi SF-36. This study provides strong evidence that the Farsi SF-36 has the potential to measure well-being status of older people. Such an application application is valid if the Vitality items are modified and new items are developed for the Well-being scale.

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Review

International Health Affairs

Education and Training

Immunity level to diphtheria in beta thalassemia patients

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Abstract

Introduction: Beta thalassemia major which is very common is a principal health problem in Iran. These patients are more often affected by several infections. The aim of the study was to determine the immunity of patients with beta thalassemia major, to diphtheria.

Methods: In this case-control study, anti-diphtheria toxin antibody concentration and serum ferritin levels were compared in 224 patients with thalassemia major and in 224 sex and age matched healthy subjects as control group. The serum concentrations of antibody and ferritin were determined by ELISA and CLIA methods, respectively. Subjects who had diphtheria antibody level >0.1 IU/ml were seen to have complete protection, between 0.1 and 0.01 IU/ml as partial protection and <0.01 IU/ml as no protection. For the analysis we used SPSS version 15 software. A two sided P-value less than 0.05 was considered statistically significant.

Results: The mean serum anti diphtheria antibody level was lower in patients with beta thalassemia major than in healthy subjects (1.51 ± 1.60 vs 2.10 ± 1.86, p<0.001). Seventy percent and 20.0% of patients and 87.9% and 12.1% of healthy subjects had complete and partial protective serum anti diphtheria level, respectively (p<0.001). Only 24.1% of anti-diphtheria antibody (IgG) was dependent to serum ferritin level in patients group (P< 0.001). Thus serums anti diphtheria antibody decreased 0.001IU/ml, when serum ferritin increased 1ng/ml.

Conclusion: In conclusion, patients with beta thalassemia major had lower anti-diphtheria antibody level than healthy subjects. Thus monitoring immunization status and recommendations for vaccine are essential for increased serum anti-diphtheria antibody concentration.

Key words: diphtheria, antibody, thalassemia, immunity

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Introduction

Beta thalassemia major which is very common (1), is a central health problem in Iran (2) with at least 800 new cases every year (1). These patients are more often affected by several infections. It is suggested a chief defect in the host defense can be caused by iron overload, splenectomy and repeated transfusion (3).

Susceptibility to bacterial infections increased in splenectomized subjects (4). Lifetime risk of developing an overwhelming post splenectomy infection and mortality rates is 1–5% and 40-70%, respectively. The spleen plays a role in the maintenance of a pool of memory B cells involved in the protection against bacterial infections (5).

According to the latest figures released by the World Health Organization, 4,530 cases of diphtheria have been diagnosed worldwide and 28 of those cases occurred in Iran in 2015 (6). The diphtheria surveillance in Iran was done according to national protocol (7, 8).

In Iran, every subject under 7 years old routinely receives 5 doses of diphtheria-pertussis-tetanus (DPT) vaccine (at 2, 4, 6 and 18 months and 4 years of age) and patients and the healthy subjects have been vaccinated against diphtheria consistent with this program.

Although survival of children with beta thalassemia major has improved, both medical therapy and the disease causes immunodeficiency (9). But others have indicated that there is no significant change in humeral immune markers in patients with beta thalassemia major (10, 11). One of the most beneficial and cost effective measures for prevention of infectious diseases, especially diphtheria, is immunization (12). Immunity to diphtheria decreases with advancing age (13). Kruger et al (14) and Xu et al (15) showed that the antibody levels of diphtheria decreased over time.

Median antibody level for diphtheria was higher in patients with acute lymphoblastic leukemia than in the control group (0.202 IU/ml vs 0.071, p<0.001) (16). In a study, only 56.8% of patients with hematologic disorders had completely protective levels of diphtheria antibody, that was lower than healthy children (88.3%) (17). Also, more than 50% patients after anti neoplastic therapy (18) and more than 83% dialysis patients (19) had lacked protective immunity for diphtheria.

Previous studies described that 56.8% of patients with hemato-oncologic illnesses (17), 17% of patients with acute lymphoblastic leukemia (20), 82% of pediatric patients with sarcoma after antineoplastic therapy (21) and 70% in Indian pre-school children (22) had completely protective immunity. Loss of immunity to previous vaccinations, necessity and timing of re-immunization remains controversial.

Antibody level of diphtheria decreased over time and also the subjects with hematologic diseases especially thalassemia major does not respond well to immunization, because of iron overload. Thus the aim of this study was to compare diphtheria antibody levels in patients with beta thalassemia major and healthy subjects.

The general objective of the current study was to investigate the immunity of patients with beta thalassemia major to diphtheria. The specific objectives were to determine the immunity of patients with beta thalassemia major to diphtheria and healthy people according to the age, gender, serum ferritin level, splenectomy and non-splenectomy status and post splenectomy time.

Material and Methods

Patients and controls had been previously vaccinated according to the Iranian national vaccination program. During 2010-2011, two hundred and twenty-four patients with major beta thalassemia referred to thalassemia ward of hospitals in Jahrom and in Bandar Abbas, Iran, enrolled in this study. Patients included 109 subjects with spleen and 115 individuals without spleen. Also, 224 healthy subjects that were similar for sex and age were considered as the control group.

Blood samples for determination of diphtheria antibodies and ferritin were collected from both groups. Five milliliters of venous blood were obtained from participants. Serum samples were stored at -80 degree centigrade until analyses were performed.

Serum antibodies against diphtheria toxin were determined using an ELISA kit (IBL, Germany). Results are expressed as international unit (IU). Serum diphtheria antibody levels greater than 0.1 IU/ml were considered as complete protection, titers 0.01 to 0.1 IU/ml were considered as partial protection and titers less than 0.01 IU/ml were interpreted as non-protection (23). Serum ferritin levels were also measured using CLIA method (Chemi-Luminescent Immunoassay Technology, Liasion, Italy, REF 313, 551).

The information and data about the patients were extracted without name by using codes and were kept confidential. This study was approved by the Research Ethics Committee of Jahrom University of Medical Sciences (ethic code: JUMS.REC.1389.65.1).

Data are presented as median ± standard deviation and percent. We used the independent-samples t-test, One-way ANOVA and chi square test to compare the means and percent in the two groups (beta thalassemia patients and healthy subjects). For the relation of antibody titers with age and serum ferritin, we used backward linear regression test. Also, the backward linear regression analysis was used for relation of antibody with ferritin and age. For the analysis we used SPSS version 15 software. A two sided P-value less 0.05 was considered statistically significant.

Results

Totally 50.9% (114) of healthy people and 50.9% patients were females. Also, the mean age of subjects between two groups was no different (p= 0.633, Table 1). Among the thalassemia group, 56.5% (65) of non-splenectomized subjects and 45.0% splenectomized subjects were female (p=0.083). The splenectomized subjects (6.85 ± 1.69 years) were younger than non-splenectomized subjects (7.37 ± 1.71 p= 0.023).

Serum ferritin level in healthy subjects was much lower than patients (p<0.001, Table 1), but there was no significant difference between the two patient groups, splenectomized (832.11 ± 568.08) and non-splenectomized (981.37 ± 592.99, p= 0.056). Serum anti-diphtheria antibody level in the healthy group was higher than in patients group (p< 0.001, Table 1).

Table 1: The mean and standard deviation of age, serum anti diphtheria and ferritin level in the two study groups

Variables	Healthy subjects, 224		Beta thalassemia major, 224		p value
	Mean	SD	Mean	SD	
Age, year	7.04	1.64	7.12	1.72	0.633
Anti-diphtheria antibody, IU/ml	2.10	1.88	1.51	1.59	< 0.001
Serum ferritin (ng/ml)	64.47	65.41	908.74	584.49	< 0.001

Although, serum antibody level against diphtheria was higher in splenectomized patients (1.60 ± 1.76) than in non-splenectomized ones (1.43 ± 1.43), there were no significant difference (p=0.448).

All participants had protective serum anti diphtheria antibody level (partial or completely protected). One hundred and ninety-seven (87.9%) of healthy individuals were completely protected against diphtheria which was significantly higher than patients (71.0%, p< 0.001) (Table 2).

Table 2: The percent of protective immunity level against diphtheria in the two study groups

Variables		Healthy subjects, 224		Beta thalassemia major, 224		p value
		Number	Percent	Number	Percent	
diphtheria immunity level groups	Partial protection (0.01 to 0.1 IU/ml)	27	12.1	65	29.0	< 0.001
	Complete protection (> 0.1 IU/ml)	197	87.9	159	71.0	

Although, the percent of complete anti-diphtheria protection was higher (75.2%) in splenectomized patients than in non-splenectomized patients (73.9%), there was no significant difference (p= 0.821).

Table 3 shows the relation between diphtheria antibody level with age and serum ferritin by backward linear regression analysis. In this model, age did not affect the relationship.

Table 3: Relation of anti-diphtheria antibody titers to serum ferritin levels in study groups

Groups		R Square	Adjusted R Square	B Coefficients		p value
				Constant	Ferritin	
Healthy subjects		0.018	0.014	2.35	-0.004	0.046
Beta thalassemia major	All patients	0.241	0.237	2.73	-0.001	< 0.001
	Non splenectomized	0.308	0.302	2.75	-0.001	< 0.001
	Splenectomized	0.191	0.183	2.72	-0.001	< 0.001

This analysis showed that only 24.1% anti-diphtheria antibody (IgG) alterations was dependent to serum ferritin level in the patients group (p<0.001), while, in healthy subjects only 1.8% of anti-diphtheria antibody was dependent to serum ferritin (p=0.045). The level of anti-diphtheria antibody decreased with intensification of ferritin level. Thus, when serum ferritin increased 1 ng/ml among patients, serum diphtheria antibody decreased 0.001 IU/ml. This model is better predicted in non- splenectomized patients; with about 31% of the serum anti-diphtheria antibody which is predictable by knowing the serum ferritin level (p<0.001).

Discussion

Although survival of subjects with beta thalassemia major has improved, both treatment modalities and the underlying disease may effect in secondary immunodeficiency. Thus these patients are at risk of attaining a variation of infectious diseases. We therefore assessed the serologic immunity against diphtheria in patients with beta thalassemia major and compared to healthy subjects.

Our study found that the mean of serum diphtheria antibody was lower in patients with beta thalassemia major than age and sex-adjusted healthy subjects. But for ferritin level it was the reverse, in other words, the level of serum ferritin was much higher in healthy subjects than in patients. Also, less percent of patients had complete antibody protection against diphtheria as compared to healthy subjects.

From the 1980s serological research showed that a high percentage of subjects become susceptible to diphtheria with advancing age. This may be due to a decrease in the level of antibody in individuals over time. Chatchatee et al in the Thai population demonstrated that subjects aged between 5 and 9 years had the highest titer of tetanus antibody, and subjects above 60 years of age had the lowest titer (24). In the present study to eliminate the effect of time and sex on the antibody levels; we used sex and age-adjusted healthy subjects as controls for patients.
We found no similar research that compared diphtheria antibody among patients with beta thalassemia major and healthy subjects.

Our study showed that the diphtheria antibody level and the percent of complete protection antibody were lower in patient groups than controls. Jahromi and Rahmanian (25) reported that mean anti-tetanus antibody titers (1.53 ± 1.71 vs 2.02 ± 2.05) and the complete protective level of anti-tetanus antibody (71% vs 87.9%) were lower in patients with beta thalassemia major in comparison to healthy persons. Also Modarresi et al reported that the patients on dialysis had less protective levels of anti-diphtheria than normal populations (19).

In the present study seventy-one percent of beta thalassemia patients were completely protected against diphtheria. Our finding is in contrast with other published results. Kown et al (17) reported that 31.5% of 146 Korean children with hematologic malignancies aged 1-17 years were completely protected against diphtheria. Also, van der Hardt et al (18), Ek et al (20) and Small et al (26) found that less than 50% patients against diphtheria, 17.0% of ALL patients against diphtheria and less than 70% of peripheral blood stem cell transplantation recipients against pertussis had complete immunity, respectively. Similarly, complete protection anti-diphtheria antibody was found in our study to be more than anti tetanus titers that were reported by Aminzade (27), Modarresi et al (19) and Kruger et al (28) in dialysis patients; but less than that Zengin and Sarper (83.3-100%) in patients with acute lymphoblastic leukemia (16).

One of the reasons for this difference in patients with beta thalassemia major may be related to high level of serum iron. Iron overload, a primary complication of both thalassemia itself and transfusion therapy, is thought to be the main causing mechanism of immune incompetence in beta thalassemia major (3). Patients with thalassemia major who had serum ferritin level more than 3000 ng/ml had lower C4 and CH50 levels (10). Recent studies on immune competence in beta-thalassemia have revealed numerous quantitative and functional defects, involving T and B lymphocytes and immunoglobulin production (3). Also, Alavi et al (29) indicated that chemotherapy has independent adverse effects on vaccine-induced antibody protection against diphtheria. In the present study, serum ferritin levels were found to be much higher in patients than in healthy subjects.

In our study, only 25.4% of the thalassemia patients had a partial protective level of IgG against diphtheria and they may susceptible to infection. Adversely, in one study conducted in beta thalassemic patients (aged 5-17 years) who were submitted for bone marrow transplantation, a high percentage (83%) of subjects had anti-diphtheria antibody levels below the protective levels (30). Zengin and Sarper (16) in their study showed that 11.1% of subjects with acute lymphoblastic leukemia had protective level for diphtheria after chemotherapy. Also, Alavi et al (29) reported that chemotherapy in hematologic malignances caused failure to achieve protective levels of antibodies against diphtheria. In another study, Aminzadeh et al found a non-protective level of IgG against tetanus in most of the hemodialysis patients (27). This alteration seems to be due to difference in mean age of study participants.

Conclusion

Our study indicated that increased serum iron levels in beta thalassemia patients decreased the level of antibody against diphtheria. Therefore, lowering the serum levels of iron may prevent further reduction of antibody levels as compared to healthy people over time. It is suggested that further studies are done.

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Genetic Variants of Toll Like Receptor-4 in Patients with Premature Coronary Artery Disease, South of Iran

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Abstract

Introduction: Ischemic cardiovascular diseases are the leading causes of morbidity and mortality in most developed and developing countries including Iran. Premature myocardial infarction has a polygenic base with a complex relation with environmental factors. Since expression of different inflammatory genes especially toll like receptor-4 (TLR4) has increased considerably in human atherosclerotic plaques, we have decided to study variants of TLR4 in premature coronary artery disease in patients in Jahrom city, Iran.

Methods: In this case-control study, 100 patients with a history of premature coronary artery diseases and 100 healthy control subjects referred to health centers in Jahrom city were studied. Target sequences of TLR4 gene were amplified by PCR amplification and digestion was done by StyI restriction enzyme (PCR-RFLP method).

Results: There was no significant difference regarding age (P>0.05). The distribution of TC heterozygote genotype in the premature myocardial infarction group is significantly higher than in the healthy group (P<0.05) but the homozygote mutated genotype showed no significant difference (P>0.05). In addition, the genotype carrying the mutated allele (TC+CC) showed a significant difference when compared to TC variant (P < 0.05). The genotype distribution in rs1927911 in both genders shows no concomitance between males and females (P>0.05).

Conclusion: According to the results derived from this study, it seems like the existence of the genotype carrying the mutated allele (TC+CC) in rs1927911's mononucleotide polymorphism of TLR gene is associated with an increased risk of premature myocardial infarction.

Key words: Premature coronary artery disease – TLR4 gene - rs1927911 polymorphism

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Introduction

Despite improvements in diagnosis and treatment of coronary artery disease (CAD), it is still among the leading causes of death and disability in the world. Cardiovascular diseases are the most common life threatening diseases in industrial societies and a rapidly growing problem in developing countries (1). MI is a complex multifactorial and polygenic disorder (2). There are several environmental risk factors correlating with CAD such as obesity, diabetes mellitus, hypertension, family history and smoking (1). Twenty percent of acute myocardial infarction patients are referred to as premature MI (3), which is defined as the first attack occurring in males aged 50 years and younger and females aged 55 years and younger (4). Premature CAD is known to be the most aggressive form of the disease (5). In recent decades, the idea of the inflammatory nature of atherosclerosis has been strongly propounded and therefore serum levels of inflammatory markers for risk stratification of cardiovascular events have been considered (6, 7). Inflammatory cells, especially macrophages, are present in atherosclerotic plaques (8).

There is a family of receptors that present in phagocytic cells like macrophages which are named as Toll like receptors (TLR) (9).

When TLRs on macrophages are activated, these lead to activation of the nuclear factor kappa B (NFkB) pathway which results in production and expression of pro inflammatory molecules (10).

TLR4 is one of the important members that is expressed by macrophages and endothelial cells in human atherosclerotic lesions (11).

Some clinical studies have demonstrated that the effects of polymorphisms of genetic variants of the human TLR4 gene, located on chromosome 9, on the progression of the atherosclerosis, is controversial (12-14).

Single nucleotide polymorphisms (SNPs) are the most common type of genetic variation in a population (15). There are 10 SNPs in the genotyping system of TLR4: Re10759930, rs2737191, rs2770150, rs1927914, rs1927911, rs5030728, rs11536889, rs1554973, rs11536897, rs11536891 (16). The rs1927911 SNP is located within the intron – coding region of the TLR4 gene on chromosome 9 (17).

Due to the lack of data about the role of TLR4 gene polymorphism in premature CAD in the literature, this study was conducted to determine the association between polymorphism in variants of TLR4 gene and occurrence of premature MI.

Materials and Methods

Design and participants
The study was retrospective, observational, and cross-sectional. One hundred patients with a history of premature coronary artery diseases and 100 healthy control subjects referred to health centers in Jahrom city were invited to participate in the study. All participants signed an informed consent approved by the Institutional Ethical Committee after a detailed orientation of the study requirements, possible risks, and benefits. The information and data about the patients were extracted without name by using codes and were kept confidential. This study was approved by the Research Ethics Committee of Jahrom University of Medical Sciences (ethic code: JUMS.REC.1394.62.9).

Demographic information
Demographic information was collected from case and control groups. This study was conducted based on the declaration of Helsinki and approved by the ethics committee of Jahrom University of Medical Sciences. All individuals had consent to participate in study and based on the testimonial they could leave the study.

Extraction of DNA and PCR
Five ml of venous blood was taken and collected in tubes containing EDTA as an anticoagulant then stored in -20 ˚C in order to extract DNA. Extraction of DNA was done by commercial kit (Cinagen Co., Tehran, Iran).

Genotyping of rs1927911 polymorphism in TLR4 gene
Genotyping of rs1927911 polymorphism was performed using restriction fragment length polymorphism (RFLP).

Amplification of DNA was done by polymerase chain reaction (PCR) in premix pipes (Bioneer Co. Daejeon, Korea). Selection of forward and reverse primers was done according to related articles. Gene sequence accuracy was confirmed by gene bank information website (http/ncbi.nlm.nih.com). Also primers gene sequence was re-checked with Gene runner software and blast program primer sequences were F: TCACTTTGCTCAAGGGTCAA R: AAACCTGCATGCTCTGCAC

To detect the rs1927911 polymorphism, StyI restriction enzyme (Frementase Co) was used. 3% Agarose gel electrophoresis was done for endorsement of the dissected sequence.

Statistical analysis
Correlation between occurrence of acute premature coronary syndrome and rs1927911 polymorphism TLR-4 gene in the case and the control groups was determined with Odds ratio (OR), Chi-square and Fisher exact tests. In the deductive part of the study, the differences in biochemical markers and demographic information were evaluated with T test (p value< 0.5 defined as significant). All analyses were done by SPSS version 15.

Results

Participants' ages were in the range of 30-50 years old. Mean of age in the case group was 41.5±4.9 years and mean of age in the control group was 42.5±6.6 years with no significant difference (P=0.197). Gender (P=0.876) and smoking (P=0.323) in case and control groups had no significant differences.

Results of study showed that 70% (70 people) of the case group had a family history of CAD and 91% of the control group had no family history of CAD. There was a noticeable difference between case and control group (P=0.000) that clarifies the obvious role of family history in occurrence of CAD. In the case group 25% of participants had hypertension (HTN), 23% had hyperlipidaemia (HLP) and 25% had diabetes mellitus (DM). There were significant differences between groups in cardiovascular risk factors: HTN (0.001), HLP (0.07), DM (0.010) (Table 1).

Table 1. Demographic data of both study groups

	NGT subjects	Premature Coronary Artery Disease	P
n (males/females)	30/70(%30/70)	32/68 (%32/68)	0.76
Age (y)	6.6±42.5	4.9±41.5	0.197
Smoking (n)	27	25	0.321
DM (n)	11	25	0.010
FHX (n)	0	2	0.000
HLP (n)	9	23	0.070
HTN (n)	8	25	0.001

FHX: family history of CAD, DM: diabetes mellitus, HLP: hyperlipidaemia, HTN: hypertension

According to the results of study there was no significant difference between CC genotype mutant of TLR-4 gene and occurrence of premature CAD (p value: 0.435) but in mix genotype CC+TC vs TT there was a significant difference between premature CAD and healthy subjects (p value: 0.021), and C-allele frequency distributions were not significantly different (P;0.093) (Table 2).
Difference between alleles of TLR-4 gene (C and T) and occurrence of
premature CAD in case and control groups is shown in Table 2 (p value: 0.013).

Table 2: Frequencies of genotypes and alleles in participants

	Controls N =100	Premature Coronary Artery Disease N =100	Value of P*	OR
TT	67(67.0%)	50(50%)		Reference
TC	5(5.0%)	23(23.0%)	0.001	0.162(0.058-0.456)
CC	28(28%)	27(27%)	0.435	0.774(0.407-1.472)
TC+CC	33(33.0%)	50(50.0%)	0.021	2.030(1.146 -3.598)
TT	67(67.0%)	50(50%)		
Allele frequency				
allele T	123(62.5%)	139(%69.5)	0.093	0.701(0.463-1.061)
allele C	74(%37.6)	61(%30.5)		

Discussion

MI is the leading cause of mortality in developed countries and the second leading cause in developing countries (1). Expression of different inflammatory genes, specifically TLR4, has increased significantly in human atherosclerotic plaques (18). 1927911 SNP located on chromosome 9 is one the polymorphisms that has always been investigated in CVDs (19).

According to the results found in this study, distribution of heterozygous genotype (TC) was meaningfully higher than that in the healthy group control but the mutated homozygous genotype did not show a meaningful difference. Besides that, when compared to TC state, the genotype carrying the mutated allele (TC+CC) did not show a meaningful difference.

Even though the distribution of the mutated C allele was higher in the healthy control group compared to the premature MI group, this difference was not meaningful.

The Logistic regression analysis of distribution of genotype in rs1927911 in both genders shows that there is no meaningful concomitance in men and women, even though the mutated C allele was meaningfully more in females than in males.

Results of a study conducted by Yanmin Song et al. in the southern Chinese province of Hunan in 2014 showed that for rs1927911 there is a meaningful difference between acute cardiac ischemia (ACI) patients and the control groups from a genotype and allele distribution but hypertension, fasting blood sugar and serum fat level with different genotypes in both ACI patients and control groups had no meaningful difference (20).

In a study done by Daniel A. Enquobahrie et al. sweeping changes of gene in PPARA (peroxisome proliferator activated receptor alpha) and TLR4 gene was accompanied by MI. A minor allele of PPARA SNP, rs4253623, was accompanied with an increased risk of MI and a minor allele of TLR4 SNP, rs1927911, with an increased risk of MI. rs1927911 minor allele, a part of TLR4-D haplotype, is accompanied with a 12% risk of MI (21).

Conclusion

According to the findings of this study, it seems like the presence of the carrying genotype of mutated allele (TC+CC) in rs1927911 single nucleotide polymorphism (SNP) of TLR4 gene is associated with an increase of premature MI.

Considering the breadth of polymorphisms of TLR4 gene and role of genetics in premature MI, in order to establish this polymorphism as a risk factor, further studies in larger populations in this area is proposed.

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Comparison of postoperative bleeding in patients undergoing coronary artery bypass surgery in two groups taking aspirin and aspirin plus CLS clopidogrel

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Abstract

Introduction: Coronary Artery Bypass Grafting (CABG) is a surgical procedure that aims to ease symptoms and reduce the risk of death in patients with coronary artery occlusion. In this surgery, healthy blood vessels from other parts of the body replace occluded coronary arteries. This surgery is done to improve blood supply to the heart. Because of its invasive nature, this procedure is associated with complications including postoperative bleeding.

Methods: The study included 68 subjects in each group. The inclusion criteria were age of 40-80 years, serum creatinine under 1.5 mg/dl, platelet count above 100 thousand per microliter, hemoglobin above 8 g per deciliter, and normal PT and PTT. The patients underwent the procedure through the on-pump method. The study population included the patients undergoing CABG in Khorramabad Heart Hospital. The convenience, consecutive sampling method was applied, based on the inclusion criteria of the study.

Results: The mean age of the patients treated with aspirin was 60.9 ± 11.05, and the mean age of the patients treated with aspirin plus clopidogrel was 60.48 ± 9.8 years. The mean FFP intake in the aspirin plus clopidogrel group during hospitalization was significantly higher than the mean in the aspirin group (PV= 0.0009). The mean cell pack intake in the aspirin plus clopidogrel group during hospitalization was higher than the mean in the aspirin group, but this difference was not statistically significant (PV=0.068)

Discussion: The rate of postoperative bleeding in the clopidogrel plus aspirin group was higher than the rate in the aspirin group, but this difference was not significant (PV=0.067). The rate of Hb, HCT, and platelets in the aspirin plus clopidogrel group at discharge was higher than the rate in the aspirin group, which was due to excess bleeding in the aspirin plus clopidogrel group compared to the aspirin group. The rate of FFP intake in the aspirin plus clopidogrel group was significantly higher than the rate in the aspirin group, which was due to excess bleeding in the aspirin plus clopidogrel group (PV=0.0009).

Key words: coronary artery bypass grafting, aspirin, clopidogrel

Introduction

Coronary artery bypass grafting (CABG) is a surgical procedure that aims to ease symptoms and reduce the risk of death in patients with coronary artery occlusion. In these patients, healthy vessels of other parts of the body are grafted to replace the occluded coronary arteries and this improves blood flow to the heart. Due to the aggressive and invasive nature of this surgery, it is associated with complications. From among the complications of this surgery, bleeding after CABG can be cited. The prevalence of this complication is so high that 17% of patients need blood transfusions after surgery and approximately 3 to 5 percent of patients require re-exploration (1). The amount of bleeding after surgery varies based on factors such as platelet count and pre-operative fibrinogen concentrations (1). Also, it should be noted that patients undergoing CABG often use antiplatelet and anticoagulant drugs due to heart disease and this issue affects the occurrence and severity of postoperative bleeding. It is expected that various antiplatelet drugs have different effects on post-operative bleeding. One of the drugs that nowadays is used as an antiplatelet drug is clopidogrel. This medication irreversibly inhibits platelet activation and aggregation (2). Various studies conducted on the effects of this drug on CABG post-operative bleeding have reported mixed results. Several studies have reported that the use of this drug has no effect on the amount of post-operative bleeding (3). In contrast, some studies have reported that the use of this drug increases the rate of postoperative bleeding (4-6). In addition, it has been reported that the preoperative use of clopidogrel with a loading dose of 600 mg increases the risk of bleeding in comparison with a loading dose of 300 mg (7). On the other hand, the use of clopidogrel in patients undergoing CABG shows benefits, which include a decline in the rates of cardiovascular events (5) and a reduction in the likelihood of replaced vessel occlusion (3).

In this study, considering the benefits that have been proposed for the use of clopidogrel plus aspirin in patients undergoing CABG, and also given the mixed results obtained from different studies, we decided to compare postoperative bleeding in patients undergoing coronary artery bypass surgery in two groups taking aspirin and aspirin plus clopidogrel.

Materials and Methods

In this study, the number of subjects in each group was 68 patients. The inclusion criteria included an age of between 40 and 80 years, serum creatinine levels less than 1.5 mg/dl, a platelet count of over 100 thousand per microliter, hemoglobin levels of more than 8 g per dl, and normal PT and PTT, and the use of the on-pump CABG for the patients. The studied population included patients who had undergone CABG in the Specialist Cardiac Hospital of Khorramabad, Iran. The convenience and consecutive sampling methods were used based on the inclusion criteria of the study.

In this study, candidate patients for angiography underwent coronary angiography by two groups of cardiologists. One group were specialists who were able to perform angioplasty and the other group was not able to perform this operation. Cardiologists who were not able to perform angioplasty prescribed aspirin (325 mg daily) for patients scheduled to undergo angiography. In contrast, given the fact that patients who are scheduled to undergo coronary angiography may need angioplasty too, cardiologists who were able to perform angioplasty prescribed clopidogrel (with a dose of 600mg per day) in addition to aspirin (with a dose of 325mg) for the patients to be ready to undergo angioplasty, if necessary. The advantage of this strategy is that it spares the patient from another procedure to perform angioplasty.

In both groups, if the findings of angiography showed that some patients needed to undergo CABG, cardiac surgeons subsequently operated on them. Therefore, some of the patients who underwent CABG had taken aspirin before surgery and others had used clopidogrel (600 mg daily) in addition to aspirin. In this study, patients were divided into two group based on the use or non-use of clopidogrel. Inclusion criteria were an age of between 40 and 80 years, serum creatinine levels of less than 1.5 mg/dl, a platelet count of more than 100,000 per microliter, hemoglobin more than 8 g/dl, and normal PT and PTT .

Exclusion criteria included a history of hereditary bleeding disorders, use of anticoagulant drugs in the previous month, having undergone CABG surgery in the past, the use of clopidogrel before the start of the current study, a history of taking clopidogrel in the aspirin group, a history of allergy to clopidogrel and aspirin, a history of cerebrovascular disease, a history of severe hepatic disease, cancer, severe bleeding or cardiac tamponade after surgery which needed surgical intervention, the need for anticoagulant drugs after surgery, and gastrointestinal bleeding after surgery.

Demographic variables, laboratory indicators, signs and symptoms of the patients, the amount of postoperative bleeding, and the amount of blood transfused (during the first 24 hours), duration of ICU and hospital stays, and duration of drain use in patients were recorded in the data collection form of the study. This form was completed by executive colleagues of the project. To describe the data, descriptive statistical methods (mean, standard deviation, and frequency percentages) and, to compare the examined variables, analytical statistical methods, including the independent t-test, chi-square, and analysis of variance were used.

Results

The mean age of the patients treated with aspirin was 60.9±11.05, and the mean age of the patients treated with aspirin and clopidogrel was 60.48±9.8. According to t-test, the difference in age between the two groups was not statistically significant (p=0.78). In the aspirin group, 42.9% of the patients and, in the aspirin plus clopidogrel group, 45.7% of the patients were younger than 60 years old. The rest of the patients of the two groups were older than 60 years old. The difference in age distribution between the two groups was not statistically significant according to a chi-square test (P=0.73).

The mean BMI in the group treated with aspirin was 27.3±4.2 and in the group treated with clopidogrel + aspirin, was 28.3±10. According to t-test, the difference in mean BMI was not statistically significant between the two groups (p=0.46). In the aspirin group, the mean EF of the patients was 46.5±10.9 percent and, in the aspirin plus clopidogrel group, was 46.2±9.2 percent, which difference was not found to be statistically significant (p=0.86). None of the patients in both groups were HIV positive or HCV positive.

Based on chi-square test, the difference in the need for blood transfusion in the studied groups during the first 24 hours after surgery was not statistically significant (p=0.8). (Table 1)

Table 1: The difference in the need for blood transfusion in the studied groups during the first 24 hours after surgery

| | | Need for blood transfusion during the first 24 hours after surgery | | |
| | | Has | Has not | Total |
		N (%)	N (%)	N (%)
Groups	Aspirin	61 (87.1)	9 (12.9)	70 (100)
	Aspirin plus clopidogrel	60 (85.7)	10 (14.3)	70 (100)

* "N" represents the number of patients in each group
** Statistical test: Chi-Square test

Additionally, according to the above table, the difference in the need for blood transfusions during hospital stay was not statistically significant between the group receiving aspirin (91.4%) and the group receiving aspirin + clopidogrel (87.1%)(p=0.41) (Table 2).

Table 2: The difference in the need for blood transfusion in the studied groups during hospital stay

| | | Need for blood transfusion during hospital stay | | |
| | | Has | Has not | Total |
		N (%)	N (%)	N (%)
Groups	Aspirin	64 (91.4)	6 (8.6)	70 (100)
	Aspirin plus clopidogrel	61 (87.1)	9 (12.9)	70 (100)

* "N" represents the number of patients in each group
** Statistical test: Chi-Square test

According to the results of a repeated measures, test differences in bleeding in each group over time was statistically significant (time effect). But the difference between the two groups was not statistically significant in any of the times (24 hours after surgery and until the removal of the drain) (group effect and the time-group interaction were not statistically significant either) (p=0.9). According to an independent t-test, the difference in the mean bleeding during the first 24 hours after surgery was not statistically significant in both groups receiving aspirin and clopidogrel + aspirin (p=0.067). Although the amount of bleeding in the group receiving aspirin + clopidogrel was more than the aspirin group, this difference was not statistically significant. Despite the fact that the group receiving aspirin + clopidogrel had more bleeding until the removal of the drain in comparison with the group receiving aspirin, this difference was not statistically significant as determined by a t-test (p=0.27).

The mean duration of ICU stay for the group receiving aspirin was 53.12 hours and in the group receiving aspirin + clopidogrel, it was 50.35 hours. This difference was not statistically significant (p=0.51).

The mean duration of drain use in the aspirin group was 106.2 hours and it was 107.4 hours in the group receiving aspirin + clopidogrel, but this difference was not statistically significant as determined by a t-test (p>0.05).

In the group receiving aspirin, 3 patients (4.3%) and, in the group receiving aspirin + clopidogrel, 6 patients (8.6%) needed reoperation, but this difference was not statistically significant, according to Fisher's exact test (p=0.24). (Table 3)

Table 3: The difference in the need for need for reoperation in the studied groups

		Need for reoperation			P-Value
		Has	Has not	Total	
		N (%)	N (%)	N (%)	0.24
Groups	Aspirin	3 (4.3)	67 (95.7)	70 (100)	
	Aspirin plus clopidogrel	6 (8.6)	64 (91.4)	70 (100)	

* "N" represents the number of patients in each group
** Statistical test: Fisher's exact test

In both groups, the average number of days of hospital stay was 6.5 days and the t-test showed no statistically significant difference in the number of days of hospitalization in the two groups. Based on the obtained results, the difference in the mean values of blood parameters before the surgery was not statistically significant (p > 0.05). Additionally, based on the results of an independent t-test, the differences in values of lipid profile, renal function and CRP indexes were not statistically significant in the two groups before the surgery (p > 0.05). (Table 4)

Table 4: The Comparison of mean and standard deviation of laboratory indices before the surgery in studied groups

Indicator type		Hb (g/dl)	RBC (µl)	Hct (%)	WBC (×10³µl)	Plt (×10³µl)	PT (Sec)
		µ ± SD	µ ± SD	µ ± SD	µ ± SD	µ ± SD	µ ± SD
Groups	Aspirin	13.6±2.2	4.6±0.87	41.14±6.3	8.6±3.3	223757±65.6	12.99±1.08
	Aspirin plus clopidogrel	14±2.07	4.7±0.72	42.07±5.5	7.8±2.9	233314±64.9	12.90±1.85
T statistics		-1.19	-0.62	-0.92	1.55	-0.86	0.34
P Value		0.23	0.53	0.35	0.12	0.38	0.74

PTT (Sec)	TG	Cholesterol	BUN	Cr	CRP
µ ± SD	µ ± SD	µ ± SD	µ ± SD	µ ± SD	µ ± SD
27.79±6.2	178.9±81.7	182.2±49.2	45.2±16.4	1.17±0.25	1.74±0.44
29.40±7.91	166.6±93.4	180.5±44	42.5±14.2	1.19±0.27	1.81.5±0.39
-1.33	0.82	0.22	1.03	-0.38	-1.01
0.18	0.4	0.82	0.3	0.7	0.31

Table 5- The Comparison of mean and standard deviation of laboratory indices in studied groups at discharge

Indicator type		Hb (g/dl)	Hct (%)	Plt (×10³µl)	BUN	Cr
		μ ± SD	μ ± SD	μ ± SD	μ ± SD	μ ± SD
Groups	Aspirin	11.1±9.7	32.9±5.2	235800±81.25	41.5±11	1±0.22
	Aspirin plus clopidogrel	9.72±1.3	29.9±4	209914±67.7	38±9	1.04±0.24
T statistics		4.15	3.90	2.04	2.03	-1.04
P Value		<0.0001	<0.0001	0.043	0.044	0.290

According to a t- test, the mean values of Hb, HCT, PLT and BUN was significantly higher at discharge in the group receiving aspirin than in the group receiving aspirin + clopidogrel. (Table 5).

Based on a t-test, there was no significant difference between the mean injected platelet units for the studied groups during hospital stay (p=0.47). The mean FFP received during hospital stay was significantly higher in the group receiving aspirin + clopidogrel than in the group receiving aspirin (p=0.0009). Additionally, the mean amounts of the packed cells received during hospitalization was higher in the group receiving aspirin + clopidogrel than in the aspirin group. But this difference was not statistically significant (p=0.068). 75.7% of the patients receiving aspirin and 80% of the patients receiving aspirin + clopidogrel needed to receive FFP during hospitalization. According to a chi-square test, this difference was not statistically significant (p=0.54). None of the patients in either group needed receiving whole blood during hospitalization. The mean postoperative bleeding at various times after surgery and Hb and HCT amounts did not show any significant difference in the aspirin-receiving group in various age groups (p > 0.05). The need for blood transfusions in younger than 60 patients in the aspirin group was 83.4% and in the older than 60 patients was 97.5% and according to Fisher's exact test, this difference was statistically significant (p=0.036). Moreover, the difference in the amount of postoperative bleeding, hemoglobin and hematocrit in patients receiving aspirin + clopidogrel was not statistically significant in terms of age groups (under 60 and 60 years and older). 81.3% of the patients younger than 60 years and 92.1% of the patients 60 years and older who received aspirin + clopidogrel needed post-operative blood transfusions. Fisher's exact test did not show a significant difference between these groups (p=0.17).

Differences in the frequency distribution of the number of grafts in both groups was statistically significant (p=0.022), but the mean number of grafts was not statistically significant (p=0.07).

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Discussion

Studies published in 1990 and 1991 indicated that the administration of aspirin preoperatively leads to further surgeries due to increased postoperative bleeding (6.6 vs. 1.7% and 6.3 vs. 2.4% in two studies) (8, 9). In subsequent studies, however, no increase in bleeding was observed. The administration of aspirin could even decrease mortalities in hospitals (10-12). In the past, concerns about bleeding lead physicians to advise patients undergoing CABG to discontinue taking aspirin three to five days before surgery. However, this general view is not recommended any more. ACCF/AHA2011 instructions recommend continuing to take aspirin or starting it before CABG surgery (13). Anemia is an independent risk factor predisposing complications and mortality after CABG. As a result, the transfer of red blood cells (RBC) is common. Blood transfusion rates have been reported to be between 40% and 90% (14). In the present study, this amount was 91.4% vs. 87.1% which was lower in the aspirin + clopidogrel group, but the difference was not statistically significant. As reported in 2010, among more than 82,000 patients from hospitals in the United States who had undergone CABG surgery with cardiopulmonary bypass in 2008, the rate of blood transfusions during surgery was 56.1% (15). In addition, the bleeding which requires re-surgery was associated with a strong need for blood transfusions, and longer ICU and hospital stays. The re-surgery rates ranged from 4% to 6% (16). However, a study has shown that during 1995-1997, there has been a reduction in the rates of re-operation down to 2% (17). In the present study too, the need for repeated OR in the aspirin receiving group was less than half of the group receiving aspirin + clopidogrel. However, this difference was not statistically significant (3.4%vs. 6.8%).

Previous randomized trials have examined dual antiplatelet therapy with aspirin + clopidogrel in cardiovascular patients. There has been observed no clinical benefits in two studies that investigated combined antiplatelet treatment as compared with aspirin alone for patients with risk factors for atherosclerosis, cerebral, cardiac or peripheral vascular disease (18, 19). On the contrary, the combination of clopidogrel and aspirin as compared with aspirin alone has demonstrated significant improvements in the outcome of patients undergoing percutaneous vascular intervention (20), and in patients with acute coronary syndrome (21-23). In our study too, no benefits were observed in the group receiving aspirin + clopidogrel. Moreover, the aspirin group showed significantly lower

postoperative bleeding (834.67±595.81 vs. 662±506.39). Also, in the group receiving aspirin the mean values of Hb, HCT, BUN, and blood platelets at discharge were significantly higher than the group receiving aspirin + clopidogrel. Additionally, the mean amount of received FFP and the need for injections were lower in the aspirin group patients than the group receiving aspirin + clopidogrel (97.5 vs. 83.13%, p=0.0009). If the above criteria be considered as indicating a good prognosis, the group receiving aspirin had a better prognosis. Often surgeons prescribe clopidogrel commonly after CABG, believing that it prevents graft occlusion, and possibly improves clinical outcomes (24, 25). Although prospective randomized controlled trial data in this area is inadequate (24), previous studies cited in cardiac surgery literature have suggested that clopidogrel may improve postoperative outcomes (25-27). In a study of off-pump CABG patients, Ebrahimi et al demonstrated that adding clopidogrel to aspirin was accompanied with a tendency toward improvements in SVG remaining open up to 6 months after surgery (26). Recently, Gao et al have reported the results of a non-randomized trial in which 197 patients received 75 mg clopidogrel plus 100 mg aspirin the day after surgery based on a weekly replacement therapy. Within 7 days, the risk of life-threatening events or major bleeding after CABG surgery did not show a significant increase in patients receiving clopidogrel 5 days prior to CABG (9.6% vs 6.3% with placebo), but the same was not true for patients who had discontinued clopidogrel five days or more before CABG (4.4% vs. 5.3%) (29). These findings are supported by several other observational studies (30-37). In our study too, adding aspirin to clopidogrel did not lead to significant differences in life-threatening events, which confirms the cited studies. However, in a study by Wang et al, there was observed a good response to adding clopidogrel to aspirin after CABG (38).

Conclusion

Given the obtained results in the present study, the following conclusions can be drawn:

1. The amount of postoperative bleeding in the clopidogrel + aspirin was more than the aspirin group. However, its P Value is not significant, but it approaches the significance level (p=0.067).

2. The platelet, Hb, and HCT is lower at discharge in the clopidogrel + aspirin group than in the aspirin group, the cause of which is higher blood loss in the aspirin + clopidogrel group in comparison with the aspirin group.

3. FFP use in the aspirin + clopidogrel group was more than in the aspirin group which is due to increased blood loss in the first group (p=0.000).

4. To get more accurate results, further research is recommended with larger sample numbers.

5. Considering the importance of the drugs aspirin and clopidogrel in the prevention of heart attacks and their importance in the health system, it is recommended that the benefits of these drugs be not overlooked in comparison with their possible disadvantages.

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Comparison of lower uterine segment thickness among nulliparous pregnant women without uterine scar and pregnant women with previous cesarean section: ultrasound study

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Abstract

Objective: To compare the   Lower Uterine Segment (LUS) thickness among nulliparous pregnant women without uterine scar and pregnant women with previous cesarean section (CS) using trans-abdominal ultrasound in the third trimester.

Methods: Three groups were included as 20 nulliparous women (group 1), 31 pregnant women with a single previous CS, and 27 pregnant women with two or more previous CS at gestational weeks 36 to 40. LUS thickness was measured by transabdominal ultrasound. The measured thickness was compared between the three studied groups and the cut-off value was determined by Receiver Operating Characteristic (ROC) curve. Uterine dehiscence during delivery was also compared between the three groups.

Results: Mean (±SD) LUS thickness in groups 1, 2, and 3 was respectively 6.05 (±2.5), 5.33 (±1.33), and 4.49 (±1.54) mm (P= 0.01). Three patients (9.7%) in group 2 has dehiscence during CS. Mean (±SD) LUS thickness in these three patients was 4.40 (±0.36) mm. In group 3, two patients (7.4%) experienced dehiscence during CS with a mean (±SD) LUS thickness of 1.2 (±0.6) mm. Cut-off value to predict uterine dehiscence and rupture was 1.7 mm with a sensitivity of 78% and specificity of 76%

Conclusions: LUS thickness was significantly lower in pregnant mothers with previous CS and this led to dehiscence in such patients. In case of LUS thickness of < 1.7 mm, the risk of dehiscence and rupture increases.

Key words: Ultrasonography; Cesarean section; lower uterine segment; scar

Introduction

Cesarean section (CS) has faced a growing trend worldwide. During a 25-year period (1990 to 2014), the average CS rate has grown from 6.7% to 19.1% translated to an average rise of 12.4% (1).

One of its consequences may be cesarean scar defect (CSD) (2). This may cause dysmenorrhea and post menstrual bleeding in non-pregnant uterus and uterine rupture or dehiscence during labor or cesarean operation (3). Dehiscence represents separation of low uterine segment with intact serosa in contrast to uterine rupture(4). Many investigations are conducted for early diagnosis of uterine rupture during trial of labor (TOL) by LUS thickness measurement(4-5) either by Trans abdominal or Trans vaginal Ultrasonography(5,6).

Lower uterine segment (LUS) thickness is one of the factors suggested to have prognostic value for uterine rupture during delivery in women with previous CS surgery (7). Uterine rupture, though rare, is a grave complication with significant morbidity and mortality (7). Hence, ultrasound examination of the LUS thickness in the third trimester has gained attention to predict possible uterine rupture and to implement appropriate obstetrical decisions.

Thinning of the LUS has been significantly associated with uterine scar defect at week 37 in a way that a threshold of 2.5 mm for LUS thickness was proposed as a risk factor (8). LUS is thinner in the third trimester compared to the second trimester. Ultrasound examination of LUS is a simple and non-invasive method which can provide useful information about the thickness of the LUS as well as prognostic value for uterine rupture. Integrating LUS measurement by ultrasound has been shown to result in lower risk of uterine rupture (9).

Although most studies have proposed cut-off values of about 2.5 to 3.5 mm for LUS thickness, there is controversy in the literature about the exact thickness that can be used for prognostic objectives (10).

Most previous studies have included patients with previous CS and investigated the risk of thin LUS with VBAC and uterine rupture (11, 9, 12). It should be noted that some limited studies included patients with and without history of CS (13-15). However, we think that more studies are required to precisely answer the question as to if there is a real difference regarding LUS thickness between pregnant women with and without history of CS. Therefore, we conducted the current study to compare the LUS thickness among nulliparous pregnant women without uterine scar and pregnant women with previous cesarean section using trans-abdominal ultrasound in the third trimester.

Materials and Methods

From December 2014 to Dec 2016 this cross sectional descriptive-analytic study took place in Imam Reza hospital, Kermanshah Iran. The study sample consisted of 78 pregnant women divided into three groups: 20 nulliparous women without previous CS (group 1), 27 pregnant women with a single previous CS (group 2) and 31pregnant women with two or more previous CSs (group 3). They were recruited consecutively in their 36th to 40th week of gestation when they presented for delivery or ultrasound examination to our university obstetric department.
The sample size was calculated using previous data about mean (SD) LUS thickness of 4.7 (1.2) mm and 6.6 (2) mm in patients with and without previous CS (9). Considering α=0.05, power= 90%, the estimated sample size was calculated as at least 20 subjects in each group (a total of 60 cases).

Inclusion criteria were singleton pregnancy, gestational age of 36 to 40 weeks, according to LMP cephalic presentation, and normal volume of amniotic fluid.

Exclusion criteria were multiple pregnancy, active labor, abnormal amniotic fluid volume, previous uterine rupture, placenta previa, fetal congenital malformations, and uterine surgical interventions other than CS.

Gestational age was estimated using the LMP and the first-trimester ultrasound report. LUS thickness was measured by trans-abdominal ultrasound (VINNO, G80) with a 3.5 MHz convex probe. The examinations were done with the bladder half-full (bladder extension at sagittal plane was 6 to 7 cm) and in the absence of uterine contractions. The LUS thickness was measured as the distance between myometrium-urinary bladder wall interface and myometrium-chorioamniotic membrane interface. The thickness was measured successively for three times by a board-certified radiologist and the mean value was documented as the final mean LUS thickness. The measurements were made in a perpendicular plane to the uterine body.

The gathered data (maternal age, gestational age, parity, and LUS thickness) were entered into a checklist. In addition, the patients were followed and the following variables were recorded at the time of delivery: Apgar scores at minutes 1 and 5, birth weight, and dehiscence at delivery.

Statistical analyses
The data were gathered and entered into the SPSS software for Windows (ver. 21.0). Descriptive indices such as frequency, percentage, mean and its standard deviation (±SD) were used to express data. The Kolmogorov-Smirnov test was used to determine normal distribution of continuous variables. One-way ANOVA (analysis of variance) was used to compare continuous data with normal distribution (maternal age, BMI, birth weight, and LUS thickness) and the Kruskal-Wallis for non-normally distributed variables (gestational age). In order to compare LUS thickness of

patients in groups 2 and 3 who experienced dehiscence during CS, the Student's t test was applied. Significance level was set at 0.05.

Ethics
The study protocol was approved by the Ethics Committee of our medical university. The study objectives were explained for the patients prior to participation and if agreed, written informed consent was obtained from them.

Results

A total of 78 subjects were included. There were 20 nulliparous women (25.6%) with a mean (SD) age of 26.16 (1.33) years, 31 with one previous CS (39.7%) with a mean (SD) age of 31.46 (0.96) years, and 27 subjects (34.6%) who had undergone CS at least twice and had a mean (SD) age of 32.5 (0.99) years. A significant difference existed among the groups regarding age (P< 0.001). Mean gestational age in groups 1, 2, and 3 was respectively 38, 37.26, and 37 weeks (P= 0.12).

There was no significant difference regarding mean (±SD) birth weight among the three groups (3,400 (±327.26) gr in group 1, 3,253.35 (±379.81) in group 2, and 3,247.35 (±388.25) in group 3); P= 0.3. Mean BMI values in groups 1, 2, and 3 were respectively 29.93, 29.89, and 29.25 kg/m2 (P= 0.79).

Mean (±SD) LUS thickness in groups 1, 2, and 3 was respectively 6.05 (±2.5), 5.33 (±1.33), and 4.49 (±1.54) mm (P= 0.01). Range of LUS thickness in groups 1, 2, and 3 was 1 to 11 mm, 3 to 8.5 mm, and 0.8 to 7.3 mm.

Three patients (9.7%) in group 2 has dehiscence during CS. Mean (±SD) LUS thickness in these three patients was 4.40 (±0.36) mm. In group 3, two patients (7.4%) experienced dehiscence during CS with a mean (±SD) LUS thickness of 1.2 (±0.6) mm. There was a significant difference regarding mean LUS thickness between groups 2 and 3 who experienced dehiscence (P= 0.03).

Paper-thin LUS was documented in 4 patients (12.9%) of group 2 with mean (±SD) LUS thickness of 4 (±0.81) mm. This finding was seen in more patients of group 3 (11 cases, 40.7%) with a mean (±SD) LUS thickness of 3.44 (±0.75) mm. Uterine rupture occurred in only one patient who was in group 3 whose LUS thickness was 2.5 mm. This was not observed by ultrasound and rupture was diagnosed during CS.

Ultrasound showed dehiscence in only one patient in the second group whose LUS thickness was 3 mm. However, three more patients in group 2 were diagnosed with rupture during CS with LUS thickness values of 4, 4.5, and 4.7 mm. In group 3, two patients were diagnosed to have rupture by ultrasound. LUS thicknesses of these two patients were 0.8 and 2.5 mm. These were confirmed during CS.
Cut-off value to predict uterine dehiscence and rupture was 1.7 mm with a sensitivity of 78% and specificity of 76% (Figure 1).

Discussion

Based on the obtained findings, those who had previous CS had significantly thinner LUS. This resulted in dehiscence and rupture in these patients. On the other hand, none of the nulliparous women with thicker LUS experienced dehiscence or rupture. The neonates' birth weight did not show difference among groups, so it is highly likely that dehiscence and rupture occurred due to thinner LUS. The obtained results are in agreement with some previous reports. In a study involving 106 patients with previous CS and 68 without, LUS was thinner in the first group with a mean value of 4.58 mm than in the second group (4.8 mm) (16).

Ultrasound can detect dehiscence by showing a defective area where no myometrial layer is seen (17). In this study, in patients with more than one previous CS, US findings were in agreement with findings during CS. The cut-off value we obtained here (1.7 mm) is very close to the reported value by a previous study (1.8 mm) (18). However, some studies have proposed higher values at 2.5 to 3.5 mm among patients with previous CS (11).

Although we observed dehiscence and rupture in patients with LUS thickness of more than 3 mm, one patient who experienced rupture had a LUS thickness of 2.5 mm. A previous study showed that none of the patients with LUS thickness of <3 mm experienced dehiscence or rupture (9). In a former meta-analysis of about 2,700 patients, sensitivity and specificity for cut-off values for LUS thickness to predict uterine defects was 76% and 92% for values between 0.6 and 2 mm (19).

Ultrasound is a non-invasive method to measure LUS thickness and its ability to predict dehiscence and rupture has been investigated previously (9, 10). One of the limitations in this study was that we were not able to gather all details about previous CS. Although CS per se is considered a risk factor for scar formation and thinner LUS, other factors can also have a role in LUS thickness. In a previous study, maternal age of more than 35 years, single layer uterine closure, and non-elective CS were factors to be associated with LUS thickness (12). All these factors can affect healing of the LUS after CS and influence the integrity of LUS.

Limitations
We intended to determine the effect of multiple previous CS on LUS thickness, and it was found that LUS was thinner in those with multiple CSs, however as the rate of dehiscence and rupture was a secondary objective; the sample size was not large enough to achieve a conclusion in this regard. Future studies with larger sample size can answer the question of the effect of multiple CSs. Another limitation is that we were not able to perform transvaginal ultrasound as some studies have demonstrated that transvaginal ultrasound provides better information about myometrial thickness than transabdominal ultrasound (20). However, this may not be regarded as a significant limitation as there is evidence of more than 90% correlation between transabdominal and transvaginal ultrasonography and a cut-off value of 2.5 mm (21).

Table 1: Apgar scores at minutes 1 and 5 in the three studied groups

	Apgar score minute 1				Apgar score minute 5			
	7	8	9	10	7	8	9	10
Group 1	1 (5%)	3 (15%)	16 (80%)	0	0	1 (5%)	3 (15%)	16 (80%)
Group 2	1 (3.2%)	3 (9.7%)	27 (87.1%)	0	0	0	4 (12.9%)	27 (87.1%)
Group 3	2 (7.4%)	3 (11.1%)	21 (77.8%)	0	0	1 (3.7%)	4 (14.8%)	21 (77.8%)

Group 1= nulliparous women without previous CS
Group 2= pregnant women with a single previous CS
Group 3= pregnant women with two or more previous CSs

Figure 1: Receiver operating curve for lower uterine segment thickness of 1.7 mm with sensitivity of 78% and specificity of 76% for predicting uterine dehiscence and rupture

ROC Curve
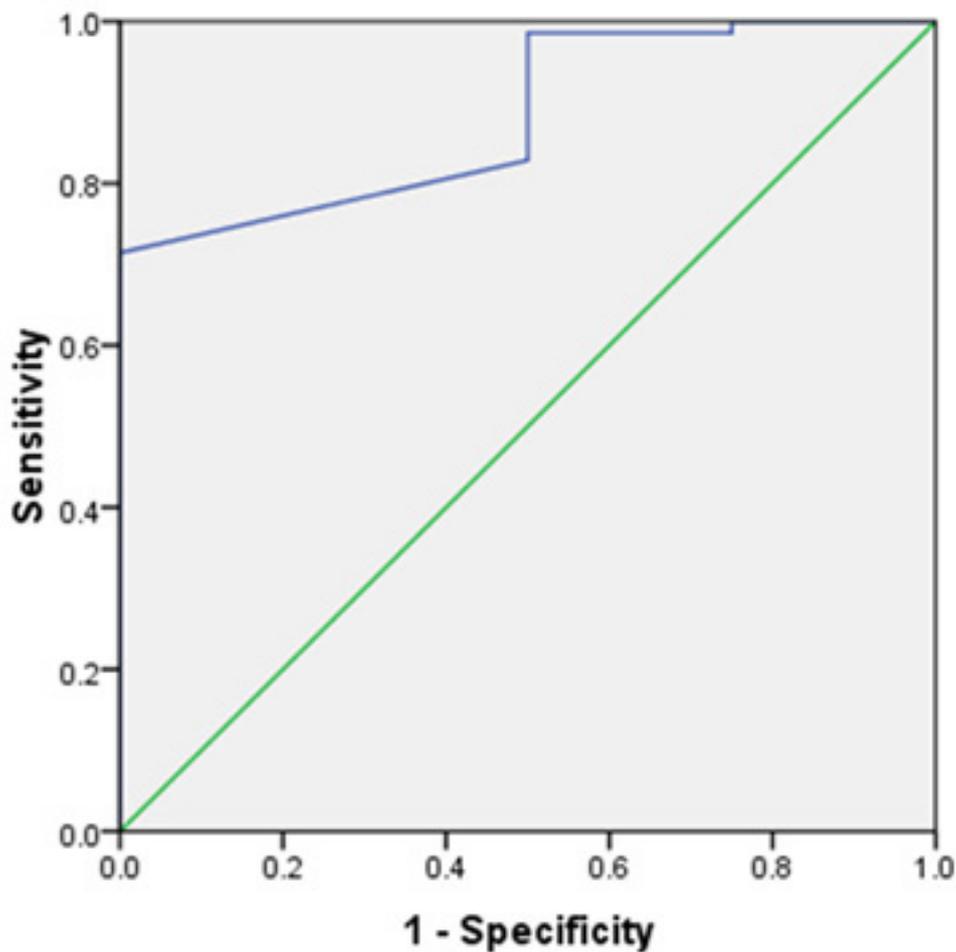
Diagonal segments are produced by ties.

Conclusion

LUS thickness was significantly lower in pregnant mothers with previous CS and this led to dehiscence in such patients. In case of LUS thickness of < 1.7 mm, the risk of dehiscence and rupture increases.

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Effect of Environmental and Behavioral Interventions on Physiological and Behavioral Responses of Premature Neonate Candidates Admitted for Intravenous Catheter Insertion in Neonatal Intensive Care Units

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Abstract

Background and Objective: Many painful procedures including intravenous catheterization are performed in the ward without taking necessary pain-reducing measures. The present study was conducted with the aim to determine the effect of environmental and behavioral interventions on physiological and behavioral responses of preterm infants during intravenous catheterization.

Materials and Methods: In the present clinical trial, 82 infants with gestational age of 30-37 weeks were randomly divided into intervention and control groups. In the preliminary intervention stage, measures such as dimming light and noise, using eye patch and ear plugs, reducing nursing manipulations, and positioning the newborn in fetal position 30 minutes before and 30 minutes after venepuncture were performed for the intervention group, but the control group received only the routine care. Data were collected using NIPS & EDIN Scale, and analyzed in SPSS-20.

Results: No significant difference was observed between the two groups in behavioral responses to pain and stress prior to intravenous catheterization (P>0.05) (P=0.13), but these responses were significantly less in the intervention group compared to the control during and after this procedure (P<0.05). Moreover, no significant difference was observed between the two groups in the mean physiological responses (P>0.05).

Conclusion: Dimming light and noise, reducing nursing manipulations, and fetal positioning during intravenous catheterization effectively reduces neonatal pain.

Key words: Environmental and behavioral interventions, physiological and behavioral responses, intravenous catheterization, preterm infant.

Introduction

The neonatal period includes the first moment of delivery to one month after birth. At this time, physical changes occur in the body and the infant learns how to respond to many forms of external stimuli (1). Over the past 25 years, the prevalence of premature babies has increased by 30 percent (2). More than 70% of preterm infants admitted to a special care nursery have spent time in a NICU (3). Many years ago, it was thought that babies and infants do not feel pain because of an immature nervous system or they feel less pain than adults. At present, it has been shown that the fiber nerves directing the pain stimulations are formed during embryonic development and in fact, term infants have the same sensitivity to pain as older infants and children do, and premature infants may be more sensitive to pain than full term infants (4). Pain as one of the defensive mechanisms of the body, indicates abnormal conditions in the body, so that relief from the pain is a basic requirement and the right of all people as well as the most important goals of medical science (5). The results of a study on neonates in the neonatal intensive care unit indicated that heel prick blood sampling was the most common procedure (56%), followed by endotracheal suction (26%) and intravenous cannula insertion (8%), and other procedures with fewer percentages included venepuncture, intubation, intramuscular injection, intravenous catheter insertion, peripheral artery catheter placement, infusion catheter, bladder urine sampling, cerebrospinal fluid sampling, and arterial sampling (6). Inadequately managed pain, for whatever reason, leads to long-term physiological, psychosocial and behavioral consequences, and through being aware of stressors that affect the ill child and their family as well as by designing and applying safe and effective interventions to eliminate or reduce stressors, caregivers should focus their attention on non-traumatic care (7). Stress and pain in newborns can lead to many complications such as such as increased hypoxia, elevated cortisol level (8), impaired nervous system development (9) and mental disorders and increased length of hospitalization (10). The infants' responses to pain and stress can be represented in three behavioral, physiological and nervous-chemical ways; however, the intensity and mode of occurrence of these responses depends upon factors such as maternal gestational age, severity of illness, and duration of admission to the neonatal intensive care unit. Behavioral responses to pain and stress in newborns include the following: crying, body movements, facial shrinkage, and decreased or impaired nutrition. Physiological responses to pain and stress in newborns include changes in blood pressure and heart rate, hypoxia, and increased oxygen intake (11). A high percentage of premature infants may experience problems that result in more than 20 days of stay in infants' care units (12). Since infants are unable to meet their needs by oral feeding, one of their basic care needs is to provide care by administering fluids, medicines and nutrition, and for this purpose, intravenous access is essential (13). Angiocath is considered to be the first choice in the newborn baby, which is ideally suited for short-term treatments (14). In this regard, many painful procedures, including intravenous

catheters placement, can be performed without the necessary measures to decrease pain (15). On the other hand, frequent intermittent catheterization puts the infant at risk of painful experiences, stress and the risk of infection and inability to control the pain caused by it, causing short and long-term complications for the baby's health (16), including increasing demand on the cardiovascular system, respiratory system, immunosuppression, increased intracranial pressure, which can lead to intravesical hemorrhage, long-term emotional, behavioral and learning disabilities (17). Pain in newborns can be controlled by non-pharmacological methods such as oral sucrose, non-nutritional sucking, breastfeeding, mother/infant skin-to-skin contact (kangaroo care), and music playback during the procedure (18). Furthermore, according to Stevens 2013, non-drug actions such as lactation, hugging, touching, massaging, cold and hot compress, the use of relaxation techniques, such as playing melodies, music and attention deviance, can effectively reduce the infant's pain (19, 20). Although the use of non-pharmacological measures in the control of anxiety is scientifically and culturally accepted, they have been forgotten due to lack of scientific advice in the pediatric wards (21). Nurses as the most important members in the treatment team, play an important role in maintaining the health and well-being of patients (22). Based on the evolutionary model, taking care of these babies allows the health care practitioner to identify the behavioral signs of the baby, such as when the baby needs sleep or is under stress due to manipulation and intervention and design a care plan adapted to his/her characteristics (23). Evolutionary care and support, integrates the evolutionary needs of newborns admitted to the intensive care unit for medical care. Key concepts in evolutionary care include the organized improvement of neuropsychological and physiological behaviors, modifying physical environment such as light, sound and heat to protect the sensory and vulnerable system, in a set of family-centered structures (24). Regarding the long-term hospitalization of premature infants in the neonatal intensive care unit and painful procedures such as intravenous catheter insertion which can cause pain and stress in the newborn, as well as the importance of evolutionary care in reducing pain in infants, this study was aimed to determine the effect of environmental and behavioral interventions on the physiological and behavioral responses of premature neonates during venepuncture procedure.

Method

The present study was a double-blind clinical trial (intervention and control group). The research population consisted of all preterm infants admitted to the neonatal intensive care unit of Alzahra hospital affiliated to Isfahan University of Medical Sciences. The babies who had the criteria for entering the research were identified. Having completed the consent form and being signed by parents, the biographical information form was completed using the medical records of the infant. Biographical data included infant's name, fetal age, birth weight, infant sex, 1 and 5 minutes Apgar score, type of delivery, number of

venepuncture attempts, and physiological information form including heart rate, respiratory rate and SpO2. In order to measure pain in infants, a NIPS checklist consisting of 6 options (facial expression, crying pattern, breathing pattern, arm and leg movement and irritability type), was used. The lowest score of pain was zero and the highest score was 7. A score greater than 3 indicated pain (25). Validity and reliability of this tool were confirmed according to Dilli study (2009) (26) and Khodaie studies (2010) (28) (r = 98). To measure the neonatal stress and discomfort, EDIN scale containing 5 items (facial expression, body movements, sleep status, communication with the nurse, and relaxation) ranging from 0 to 15 was employed; its validity and reliability were confirmed by Debillon et al., (2001) (α = 0.92) (28). In order to study the physiological criteria, Saadat Monitoring manufactured by Pooyandegan Rayan-Sanat, Tehran, Iran was used and the equipment was calibrated by medical equipment engineers prior to use. After confirmation by the Ethics Committee coded by IR.SBMU.RETECH.REC.1395.587 and obtaining written permission from the authorities, the researcher visited the Neonatal Intensive Care Unit of Al-Zahra Hospital in Isfahan to collect samples and by explaining the aims of the study for the authorities and staff of the neonatal intensive care unit, sampling was performed. According to the sample size formula, 41 neonates (in each group) were selected for participation in the study and were randomly assigned (colored beads) to two, intervention and control, groups.

Then, the environmental and behavioral interventions including closing the eyes of the newborns with an eye patch to decrease light, closing the ears of the newborns with ear plug to reduce the auditory stimuli and fetal positioning using the nests provided by the researcher, were implemented in the ward by the researcher. After 30 minutes of interventions, an intravenous catheter insertion was performed by an experienced nurse while interventions continued. At the same time, another nurse who had a work experience of at least one year in the neonatal ward and knowing how to fill out the measurement tools, completed the checklist 2 minutes prior to the venepuncture, during the venepuncture and 5 minutes later and 30 minutes after the venepuncture while interventions continued. Physiological data and related checklist were completed and samples were taken out after an hour of relevant study. For each studied neonate, no environmental and behavioral interventions were performed in the control group, but all the information gathering and checklists completing procedures were implemented and recorded as the first one. Data analysis was performed using SPSS version 20. In descriptive statistics, descriptive indicators such as mean and standard deviation were reported. The repeated measures analysis of variance was used to compare the two groups at different times. Also, for comparing demographic indices in two groups, independent t-test, Mann-Whitney and Chi-square test were used.

Findings

The results indicated that the mean gestational age of infants was 33.3 ± 2.2 weeks and the mean weight of newborns was 1871.2 ± 547.32 g. There was no statistically significant difference between the mean 1 and 5 minutes Apgar score and the mean number of venepuncture in the two groups [Table 1]. The fetal age of all subjects was 33 weeks.

Table 1: Frequency distribution of neonatal demographic variables in both intervention and control groups

Variable			Intervention group (n=41)	Control group (n=41)	P-value
Gestational age (week)			33.5 ± 2.2	33.1± 2.2	43%
Birth weight (g)			1974 ± 58.6	1768.94 ± 514.04	10%
Sex		Female	41.15 (n=17)	58.5 (n=24)	12%
		Male	58.5 (n=24)	41.5 (n = 17)	
1 minutes Apgar			6.04	6.4	37%
5 minutes Apgar			8.1	8.3	10%
Type of delivery		Cesarean section	90.2 (n = 37)	85.4 (n = 35)	50%
		Normal	9.8 (n = 4)	14.6 (n = 6)	
Number of venepuncture attempts			1.2	1.3	46%

The mean heart rate in both groups was initially found to be increased during venepuncture and then decreased over time (P <0.05), but the results showed that there is no significant difference between the mean heart rate at different times between the two groups (P> 0.05) [Table 2]

Table 2: Comparison of mean heart rate at different times between the two groups

Time	Intervention group		Control group		P-value[1]
	Mean	Standard deviation	Mean	Standard deviation	
2 minutes before venepuncture	15.09	17.1	149.9	18.8	79%
During the venepuncture	153.5	17.8	155.7	17.9	57%
5 minutes after the venepuncture	148.3	16.5	147.3	16.3	79%
30 minutes after the venepuncture	145.2	17.2	141.8	16.4	35%
P-value	0.008		<0.001		

The mean of respiratory rate in the intervention group was 59 and in the control group 58. Although the mean respiratory rate was higher in the intervention group, the results showed that there was no statistically significant difference in the respiratory rate over time in both groups (p> 0.05) [Table 3]

Table 3: Comparison of mean respiratory rate at different times between the two groups

Time	Intervention group		Control group		P-value[2]
	Mean	Standard deviation	Mean	Standard deviation	
2 minutes before venepuncture	59.07	7.1	58.6	4.9	75%
During the venepuncture	59.12	7.1	58.9	5.1	86%
5 minutes after the venepuncture	59.10	7.02	59.11	5.1	99%
30 minutes after the venepuncture	50.14	58.7	58.7	5.1	70%
P-value	0.93		0.51		

The mean of arterial oxygen saturation in the intervention group was 94.875 and 94.7 in the control group. Although the mean of arterial oxygen saturation in the intervention group was higher, the results showed that there was no statistically significant difference in the mean arterial oxygen saturation during venepuncture in both groups (p> 0.05) [Table 4].

Table 4: Comparison of mean SP02 at different times between the two groups

Time	Intervention group		Control group		P-value[3]
	Mean	Standard deviation	Mean	Standard deviation	
2 minutes before venepuncture	95.1	2.3	94.7	3.5	50%
During the venepuncture	94.8	2.6	94.7	3.2	88%
5 minutes after the venepuncture	94.9	3.4	94.6	4.6	75%
30 minutes after the venepuncture	94.7	2.9	94.8	2.7	92%
P-value	0.81		0.51		

There was no statistically significant difference between the mean pain intensity score in the neonates two minutes before the venepuncture and 30 minutes after the venepuncture between the intervention and control groups (p> 0.05). However, the mean score of pain in the intervention group was significantly less than the control group during the venepuncture and 5 minutes after the venepuncture (p <0.05) [Table 5].

Table 5: Comparison of mean pain intensity at different times between the two groups

Time	Intervention group		Control group		P-value[4]
	Mean	Standard deviation	Mean	Standard deviation	
2 minutes before venepuncture	0.5	0.09	0.6	0.1	0.41
During the venepuncture	0.8	0.1	3.04	0.2	<0.001
5 minutes after the venepuncture	0.4	0.09	1.6	0.2	<0.001
30 minutes after the venepuncture	0.3	0.08	0.7	0.2	13%
P-value	0.12		<0.001		

There was no significant difference between the mean severity of stress and discomfort scores in the neonates two minutes before the venepuncture in two intervention and control groups (p = 0.13). However, the mean of stress and discomfort scores in the intervention group was significantly less than the control group during and 5 and 30 minutes after the venepuncture (p <0.05) [Table 6].

Table 6: Comparison of mean stress score at different times between the two groups

Time	Intervention group		Control group		P-value[5]
	Mean	Standard deviation	Mean	Standard deviation	
2 minutes before venepuncture	0.3	0.08	0.5	0.1	0.13
During the venepuncture	0.4	0.09	2.7	0.2	<0.001
5 minutes after the venepuncture	0.1	0.05	1.5	0.2	<0.001
30 minutes after the venepuncture	0.05	0.03	0.7	0.2	<0.001
P-value	0.10		<0.001		

Discussion

There are many studies worldwide about some of the environmental interventions (light and noise reduction), neonatal physiological and behavioral responses (heart rate, respiratory rate and arterial oxygen saturation) and various pain assessment methods, but no research has been found in relation to the effect of environmental and behavioral interventions on the physiological and behavioral responses of premature infants candidates for intravenous catheter insertion admitted to the neonatal intensive care unit. The results of this study showed that although the average heart rate in the two groups was different and was firstly increased during the venepuncture and was decreased over time, no significant difference was found between the mean heart rate at different times between the two groups. The mean respiratory rate and arterial oxygen saturation were higher in the intervention group, but these changes did not show a statistically significant difference in any of the two groups over time. The results of this study are in line with Marilyn's study 2013 (29) in Canada as well as the study by Jacques Sizun (30) in France in 2002. The results of this study showed significant physiological changes (mean SpO2 and heart rate) among newborns with evolutionary care before and after weighing compared with the control group, but the rate of hypoxic attacks was decreased significantly, which was in line with the results of studies by Johnston et al. (31) and Taheri et al. (32) in 2007-2008. In terms of heart rate and respiratory rate, the results of this study were consistent with the study of Taheri et al., but did not have an agreement on the amount of arterial oxygen saturation. This discrepancy can be due to the difference between

the procedures conducted in the study. The results of this study are consistent with the results of the study by Slevin et al. (33) in 2000. In addition, the results of this study are consistent with the results of the research by Abdeyazdan et al. (34) (2013), for the respiratory rate, but are inconsistent in terms of oxygenation rate. This discrepancy in outcomes can be attributed to the difference between the interventions in the study. The results of this study are not consistent with the results of the study by Celine Catelin and colleagues (35) in France in 2005. Their study showed that the implementation of environmental and behavioral interventions such as (closing baby's eyes and ears, non-nutritious diet, kangaroo and family-centered care, shaking the baby and putting the baby in a fetal position) during the weighing process resulted in significant changes in physiological criteria; it suggests that these interventions have led to a decrease in respiratory rate and a decrease in heart rate, and an increase in arterial oxygen saturation, which can be due to the low number of samples in each group (15 neonates for each group). However in the recent study, increasing the number of neonates in each group (n = 41) as well as different procedures in the study could be the reasons for discrepancy in the results. Regarding the embryo's position, the results of this study are not consistent with the results of the study by Reyhani et al. (2011) in Mashhad (36). This discrepancy can be attributed to individual differences, demographic characteristics of infants, providing different nursing care in infants' intensive care units and different fetal age. Moreover, the results of this study are not consistent with the results of the study by Nasimi et al. (2014) in Mashhad (37). This discrepancy can be due to the different procedures conducted in the study; these studies have been done using an invasive procedure during a venepuncture, while the study by Nasimi et al., has been conducted with normal procedures in the ward. Other results obtained from this study also showed that there was no significant difference between the mean score of pain in newborns 2 minutes before venepuncture and 30 minutes after venepuncture between the intervention and control groups (p >0.05); but the mean score of pain in the intervention group was significantly less than that of the control group during and 5 minutes after the venepuncture (p <0.05). Additionally, there was no significant difference between the mean stress intensity and discomfort in the neonates 2 minutes before the venepuncture between the intervention and control groups (p = 0.13), but the mean score of stress and discomfort in the intervention group was significantly less than that of the control group during as well as 5 and 30 minutes after the venepuncture. The results of this study were in line with the results of the study by Celine Kathleen et al. (2005). Also, the results of this study are consistent with the results of the study of Reyhani et al. (2011) implying that the fetal position decreased the pain intensity of newborns in the intervention group compared to the control group.

Conclusion

According to the results, we can conclude that there are no environmental and behavioral interventions that affect the physiological and behavioral responses of the premature infant, so further research is recommended.

Given the advantages of reducing pain and stress during the intravenous catheters insertion in premature infants, their low cost, the lack of specific equipment and the need for evolutionary care, it is recommended to use these interventions in order to decrease the pain of premature neonates during painful procedures including venpuncture.

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Effect of 8 weeks Rhythmic aerobic exercise on serum Resistin and Body Mass Index of overweight and obese women

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Abstract

Resistin plays an important role in obesity-related diseases through metabolic processes and the immune system. The purpose of this study was to evaluate the effect of 8 weeks aerobic exercise on the amount of resistin and the Body Mass Index (BMI) of overweight women. This study was carried out through semi-experimental method. To this end, 34 overweight and obese women (aged 40±10, BMI≥25) participated in the study voluntarily and were randomly divided into experimental (17) and control (17) groups. The experimental group started the 8-week exercise program performed in three sessions a week (51 minutes per session) with 66% of the maximum heart rate in the first week which gradually and along with the exercise progression increased to 86%. Training sessions began with warming up then continued with the main part of the exercise including low impact and high impact aerobic moves in the standing positions and then back to the sitting initial position. The exercise (experimental) group participated in an 8-week training program (3 sessions a week) while the control group was asked to keep their normal life during the study period as it was before. Blood samples were taken in two stages, first 48 hours before the tests and second 48 hours after the last aerobic training session. Serum resistin concentration was calculated through ELISA (enzyme-linked immunosorbent assay) method using its special kit. The Shapiro-Wilk test was used to determine the consistency and nature of information about the subjects in the research groups. In order to analyze the data, the paired t-test was used to examine the intra-group differences and covariance test at a significant level of $P \leq 0.05$ was performed to measure the inter-group differences. SPSS21 software was also used to conduct statistical calculations. Data analysis indicated that the 8-week exercise program had a significant effect on BMI (P=0/001), body weight (P=0/000), and resistin (P=0/001). In addition to reducing weight and lowering BMI, aerobic exercise can also decrease resistin levels in overweight and obese women which can be indicative of a lower risk of developing metabolic and cardiovascular diseases.

Key words: aerobic exercise, resistin, body mass index, overweight

Introduction

Today, both developed and developing countries are facing a lifestyle of low physical activity spreading among people, which is normally followed by some side effects such as increased prevalence of cardiovascular diseases and early mortality (1). In most cases, premature coronary artery diseases are directly associated with the number, severity and acquiring of atherosclerosis factors (2). Adipose tissue is not just an energy saver, but can also play an important role in insulin resistance through production and irregular discharge of a number of proteins called adipocytokines (3).

Adipocytokine resistin weighs 11.3 kDa (4) and belongs to the cysteine-rich protein (CRP) family called resistin-like molecules also known as and found in inflammatory zone-2 (FIZZ-2) (5,6). This hormone is also directly related to atherosclerosis risk (7). Increasing level of resistin occurs mainly in inflammatory conditions which stimulate and relieve proinflammatory cytokines (8). Little research has been done on the effect of physical activity on resistin levels. Jamurat et al (2006) reported that a sub-intensive aerobic exercise session in healthy and overweight men did not make any significant changes in resistin levels (9). In their study, Jones et al (2009) examined the effect of 8 months of aerobic exercise on resistin levels and lipid profile and suggested that the exercise lowered resistin levels (10). Balducci et al (2009) indicated that resistin decreases in diabetic and overweight patients after 12 months of regular physical activity (11). In another study, Juan et al (2007) revealed that 8 weeks of aerobic exercise had no significant impact on serum resistin of obese people. Resistin expression in adipocytes decreases in fasting condition and increases with nutrition. They also declared that exercise would not reduce resistin in the absence of weight loss (12). Dastani and colleagues reported that 8 weeks of aerobic exercises with an intensity of 50-60% of maximum heart rate resulted in a significant decrease in body composition and a significant increase in serum resistin of subjects (13). While Rashid Lamir et al (2013) found that 8 weeks of aerobic exercises with an intensity of 70-80% of maximum heart rate in active women led to a significant increase in resistin and a significant reduction of their body composition (14). Such contradictions in research results can be influenced by various factors such as amount of fat and its distribution, inflammatory conditions, hormones and other factors including the type and intensity of exercise. Therefore, there is a need for further research to better understand the factors controlling the synthesis and release of resistin and to clarify its role. It is also not clear whether changes made in adipose tissue by exercise can reduce resistin or not. Given little research conducted on the effect of long-term exercise on serum resistin levels and the importance of examining this new adipokine in obese people as well as increasing interest of women in aerobic exercises, this study aims to investigate the effect of 8 weeks aerobic training on resting levels of resistin and some metabolic risk factors in obese women.

Materials and Methods

After recall papers were distributed among women of the population from Zahedan, 34 overweight and obese women were selected voluntarily and through convenience sampling method on the basis of inclusion/exclusion criteria. Inclusion criteria were 1) being overweight or obese (BMI≤25), 2) a minimum age of 30 and a maximum age of 50.

Research exclusion criteria were 1) having cardiovascular diseases, severe hypertension, type 1 and 2 diabetes, thyroid-related diseases, 2) taking medicine, 3) smoking and alcohol use, 4) lack of participation in any regular exercise program during the past 6 months. Subjects had no particular diet during the research period. Because of the experimental nature of research and observance of ethical principles, the consent form for participation in the study and medical record questionnaire were completed by subjects. Then, subjects were randomly divided into two exercise (experimental) (17) and control (17) groups. The exercise group participated in an 8-week training program (3 sessions a week) while the control group was asked to follow their normal life routine during the study.

The exercise program included 8 weeks of aerobic training consisting of 3 sessions per week, 51 minutes per session which started with 66% of the maximum heart rate during the first week and gradually increased up to 86% as the training process progressed. Each training session consisted of warming up (stretching and running slowly for 11 minutes), the main part including low impact and high impact aerobic moves in standing position (41 min) and returning to the initial seated state (11 min). It should be noted that the control group did not attend any regular exercise activity during the research. The maximum heart rate of participants was calculated using Polar heart rate monitor. The exercise protocol was performed in an indoor sport hall with suitable ventilation system at the same temperature and for the same hours all 8 weeks.

Blood samples were taken from participants at the laboratory between 5 to 8 in the morning while fasting over two stages, first 48 hours before the tests and second 48 hours after the last aerobic session in order to exclude the effect of the exercise. Resistin serum concentration and lipid profile were measured using Human resistin ELISA kit made by EASTBIOPHARM Co., and Pars Azmoon kit according to the manufacturer's instructions.

The Shapiro-Wilk test was employed to determine the consistency and naturalness of information about the subjects in the research groups. In order to analyze the data, the paired t-test was used to examine the intra-group differences and covariance test at a significant level of P≤0.05 was employed to measure the inter-group differences. SPSS21 was also used to perform statistical calculations.

Findings

As shown in Table (1), there was no significant differences between subjects in terms of age, weight and body composition before the research protocol was implemented. Data analysis implied that the 8-week exercise program had a significant effect on BMI (P=0/001), body weight (P=0/000), and resistin (P=0/001).

Table 1. The average variables for the control and experimental groups in the pre and post-test			
Variable	phase	control group	experimental group
Height (cm)	Pre-test	161.1±*5.1	160.2±6.6#
Age (year)	Pre-test	39.7±6.2	37.1±7.3
Weight (kg)	Pre-test	75.6±9.2	80.7±9.7
	Post-test	75.6±8.9	78.8±9.7#*
BMI (2kg / m)	Pre-test	29.1±2.4	31.4±2.8
	Post-test	29.1±2.3	30.7±2.9#*
resistin (mg / dl)	Pre-test	8.38±0.84	8.09±0.75
	Post-test	8.34±0.81	7.22±0.5#*
a Data are shown as mean ± standard deviation.			
# T test for dependent samples is significant (significant difference in the experimental group before and after 8 sessions) (p < 0.05).			
* Covariance test is significant (significant difference of groups' post-test after eliminating the effect of pre-test) (p < 0.05).			

Discussion and Conclusion

The results of this study revealed that BMI and serum resistin levels decreased significantly after 8 weeks of aerobic exercise. Such change made in resistin levels has also been reported in many previous studies. In one of them, 16 weeks of regular aerobic exercise at 50% to 85% VO2MAX intensities in overweight patients with type 2 diabetes resulted in a significant reduction of resistin (15). Further, 8 months of regular aerobic exercise of overweight adolescents led to a significant reduction of resistin level (16). The results of the present research was not consistent with Persephin et al (18) and Juan et al (12). Thus, it can be stated that changes in resistin amounts result from physical exercises. Contradiction between the present article and other studies can be attributed to differences among exercise interventions (duration, type, intensity) as well as subjects. In the present study, body weight changes of the training group were directly related to resistin changes. As a matter of fact, a significant reduction of body weight after exercise was associated with a decrease in resistin level. In some other studies, it was confirmed that aerobic exercise affects weight loss and subsequent resistin decrease as factors contributing to increased insulin function and reduced insulin resistance (18,19). Youn et al (2004) reported that 2 months aerobic exercise resulted in weight loss which caused a significant decrease in resistin (18). As can be seen, none of the studies mentioned above have been similar in terms of exercise intensity and duration.

Increasing resistin gene expression disrupts the muscle's glucose metabolism and raises glucose intolerance. Therefore, resistin may have a crucial role in insulin resistance or glucose homeostasis (20). However, the physiological effect of resistin on resistance and obesity has not been clarified yet (21). Moreover, some researchers have suggested that resistin is directly correlated with body mass index, body fat and glucose and insulin in obese people (21,22). Some previous studies have pointed to the impact of a healthy, balanced diet along with a regular exercise program on reducing blood resistin levels as well as lowering fat mass due to weight loss in response to the diet and physical training which ultimately results in a decrease in serum resistin (23). Generally speaking, long-term physical exercise seems to reduce the amount of resistin as it decreases body fat percentage and BMI. All controversies in articles may be caused by failure to significantly lose weight, people's different and incontrollable genetic backgrounds, differences in type, intensity and duration of exercises or subjects participating in the studies.

The findings indicate that serum resistin concentrations are improved after 8 weeks of aerobic exercise which result in reduction of body mass index. Adipokine ideal levels can play an important role in preventing cardiovascular and metabolic diseases. Overall, the results of this study bring us to the conclusion that continuous aerobic exercise not only results in weight loss but also reduces serum resistin of overweight women which can help us reach a better understanding of the role of regular physical activity in lowering the risk of developing cardiovascular diseases and diabetes, although, more research is needed to be conducted on its long-term effect.

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Study of changes in leptin and body mass composition with overweight and obesity following 8 weeks of Aerobic exercise

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Abstract

Introduction:
Obesity causes diseases such as coronary artery disease, mellitus diabetes, hypertension, cancer and stroke. The purpose of this study is to investigate changes in leptin and body mass composition in women with overweight and obesity after 8 weeks of aerobic exercise.

Method: The research method is semi-experimental. 34 women with overweight and obesity (40 ± 10 years, 25 ≤ BMI) volunteered and were randomly divided into experimental (17) and control (n = 17) groups. The training group started an 8-week training session with three sessions per week (51 minutes for each session) with 66% maximum heart rate in the first week and gradually reached 86% of the maximum heart rate with the progression of the training program. Each training session included warming up; the main part of the exercise included the implementation of low impact and high impact aerobic movements, in the standing position and back to the original sitting position. The control group was asked to maintain their normal life during the study period. Blood samples were taken in two phases: one was taken 48 hours before the tests and the other was taken 48 hours after the last aerobic training session. Serum leptin concentration was calculated using ELISA method using special kit. Shapiro-Wilk test was used to determine the consistency and normality of the information about the subjects in the research groups. For analyzing the data and considering the intra-group differences, the paired t-test was used and covariance test was used at the significance level of P≤0.05 to investigate the inter-group differences between the groups. SPSS 21 was used to perform statistical calculations.

Results: Data analysis showed that 8-weekly sport exercises had a significant effect on BMI (P = 0.001), body weight (P = 0.000), and leptin (P = 0.001).

Conclusion: Aerobic exercise can lead to weight loss and leptin. This exercise can be used as a non-invasive way to treat obesity and prevent its complications.

Key words: Leptin, Body Mass Index, Aerobic exercise, overweight

Introduction

The global spread of obesity is seen in all age groups, so that about 250 million people who are about 7% of the world's current population are obese and two to three times of this amount are overweight (1). According to the World Health Organization reports, the number of obese and overweight people will increase by about 1.5 billion in 2015 (2). The prevalence of abdominal obesity in Brazil, France and the United States is reported to be 39.2%, 33.3% and more than 50 % respectively (3.1). Studies in different cities of Iran indicate a high prevalence of abdominal obesity in the population, so that the prevalence of abdominal obesity in these cities is as below: Tehran (over 76%), Rafsanjan (54.7%), Isfahan (84.6%), Arak (66.8%), Najaf Abad (82.2%) and Mazandaran province (82.2%) (4-6). Published statistics by the Institute for Endocrine Sciences and Metabolism of Shahid Beheshti University of Medical Sciences and Health Services showed that the prevalence of abdominal obesity increased from from 67.1% to 83.1% in the years 2002- 2009 (7).

The discovery of leptin hormone in 1995 has led to advances in obesity research. Leptin that is produced by the ob-gene is a protein hormone that is composed of 129 amino acids with a molecular weight of 16 kDa (8-9). This hormone is mainly secreted from adipose tissue and plays an important role in regulating body weight and energy homeostasis in the body. Leptin is actually an alert mechanism for regulating body fat. The higher adipose tissue contains more leptin and the lower adipose tissue secretes less leptin (8).

Laboratory studies are under way to better understand the function of leptin. Part of this research is the study of the effects of exercise on leptin levels. Several studies have shown that low-fat diet and physical exercise lower blood levels of leptin (9) and since regular body exercises play a crucial role in losing weight and body fat, if leptin levels are affected by exercise, it can explain how exercise affects obesity. Also, those who exercise regularly achieve better weight stability and metabolic fitness (1). Individuals who perform a particular exercise receive better results in reducing bodily mass than those who do not follow specific exercise (11). Leptin is associated with increased energy intake, reduced appetite and increased body temperature (12). In addition, leptin density significantly correlates with body mass index (BMI) and body fat percentage (12).

Limited studies have been conducted on leptin and have reported different outcomes. Azizi (2011) examined 8 weeks of running on a treadmill with an intensity of 65-85% maximum heart rate and reported that the leptin level significantly decreased in the training group but this decrease was not significant in comparison with the control group (13). Also, Akbarpour (2013) showed that 12 weeks of aerobic training on obese men with cardiovascular disease resulted in a significant decrease in leptin in the experimental group compared to the control group (14). Hejazi et al. (2014) investigated the effects of leptin changes after 12 weeks of aerobic training, which

was performed 3 days a week and with an intensity of 75-65% of the heart rate in obese middle-aged women. They reported that exercise significantly decreased leptin (15). While Weltman et al. (2000) noted that a high intensity exercise session does not change the amount of leptin in the blood (16).

This contradiction in research results can be influenced by various factors such as the amount of fat and its distribution, inflammatory conditions, hormones and other factors, including the type and intensity of exercise. Therefore, more research is needed for understanding the mechanisms that control the synthesis and release of leptin and in clarifying the role of leptin better. Thus, according to little research done on the effect of long-term exercise on serum leptin levels and also given the importance of examining this new adipokin in obese people and the increasing interest of women in aerobic exercise, the aim of this study is to evaluate the effect of 8 weeks of aerobic exercise on resting levels of leptin and lipid profiles in overweight and obese women.

Materials and Methods

After distributing recall papers, among women, 34 overweight and obese women were selected voluntarily and available from Zahedan on the basis of entry and exit criteria. The criteria for entering the study were: having overweight and obesity of BMI 25≥ and a minimum age of 30 years and a maximum age of 50 years. Also, the criteria for leaving the research were: 1- Cardiovascular disease, severe hypertension, type 1 diabetes mellitus, thyroid-related diseases, 2- drug use, 3- smoking and alcohol consumption 4. Non-participation in any regular exercise during past 6 months. Samples should not have any particular diet at the time of the research. Due to the experimental nature of research and observance of ethical issues, at first, the consent form of participation in the research and the medical records questionnaire were completed by the subjects. Then subjects were randomly divided into two groups of training (17 people) and control (17 people). The training group participated in an 8-week training program and three sessions per week, while the control group was asked to maintain their normal life during the study period.

Aerobic exercise program included 8 weeks aerobic training, 3 sessions per week and 51 minutes each session which started with 66% of maximum heart rate in the first week and gradually increased to 86% of the heart rate with the progression of the exercise program. Each training session consisted of warming up (stretching and running slowly for 11 minutes), the main part of the exercise included performing low impact and high-impact aerobic exercises (41 minutes) in standing position and returning to the initial state in sitting position (11 minutes). It should be noted that the control group did not attend any regular exercise at any time during the course of the research. The maximum heart rate of the participants in the exercise group was calculated using the Pollard pulse rate. The exercise protocol was carried out in a covered

sports hall with proper ventilation and it was the same for all 8 weeks in terms of temperature and operating hours.

Blood samples were taken in two stages; one was taken 48 hours before the tests, and the other was taken 48 hours after the last aerobic exercise session in order to eliminate the effect of the exercise, in the laboratory between 5:00 and 8:00 am in a fasting state. Serum vaspin concentration and lipid profile was measured by ELISA method and by using a special kit of Human LEPTIN of EASTBIOPHARM Company according to the manufacturer's instructions.

Shapiro-Wilk's test was used to determine the consistency and normality of the information about the subjects of the research groups. In order to analyze the data, paired t-test was used to examine the intra-group differences and to examine the inter-group differences between research groups; covariance test was used at a significant level of P≤0.05. SPSS 21 was used to perform statistical calculations.

Findings

As shown in Table 1, subjects prior to the implementation of the research protocol did not have a significant difference in terms of age, weight, and composition of the body. Data analysis showed that 8-weekly exercise had a significant effect on BMI (P = 0.001), body weight (P = 0/000), and leptin (P = 0.001).

Discussion and Conclusion

The main findings of this study were significant reduction in serum leptin levels, BMI and weight in overweight and obese women. Exercise affects body composition, and carbohydrate and fat metabolism, and considering the effect of exercise activities on serum leptin levels in energy balance and glucose hemostasis is very important (17). In confirmation of the present study findings, some studies that have improved body readiness level and have an effect on body composition, have reduced serum leptin (17). The size of the fat mass, especially the abdominal fat, plays a special role in the level of blood leptin. In obese people, elevation of adipose tissue was associated with increased leptin and increased leptin resistance (18). Of course, in one study, after 60 minutes of aerobic exercise activity for 7 weeks, no significant changes were observed in the level of blood leptin (19). These findings were also observed in some other studies with different intensity and duration of training periods (16). Fataru et al. (2005) stated that 6 months of exercise (3 days a week) would lead to a decrease in blood leptin, with a decrease in subcutaneous fat and body mass index which is consistent with the findings of the present study (18). Gökbel et al. (2009) indicated that leptin concentration significantly decreased in long term aerobic exercise immediately after exercise, 24 and 48 hours after exercise, and in the re-initiation period (20). Oazaki et al. (2010) also investigated the effect of moderate-intensity aerobic exercise (50% maximal oxygen consumption) and diet for 1 week on fat loss and leptin concentrations in non-active obese and non-obese middle-aged women. Based on these findings,

Table 1: The average variables for the control and experimental groups in the pre and post-test				
Variable	Phase	control group	experimental group
Height (cm)	Pre-test	161.1±*5.1	160.2±6.6#
Age (year)	Pre-test	39.7±6.2	37.1±7.3
Weight (kg)	Pre-test	75.6±9.2	80.7±9.7
	Post-test	75.6±8.9	78.8±9.7#*
BMI (2kg / m)	Pre-test	29.1±2.4	31.4±2.8
	Post-test	29.1±2.3	30.7±2.9#*
LEPTIN (ng / dl)	Pre-test	35.83±26.74	39.53±23.89
	Post-test	38.12±25.25	28.21±21.65#*
a Data are shown as mean ± standard deviation.			
# T test for dependent samples is significant (significant difference in the experimental group before and after 8 sessions) (p < 0.05).			
* Covariance test is significant (significant difference of groups' post-test after eliminating the effect of pre-test) (p < 0.05).			

leptin concentration and fat mass decreased, but decrease in leptin concentration was not associated with weight loss (21).

However, Bijeh et al. (2009) did not observe significant changes in body weight and body mass index and blood leptin levels by assessing the effect of 6 months of aerobic exercise on leptin level, cortisol, and insulin and serum glucose in middle-aged lean women. The reason for this discrepancy can be that regular physical activity is likely to reduce serum leptin levels if the body mass index is significantly reduced. In short, the decrease in the concentration of leptin after long-term exercises (more than 60 minutes) is assigned to overnight leptin reduction and hormonal changes due to exercise. Extremely long exercises that caused significant energy imbalances, affected periodical and overnight Leptin changes (23). However, the effect of leptin on physical activity and the return period to initial state is still unknown. There are some reasons that can explain the changes in the response of leptin to physical activity (17). Regarding all of these, it is believed that sports activities can play an important role in energy costs due to several factors, including weight loss and also can alter the response of leptin by effecting on hormonal concentrations (insulin, cortisol, growth hormone, catecholamine and testosterone) and metabolites (free fatty acid, lactic acid, and triglycerides)

Type of exercise is one of the factors influencing leptin levels (24). Long-term mild activity that consumes 900 kilocalories of energy, reduces leptin concentrations for more than 2 days after exercise, while high-intensity short-term activity with an energy consumption of approximately 200 kcal has no effect on leptin levels (24). The amount of exercise activity can have a significant effect on the levels of leptin, which is independent of the effects of exercise on the balance of energy (24).

 The duration of exercise is one of the important determinants of severity that affects serum leptin levels (25). Studies are focused on leptin and short-term exercise. The severity and duration of activity, the nutritional status of individuals, the hours of blood transfusion, the caloric imbalance, the cyclic rhythm of leptin, etc. are affected by exercise (26). People with higher degrees of obesity are more resistant against leptin and therefore require a greater amount of exercise to affect leptin levels (27).

 In summary, it may be said that aerobic exercise may be a suitable treatment for obesity and additionally if diet is used properly, it will have more beneficial effects.

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A reassessment of factor structure of the Short Form Health Survey (SF-36): A comparative approach

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Abstract

Background: The factor structure of the Short Form Health Survey (SF-36) and its application to older people in Eastern countries has been the focus of limited research. Four theoretical and experimental factor structures of the SF-36 were tested and compared here to establish a best-fitting model for Iranian older people.

Methods: A sample of 391 participants (60 -89 years) years completed the Farsi SF-36. A confirmatory factor analysis assessed the fit and viability of the measurement model. Three theoretical and experimental factor structures of the SF-36 were tested using an exploratory principal component analysis to explore the factor solution of the Farsi SF-36.

Results: An exploratory factor analysis identified the two factor solutions (mental and physical) to be the same as the original US model, but the fit indices of the confirmatory factor analysis identified the two and three factor model (mental, physical and well-being) to be the same, making the latter more extensive for use with older people.

Conclusion: This study provides strong evidence that the Farsi SF-36 has the potential to measure well-being status of older people. Such an application is valid if the Vitality items are modified and new items are developed for the Well-being scale.

Key words: Health–related Quality of life, SF-36 Health Survey, older people

Introduction

Measuring the health-related quality of life (HRQoL) of older people has a prominent position in gerontology as an indicator for monitoring the health status of older people. Such monitoring forms the basis for clinical decision-making and gerontological research outcome measures. Of the several instruments for measuring HRQoL, the SF-36 Health Survey is the most widely used in health research (1, 2) and is known for its high standard of reliability and validity (3, 4). The SF-36 accentuates both the practical and popular nature of the questionnaire in both clinical settings and research. It has been translated into more than 20 languages (5). The SF-36 enables policy makers to involve older people in the decision making process about their own health with a comprehensive and short instrument (6). The SF-36 has been validated for use with older people, and its applicability and suitability are well documented (5, 7, 8), however, those versions cannot be used with Iranian older people due to lack of cultural equivalence. The existing Farsi SF-36 was translated and validated for use with a general population by an Iranian research team in 2005 (9), however, it cannot be used directly with older people owing to their heterogeneous characteristics (6). There is also controversy surrounding the numbers of underlying dimensions measured by the different translated versions of the SF-36 compared to the US original SF-36 (10-12). Therefore, a lack of a validated Farsi SF-36 for elderly and controversy about the number of underlying dimensions measured by the SF-36 highlights the need to conduct a new psychometric analysis. This study therefore investigates the factor structure of the Farsi version of the SF-36 in older people to find the best-fitting model for this population group.

Materials and Methods

Participants: A sample of 391 participants (197 males and 194 females) were randomly selected from the Tehran population and they ranged in age from 60-89 years. The inclusion criteria were age of 60 years and older and Abbreviated Mental test score ≥ 6. The participants were asked to complete the existing Farsi SF-36 (9), which took about 20 to 30 minutes. The research was approved by the ethics committee of the University of Social Welfare and Rehabilitation Sciences (USWR.REC.7393.162). Written informed consent was obtained from each participant.

Instrument: The SF-36 Health Survey assesses the mental and physical health status and eight generic health concepts including Physical Functioning (PF); Role Limitations due to Physical Health (RP); Bodily Pain (BP); General Health (GH); Vitality (VI); Social Functioning (SF); Role limitations due to Emotional Health (RE); and Mental Health (MH). The SF-36 has been translated for use in several countries as part of the International Quality of Life Assessment (IQOLA) project (13, 14), and has demonstrated reliability and validity across diverse samples (3). The scale has 36 items that are scored and summed according to a standardized protocol and expressed as a score on a 0-100 scale for each of the eight health concepts,

with higher scores representing a better health status (15). The psychometric testing of the Farsi version of the SF-36 followed the procedure of the IQOLA project (9).

Data analysis: A confirmatory factor analysis (CFA) on item level using LISREL 8.4 (16) assessed the fit and viability of the measurement model which was developed from the original US model (Model A) (15). The chi-square is significant at p <.001 and an adequate fit is < 2.0. The point estimate of the Root Mean Square Error of Approximation (RMSEA) and its upper confidence limit for the model should be less than 0.05 (17). The Expected Cross-Validation Index (ECVI) (6.08) should be less than the ECVI for the saturated model (3.23) (16). An exploratory principal component analysis (PCA) was conducted to explore the factor solution of the Farsi SF-36 with both orthogonal and oblique rotations. In this analysis, three alternative models were examined to explore the best fitting model. These alternative models were a one-factor model (model B), a three uncorrelated second order factor model (model C) based on previous studies (18), and an eight-factor model (model D). Figure 1 depicts the diagrams of these three models and the original US model (Model A).

Results

Descriptive statistics
The test of normality of the scale scores showed the distributions of all study variables were negatively skewed (Table 1 - page 48). The α-coefficient for the VI was very low, and for SF and MH were also below typically accepted standards. On the other hand, Cronbach's alphas were adequate for the GH, RE, Physical and Mental components, and good for PF, RP and BP.

Testing the Sf-36 factor structure models
Four CFA models were developed to confirm the factor structure of the Farsi SF-36. This analysis served to confirm Model A, the original US model, which is a comparison of the three competing models to ascertain the extent to which the Model A would demonstrate a superior fit to the three alternative models. Model B, the first alternative model was developed to load all items of the SF-36 into a single health construct. The second alternative model, Model C, was developed from the three summary measures of mental, physical and well-being (18). The third alternative model, Model D was then developed based on the eight factors that aggregate the 36 items of the SF-36.

Table 2 indicates how Model B provided a poor fit for this data. While a significantly greater model fit was observed for the original US model (Model A) and Model C and D; when compared to Model B, these models did not demonstrate a good fit. Models A, C and D however, provided a relatively better fit for this data. An examination of model fit statistics revealed mixed evidence for a good model fit, where all models did not fit the data well, according to the significant chi-square index, the relative chi-square per degrees of freedom and the RMSEA (17). The Comparative goodness-of-fit and Incremental Fit Index for these models indicated more than an acceptable model fit, but the goodness-of-fit
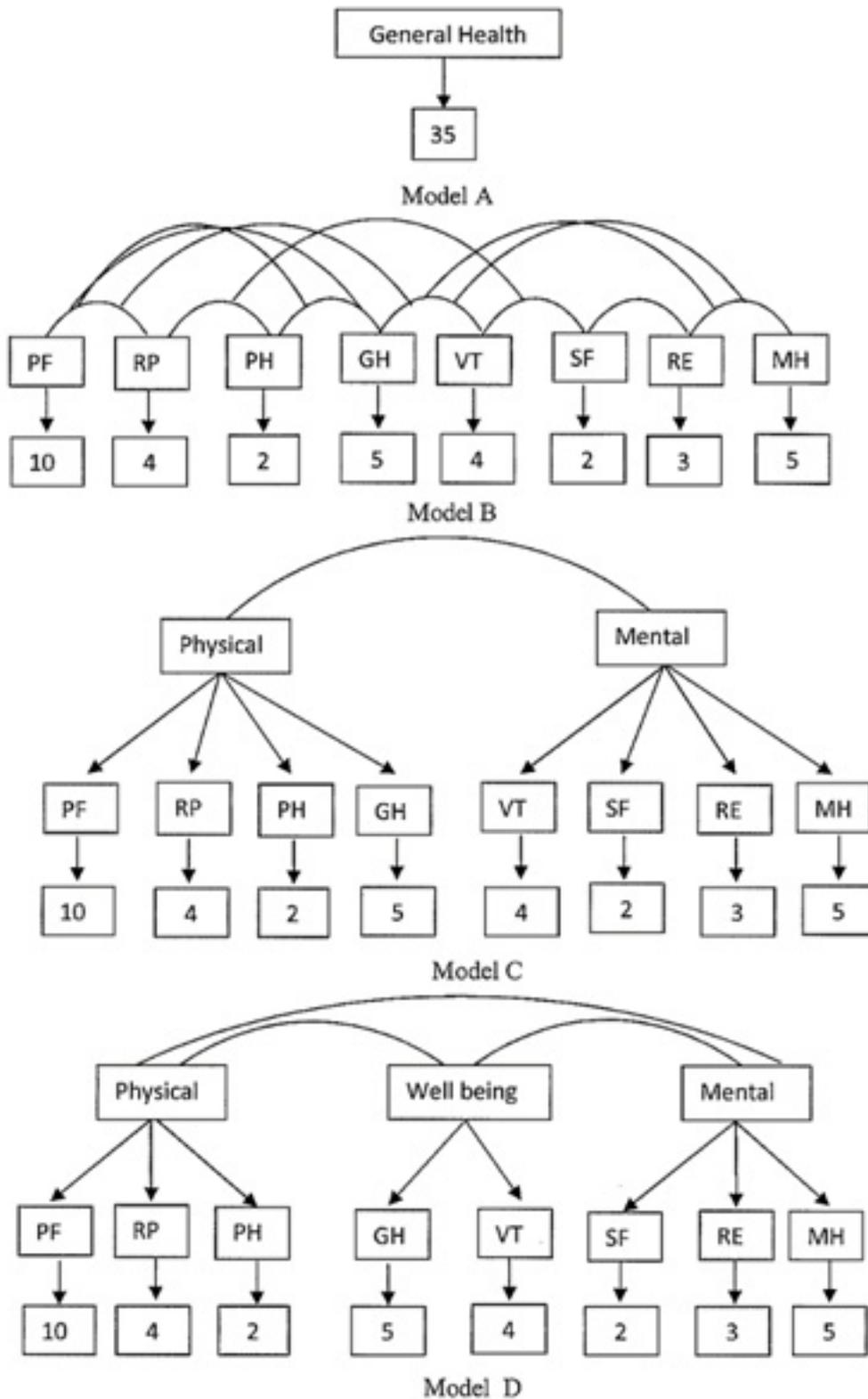
Figure 1. Path diagrams of models A, B and C of the Farsi version of the SF-36.
Note: Digits in the squares indicate the number of items (indicators). Model A, included the items belonging to one general factor (General Health), Model B included items placed in the eight factors (first order CFA), Model C included a hierarchy CFA model based on the original taxonomy model.

Table 1: Descriptive statistics and K-S test of normality of Persian SF-36 scales and summary measures

subscales	M	SD	skewness	kurtosis	D	α
PF	60.3	31.6	-0.48	-1.00	2.5**	0.93
RP	62.1	39.5	-0.49	-1.30	4.9**	0.83
BP	65.3	30.0	-0.32	-1.07	3.7**	0.83
GH	58.9	21.7	-0.29	-0.39	1.28	0.74
VI	59.1	22.7	-0.13	-0.43	1.27	0.49
SF	76.4	28.4	-0.84	-0.05	4.4**	0.69
RE	63.9	39.5	-0.58	-1.22	5.4**	0.76
MH	66.4	21.0	-0.47	-0.20	1.5*	0.66
Physical	61.3	21.7	-0.28	-0.74	1.3	0.74
Mental	64.8	19.7	-0.47	-0.15	1.4*	0.72

PF= Physical Functioning; RP=Role-Physical; BP= Bodily Pain; GH= General Health; VT= Vitality; SF= Social Functioning; RE = Role-Emotion; MH= Mental Health. D = Kolmogorov-Smirnov (K-S) test of normality. α = Cronbach's alpha. ** P<.01. * P<.05

Table 2: Factor loadings, communalities, mean and standard deviation of the scales of the Farsi SF-36, a two factor solution

Scales	Factors varimax I	Factors varimax II	Factors oblimin I	Factors oblimin II	Descriptive statistics M	Descriptive statistics SD	Descriptive statistics h²
PF	.818		.774		60.3	31.6	.67
BP	.700		.768		65.4	30.1	.51
GH	.666		.755		58.9	21.7	.59
RP	.563	.433	.663		62.0	39.4	.61
RE		.807		.796	63.9	39.5	.66
SF		.751		.774	76.5	28.4	.60
MH		.587		.668	66.4	21.0	.49
VT	.441	.478		.581	63.9	22.7	.42
Eigenvalue	3.59	.945					
% variance	44.8	11.8					

Note. PF= Physical Functioning; BP= Bodily Pain; GH= General Health; RP=Role-Physical; RE = Role-Emotion; SF= Social Functioning, MH= Mental Health, VT= Vitality. h2= communality. Factor loading > 0.4. Cross-loaded items > 0.4.

Table 3: The Goodness of Fit Statistics for CFA Modified and non-modified two and three summary measure models of the Farsi SF-36

Models	χ2	df	χ2 / df	CFI	GFI	IFI	NFI	RMSEA	ECVI
First order									
Model A	1258.09**	551	2.33	0.91	0.75	0.91	0.89	0.057	3.63
Model B	5057.67**	560	9.03	0.80	0.45	0.80	0.78	0.144	6.08
Model C	1256.99**	548	2.29	0.91	0.75	0.91	0.89	0.058	3.64
Model D	1189.72**	531	2.24	0.92	0.76	0.92	0.90	0.056	3.56
Higher order									
Before modification									
Model E	99.2 **	19	5.2	0.95	0.94	0.94	0.94	0.104	0.34
Model F	103.5**	17	6.08	0.95	0.94	0.95	0.94	0.114	0.36
After modification									
Model E	22.3	15	1.48	0.99	0.98	0.99	0.99	0.035	0.16
Model F	24.7*	13	1.90	0.99	0.98	0.99	0.97	0.048	0.18

Note: Model E included the two summary measures belonging to one general factor (General Health), Model F included the three summary measures belonging to one general factor. CFI= Comparative Fit Index, GFI=goodness of fit index, IFI= Incremental Fit Index, NFI= Non Normed Fit Index, RMSEA=Root Mean Square Error of Approximation, ECVI= Expected Cross-Validation Index. ECVI for Saturated Model=0.18. * P< .05. ** P< .001

index for all models was lower than the accepted criteria. Together, these results indicate that the one-factor did not provide a good fit for this data, and the three alternative models are the same, according to the fit indices, along with the fact that their overall fit did not appear across the model fit statistics.

Farsi SF-36 factor structure

A PCA of the eight scales was conducted with orthogonal and oblique rotations to explore the factor structure of the Farsi SF-36, and examined how many summary measures were extracted in the Iranian sample. The analyses demonstrated only one factor could be extracted with eigenvalues over 1, and explained a total 44.9% of the observed variance. The original two measure model and the three uncorrelated measures were examined and a scree-test was used to determine the proper number of several factor solutions. The results showed that the first two factors represented the main sources of variance in the data matrix. However, the results of orthogonal rotation

showed the RP and VT had high factor loadings on both factors. The results of the oblimin rotation however, showed a better fit of the original measurement model because all eight scales were loaded on their appropriate factors. The explained variance by the two extracted factors was 56.7%.

The communality, eigenvalues and factor loadings for the two rotated factors using varimax and oblimin rotations are presented in Table 2, along with the means, and standard deviations for all eight scales.

One General Health Construct

A second order CFA based on the two factor model (Physical and Mental) and three factor model of adding General well-being, were loaded on a one general health conception. This analysis served to explore and determine the underlying latent trait in the SF-36 that aggregates the summary measures (Figure 2).
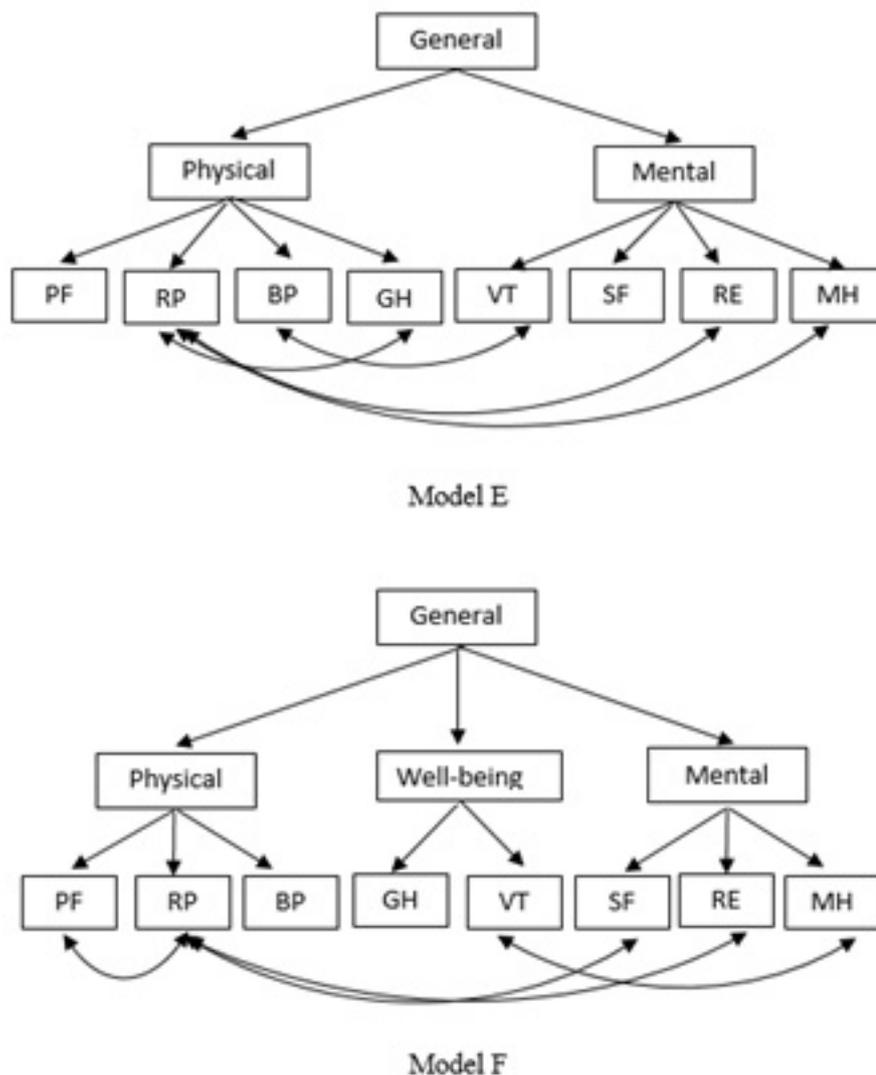
Figure 2. Path diagrams of second order models E and F of the Farsi SF-36. Model E, included the two summary measures belonging to one general factor (General Health), Model F included the three summary measures belonging to one general factor.

Table 3 shows how both models demonstrated an unacceptable fit of this data. The chi squares were significant, with p < 0.05, the relative chi square was higher than 2, and the RMSEA was higher than 0.05. However, the goodness-of fit indices were acceptable and confirmed both models.

One strategy to improve the models was to add the correlations between error terms which were specified, when suggested, by high modification indices and also where theoretically defensible. In Model E, the correlated errors were added between RP items with GH, RE and MH, and between BP-VT. The correlated errors in model F were added between RP with PF, SF, RE and MH, and between MH-VT.

An examination of model fit statistics after modification revealed adequate evidence for a good model fit. However, in both Models the RP scale had the most error correlations with the other scales, but its pattern of correlated errors was different in the models with GH, RE and MH.

Discussion

A comparative approach of the four factor structure models of the Farsi SF-36 is presented here.

Reliability
The Farsi SF-36 has shown satisfactory internal consistency reliability (>0.70) for all scales except VI, SF and MH, with the highest value for PF. Similar results for PF have been reported in other countries (19), which was to be expected given that the PF scale has 10 out of 36 items of the SF-36. Such a large set of items increases the Cronbach's α. A very low level of reliability has been reported for the VI in other studies conducted with older people and patients with chronic conditions (10, 20, 21). These studies determined whether the lower internal consistency of the SF-36 VI scale is due to the study sample or cultural differences, although this deserves further study. Additionally, the SF scale results for internal consistency reliability were below typically accepted standards in Iran, suggesting a decreased level of social abilities among older adults. The fact that this result was consistent with other studies (20, 22, 23) raises the question of whether only two items in the SF scale are adequate for assessing the concept of social functioning.

Factor structure
Both two and three factor models were confirmed in the Iranian older population, however a comparison of fit indices of the higher order two-factor model, Model A with two summary measures, and higher order three factor model, Model C with three summary measures, showed no differences between these two models. This result means it is not possible to show a preferred model for older people and suggests the instrument is conceptually equivalent with the original version. However, the question remains about how many scales could be extracted from this concept.

The two factor model (mental and physical) showed PF, RP, BP and GH to correlate with physical health component, and VI, SF, RE and MH with the mental dimension. These results are consistent with other studies (24) and confirmed the Farsi SF-36 met the psychometric standards hypothesized in the original model for physical and mental health.

The results of testing a three second-order factor are consistent with the study conducted across nine countries (18) and Rasch validation of the SF-36 in Korea (25). The third factor, interpreted as general well-being in this data, was the result of clustering GH and VI, as in previous studies, and interpreted for the mixed factor content of GH and VI (18). The reason for such a divergent result between this and previous studies that confirmed the two-factor model may be the difference in separating elderly from the other population group. Another reason for this divergent result is that cultural value plays a role in the interpretation of these differences, and Iranian elderly tend to put more value on items related to well-being compared with other population groups and cultures. Therefore the three-factor model makes the Farsi SF-36 particularly suitable for use in the assessment of older adults, as its three scales make it more appropriate to identify older people's needs. Such data makes it possible to develop a more precise care plan, since the more factors indicate a greater identification of the underlying latent trait. The three factor model will be achieved by slightly modifying items on the VI scale and developing items for the well-being scale.

Conclusion

The Farsi SF-36 has generally accepted psychometric properties, with empirical evidence showing that developing items for the third factor of well-being would be useful to better identify the needs of older people.

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Evaluation of seizures in pregnant women in Kerman – Iran

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Abstract

Background and Objectives: Seizure occurs in 0.5 to 1 percent of pregnant women, marking it as one of the most prevalent serious neurological disorders during pregnancy. Women with epilepsy face a greater threat of pregnancy-related adverse effects. The effects of seizures on pregnancy and its maternal and fetal adverse effects, necessitates the study of the prevalence of pregnancy seizures, an issue ignored by previous studies conducted elsewhere.

Method: The present study is a descriptive-analytical research. The participants included women who were referred to delivery centers of Kerman (public and private) for childbirth. The exclusion criteria were lack of cooperation and consent of the subjects for sitting the interviews.

Results: Among 3,807 admitted pregnant women, 38 cases (1%) experienced epileptic seizures. Among the participants, 2,125 subjects were admitted to public hospitals and 1,682 subjects to private hospitals. Seizure recurrence remained constant in 58% of the subjects, declined in 21%, and increased in 21%. Twenty four cases (0.63%) had a history of prepartum seizures, and 14 cases (0.36%) experienced seizures for the first time during pregnancy, with eclampsia as the most prevalent cause. Patients of public hospitals had lower levels of education and higher number of epileptic seizures. Average age of patients experiencing epileptic seizures was lower than the non-epileptic cases. Seizures were observed more in nulliparous women.

Conclusion: More than 6 in 1,000 pregnant women suffer from epilepsy. Eclampsia is the most prevalent cause. Epileptic seizures increased in 21% of epileptic pregnant women, and declined in 21% of the cases.

Key words: seizure, epilepsy, pregnant, women

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Introduction

Seizures are referred to as the temporary physiological dysfunction of the brain, caused by the abnormal electrical and excessive discharges of cortical neurons, and epilepsy is the unexplained and unpredicted repetition of these attacks (1-5). Women with epilepsy have a greater risk of pregnancy-related adverse effects, including cesarean section, preeclampsia, pregnancy-induced hypertension, premature contraction or preterm labor, postpartum hemorrhage, possibility of stillbirth, and microcephaly. Also, the risks of mental retardation and afebrile seizures are increased in their infants. Women with a history of pregnancy seizures are likely to experience epilepsy-related adverse effects including status epilepticus and increased epileptic seizures(2). Uncontrolled seizures influence maternal and fetal mortality and morbidity; tonic-clonic seizures may cause physical damage and spontaneous abortion , hypoxia, acidosis and intracranial hemorrhage in the fetus; also fetal bradycardia is possible during the mother's seizures. The etiology of epileptic seizures in pregnancy includes epilepsy of unknown cause, metabolic disorders, eclampsia, and cerebral sinus thrombosis, causing pregnancy and postpartum seizures(4, 6). Convulsion has occurred in 0.5-1% of pregnancies(6), and is one of the serious neurologic disorders in pregnancy(6, 7).

The most seizure attacks occurred in pregnant women, who have history of epilepsy (8). Another study reported that 1 in 200 pregnant women experience seizures(9).

In India, 2.5 million women are experiencing epileptic seizures, almost half of whom are at fertility ages(10). Approximately 1 million women of childbearing age in the US have seizures, among whom 20 thousand go into labor, annually (2, 3, 5, 11, 12).

In a study in the US on 45,000 pregnant women, 21.4 cases per 1,000 experienced non-eclamptic seizures before or during pregnancy(13). According to estimations, 3 to 5 per 1,000 births are related to women with epilepsy (2-4, 11) . Another study in Europe in 2013 reported that pregnant women comprise 25% of all epileptic patients, and most of these women are in need of long-term treatment with antiepileptic medications. Approximately 3-4 out of 1,000 pregnancies concern women with a history of epilepsy and 1,800-2,400 infants in Britain are born from women with a history of epilepsy, most of whom have healthy pregnancies and infants(14).

In a study conducted between 1991 and 2000, at Vali-Asr Hospital of Tehran, out of 21,000 admitted pregnant women, 53 cases had epilepsy; of these women 55% were nulliparous and 45% multiparous; 82% had generalized epilepsy, 14% had focal epilepsy, and 4% had other types. Epileptic attacks occurred in 34 subjects (70%) during pregnancy, and the number of attacks increased in only 15 patients (32%) and declined in 9.5%; 58.6% showed no change in the seizure frequency. This study reported that the cause of increased epileptic attacks may be due to the discontinuation of anti-epileptic medication and pharmacokinetic and pharmacodynamic changes of these medications during pregnancy, as well as, insomnia, stress, and anxiety(10) .

Epilepsy control must be handled adequately, as the frequency of attacks increases in 15 to 30% of the cases. Pregnancy-induced changes of anti-epileptic medications are an important agent(8). Due to reduced serum albumin and increased hepatic and renal clearance, and increased emission volume, the blood level of anti-epileptic drugs falls in pregnancy(5, 8, 9, 12, 15), causing a changed control over epileptic attacks in pregnancy. Mother's compliance and acceptance is, however, another important factor (5, 15).

Fear of fetal adverse effects is a major issue in pregnancy(12), accompanied by nausea, vomiting, and sleep disorders of the mother(5). One of the most important predicting factors is the frequency of attacks in pregnancy versus the prepartum years(16).

It has been shown that sex hormones influence epileptic attacks, as estrogen decreases the threshold and progesterone increases it (17).

Nearly 1-2% of epileptic women are afflicted with status epilepticus, which causes mortality and morbidity (8).

Preconception counseling, as well as monitoring drug serum levels, along with drug and dosage adjustment and providing patients with the information concerning their condition, can help decrease the frequency of attacks (10).

Seizures are the most probable to appear in the first trimester of pregnancy and upon delivery (8). Women with epilepsy who take anti-epileptic medication are likely to suffer from an increased risk of caesarean and hemorrhage(12, 15), yet they do not experience increased risks of premature contractions or preterm labor (2).

The present study was conducted in Kerman with regard to the prevalence of pregnancy seizures and the importance of maternal and fetal adverse effects. It must be mentioned that this study is unprecedented.

Methods

Patient Selection: This is a descriptive-analytical study. The participants of the study were women who referred to delivery centers of Kerman (public and private) for childbirth. The patients were initially asked to fill out the questionnaire developed by Placencia et al (18-20) for screening, containing 9 questions. The questionnaires were also filled out by Hospital obstetricians, who had previously received the required instructions by a faculty member neurologist. Suspicious patients were then examined by a neurologist who filled out the complementary questionnaire, including the demographic information of the patients, type of epilepsy, history of attacks, pregnancy condition, and medications used. A case of epilepsy was approved by

biography, physical examination, and EEG. Patients with approved epilepsy underwent lab assessment, imaging, including MRI and CT scan, and lumbar puncture, when required.

Sample Size: Considering the fact that epileptic seizures are reported in 1% of all pregnancies (5), the population of this study comprised 3,800 cases admitted to public and private hospitals. Since the cause of epileptic seizures in pregnant women is different from others and certain types are more frequent in pregnancy, there was no need for a control group in this study.

Exclusion Criteria: The exclusion criteria were non-cooperation and dissent of participants to sit interviews or non-cooperation of the pertaining delivery wards for patient screening. This study aimed at determining different types of epilepsy (idiopathic or secondary causes) and comparing epilepsy prevalence in nulliparous and multiparous cases, as well as between pregnant women with a prepartum history of seizures and those with no such history. Furthermore, the comparison of epilepsy prevalence according to the admitted medical centers (public and private hospitals) was determined according to the prevalence of seizures in pregnant women in each subgroup and a 95% confidence interval.

Comparison of prevalence between the groups was carried out using chi-squared test.

This study was conducted subsequent to obtaining informed consent from the participants, describing the study objectives, and commitment to confidentiality.

Results

Out of 3,807 pregnant women who were admitted to public and private hospitals of Kerman in the last month of their pregnancy, 38 subjects had experienced seizures (epileptic patients and those who experienced their first seizure in pregnancy).

Age of the epileptic patients ranged from 15 to 33 years, at an average age of 28.1274 ± 5.60687 years; it was 24.6579 ± 6.14267 for patients with epileptic attacks, and 28.1624 ± 5.60687 for patients without epileptic attacks, and the difference was significant (P=0.001).

In this study, out of the epileptic patients (a total of 24), 11 cases were nulliparous and 13 cases were multiparous, while, a total of 901 subjects were nulliparous which was statistically significant (P=0.017). A number of 2,125 cases were admitted to public hospitals and 1682 cases referred to private hospitals. Incidence of epileptic attacks was 31 cases among those admitted to public hospitals and 7 cases in those admitted to private ones, indicating a significant difference (P=0.001). (Table 1).

The degree of gravidity and parity in customers of public and private hospitals showed no significant difference, yet, the number of abortions was higher in public hospitals,

which was statistically significant (P=0.000) (Table 2). In total pregnant women these factors are shown in Table 3.

Customers of public hospitals had lower education. The majority of pregnant women in the public sector were less than high school diploma, while, those in the private sector held higher than high school diploma (P=0.000). In this study, the number of epileptic patients was directly associated with the education level (P=0.039) (Table 1).

Out of the 24 epileptic pregnant women, 20 were receiving antiepileptic medications (7 patients under multi-drug and 13 under single-drug regimens); in 2 cases, the epilepsy was controlled and the treatment was discontinued, and 2 cases did not take any medications. Epileptic attacks were controlled in only 1 case among the multi-drug patients (%14), while they were controlled in 7 cases of single-drug patients (54%), approximately 4 times the former group. The frequency of attacks declined in 5 cases (21%), increased in 5 (21%), and was unchanged in 14 cases (58%).

Of all the patients experiencing epileptic attacks, 24 had epilepsy (2 cases did not take antiepileptic medications, and 2 cases had discontinued their medications after controlling seizures), 13 cases were non-epileptic, and 1 case had a childhood experience of febrile seizure.

Among the 38 cases with a history of seizures, 27 cases had seizures in pregnancy, and the remaining 11 cases experienced no seizures in pregnancy; 6 cases had a family history of epilepsy.

Out of the 27 women with pregnancy seizures, 13 subjects had a history of epilepsy, 14 cases experienced seizures for the first time in their pregnancy; out of 11 cases without pregnancy seizures, 8 cases had a history of active epilepsy. In 2 cases who did not take medications seizures were controlled, and one subject had an experience of seizures once in her childhood.

Out of 22 patients with active epilepsy, 5 had a history of myoclonic jerk. No myoclonic jerks were reported in patients with inactive epilepsy or those experiencing their first epileptic seizure in pregnancy. Table 4 portrays the occurrence of different epileptic seizures in the patients.

Concerning the anti-epileptic medications, 13 cases received single-drug regimens (9 cases, carbamazepine; 2 cases, lamotrigine; 2 cases sodium valproate) and 7 subjects received multi-drug regimens (3 cases, lamotrigine and levetiracetam; 2 cases, carbamazepine and levetiracetam; 1 case, carbamazepine and sodium valproate; and 1 case, carbamazepine and lamotrigine).

In the present study, 11 cases had a history of abortion, out of whom: 2 cases experienced cerebral vein thrombosis (CVT) and 1 case, eclampsia; 6 cases had epilepsy; 1 case had Arterio-Venous Malformation (AVM), and 1 case had brain tumor. Six cases of epileptic patients (24%) had a history of abortion, whereas, in the remaining participants, 654 cases out of the total 3783 subjects (17%) had

Table 1: Relationship between education and seizures in pregnant women and type of Hospital

	Hospital	School + Illiterate	High School	Bachelor	Ms +PhD
Patients	Public	864	744	463	54
	Private	183	834	621	44
Seizures	No	1032	1562	1079	96
	Had	15	16	5	2

Table 2: Relationship between seizures and some pregnancy factors

		Sum of Squares	Df	Mean Square	F	Sig (ANOVA)
Gravidity	Between Groups	375.190	3	125.063	78.839	0.000
	Within Groups	6032.727	3803	1.586		
	Total	6407.917	3806			
Parity	Between Groups	339.484	3	113.161	82.263	0.000
	Within Groups	5231.442	3803	1.376		
	Total	5570.926	3806			
Abortion	Between Groups	0.862	3	0.287	2.007	0.111
	Within Groups	544.064	3803	0.143		
	Total	544.926	3806			

Pregnant women with higher levels of education referred to private hospitals more (P=0.000). The pregnant women with higher education have lower number of seizures (P=0.039).

Table 3: Relationship between hospital type and a number of pregnancy factors

	Hospital	N	Mean	Std. Deviation	P value
Gravidity	Public	2125	2.6551	1.37611	
	Private	1682	2.5470	1.18858	0.009
Parity	Public	2125	1.4442	1.29802	
	Private	1682	1.3603	1.08685	0.030
Abortion	Public	2125	1.1934	0.39507	
	Private	1682	1.1474	0.35465	0.000

Table 4: Type of seizures in pregnant women

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Tonic-Clonic	29	0.8	76.3	76.3
	F-G	1	0.0	2.6	78.9
	JME	5	0.1	13.2	92.1
	CPS	3	0.1	7.9	100.0
	Total	38	1.0	100.0	

experienced abortion previously, indicating a significant difference (P=0.000). However, there was no significant difference in the increasing cases of epilepsy, between pregnant women with a history of abortion and those without such history (P=0.111). The difference between the degree of parity and gravidity between women with a history of seizures and those with no such history was significant (P=0.000) (Table 2).

For all the patients with a history of eclampsia, epilepsy, CVT, and AVM, pregnancy seizures occurred in the third trimester (except for a CVT patient who experienced seizures in month 2).

Only 5 out of 38 patients (total number of patients) had an abnormal neurological examination. According to the assessments, one case was caused by AVM, another case by trauma, one case by tumor; epilepsy in 24 cases had unknown etiology. The causes of the first seizures in pregnancy were eclampsia in 7 cases, CVT in 3 cases, and TTP in one case.

Discussion

In the present study, out of 3807 pregnant women admitted to public and private hospitals of Kerman in their last month of pregnancy, 38 cases (0.99%) had previously experienced seizures. In a study in the US on 45,000 pregnant women, 21.4 cases per 1,000 individuals were reported to have experienced one non-eclamptic seizure during or before pregnancy(2). A study in Vali Asr Hospital of Tehran in 1991, reported 53 epileptic cases out of 21,000 pregnant women (10). The pregnancy prevalence in a study in London was reported at 0.5-1%(21). An Australian study claimed that 1 in 200 pregnant women experience seizures(9).

Out of the total referrals, 2,125 women were admitted to public hospitals and 1,682 women to private hospitals. The prevalence of seizures was significantly higher in patients admitted to public hospitals (P=0.001). Numerous causes to this are: 1. Patients with complications who are more likely to experience epilepsy are referred to teaching (public) hospitals; 2. Patients of private hospitals hold higher education, and according to studies in this region, lower education is directly associated with epilepsy; 3. This study, also, revealed that the education of pregnant women in public hospitals is lower, matching the results of a 2011 study in Kerman, indicating a significant relationship between the incidence of epilepsy and lower education (22). Our findings were similar to those of studies conducted in the US (23), Vietnam(24), and Turkey (25), whereas, in his study in England, Ferro did not report such a relationship (26); 4. The degrees of gravidity and parity and abortion were higher in women admitted to public hospitals, which was only significant in case of abortion. This may have caused the increased cases of epilepsy. In a study in Canada on 55 pregnant epileptic women, it was shown that 42 patients were admitted to public hospitals and 13 patients to private hospitals (P=0.000)(27).

The age of our patients ranged from 15 to 33. A study in Italy reported the age of pregnant epileptic patients between 15.3 to 43.5 years (28). The decline of the childbearing age in Iran is due to cultural conditions. The important point is that, the age of pregnant women who experienced epileptic seizures was lower than others (24.6 years compared to 28.1 years). A study in England reported the average age of epileptic patients (38 cases) at between 11 to 35 years old(29). The average age of pregnant epileptic patients is reported at 26 years by a study in India (30). This difference arises from cultural conditions.

Among our patients, 6 cases (15.7%) had a family history of epilepsy. This rate was 17.3% in a study in Kerman, in 2011 (22), close to that of a study in Turkey (14.3%) (25).

In the present study, out of patients with a history of epilepsy (24 cases), 14 patients were multiparous and 10 cases were nulliparous, while, 901 women in the population were nulliparous, indicating a significant difference. A study in England reported 12 multiparous cases out of 38 participants (P=0.000) (29).

In another study in Canada it was observed that there was no relationship between worsening of seizures and the childbearing age, parity, toxemia, a family history of epilepsy, age at onset of pregnancy, and preterm labor. The most prevalent complication in these patients was preterm labor, occurring in 8 cases (27). Preterm labor or abortion occurred in 2.6% of the cases in a study in Italy (28).

Eleven of our cases had a history of abortion, out of whom: 2 cases experienced cerebral vein thrombosis (CVT) and 1 case, eclampsia; 6 cases had epilepsy; 1 case with Arterio-Venous Malformation (AVM), and 1 case had brain tumor. Six cases of the epileptic patients (24%) had a history of abortion, while, for the remaining participants, 654 cases, out of the total 3,783 subjects (17%), had previously experienced abortion, indicating a significant difference (P=0.000). However, there was no significant difference in the increasing cases of epilepsy, between pregnant women with a history of abortion and those without such history (P=0.111).

We observed a significant difference between the degree of parity and gravidity between women with and without a history of seizures (P=0.000).

None of our patients experienced status epilepticus, similar to our Canadian counterpart(27), however, in the study conducted in Italy, 21 in 3,415 cases (0.6%) experienced status epilepticus (28). The similar study in England reported 2 patients with status epilepticus (29).

For all the patients with a history of eclampsia, epilepsy, CVT, and AVM, pregnancy seizures occurred in the third trimester (except for a CVT patient who experienced seizures in month 2).

The study in Canada reported exacerbation of seizures in early pregnancy (27). In England, the frequency of seizures rose in the first trimester (29). Yet, in Italy, the exacerbation of seizures was reported in 29% of the cases in the first trimester, 32% in the second trimester, and 39% in the third trimester (28). We have no explanations for these differences.

Seizure recurrence declined in 5 cases (20%), increased in 5 cases (20%), and remained constant in 15 cases 60% of the subjects.

In the study in England, out of 38 pregnant women with idiopathic epilepsy, seizure frequency increased in 45.2% of the cases, remained constant in 50%, and declined in 4.8% (29).

Pregnancy in the Australian study increased seizures in 24% of the subjects(9). Seizure frequency in the Canadian study increased in 9, remained constant in 14, declined in 4 cases, and was unknown for the rest of the participants(27). In Italy, pregnancy seizures were unchanged in 70.5% of the patients, declined in 12%, and increased in 15.8% of the cases(28). A study in Texas reported a decline in

the seizures in 3-24% of the subjects, a rise in 14-32%, and no change in 54-80%; 84-92% of the patients were pregnancy seizure-free (4). The study in England showed a positive relationship between seizure frequency 2 years prior to pregnancy and increased seizure frequency in pregnancy. Patients with more than one seizure per month had a higher risk of exacerbation in pregnancy, whereas, only 25% of patients whose seizure intervals were more than 9 months, got worse (29). However, in the study by Rosciszewka and Grudzinska in 1970, no such relationship was reported (21).The average age of onset of seizures was lower in subjects with increased seizures (12.6 years old), compared to others (16.1 years), yet, insignificant. In the present study we did not take into account the age of onset of seizures in epileptic patients.

Of the referrals, 24 cases were epileptic, with 2 cases of inactive and 22 cases of active epilepsy.

Out of the total patients, 25 cases had a history of seizures, while 13 cases did not. Out of the total 27 cases with pregnancy epilepsy, 13 cases already had epilepsy, while, 14 cases experienced seizures for the first time in their pregnancy. From the 38 cases with previous seizures, 11 cases had no pregnancy seizures (8 cases had a history of active epilepsy, 2 cases had non active epilepsy, and one of the patients experienced epilepsy in her childhood only once), while, 27 cases experienced pregnancy seizures. Six cases had a family history of epilepsy and 32 had no such history. In a study in England, in 1974, 59 pregnant women had epilepsy, out of whom, 14 cases experienced their first seizure in pregnancy: 7 cases in the first pregnancy, 5 cases in the second, one case in the third, and one case in the fifth pregnancy. Thirty eight cases had idiopathic and 7 cases had symptomatic epilepsy. In the former group, 11 cases had only one seizure, and 5 cases had recurrent seizures in the very same pregnancy (29). In Canada, 55 patients had a history of idiopathic epilepsy and 3 cases experienced seizures in pregnancy for the first time (27).

In our study seizure attacks occurred in the third trimester of pregnancy, except one case of CVT, which was in the second month. The 8 cases who were epileptic had frequent attacks.

The England study reported pregnancy seizures from week 10 to 38, one case upon delivery, and one case postpartum (29). None of the cases had seizures upon delivery in the study in Australia and seizure recurrence in pregnancy was reported between 30 and 50% in the study conducted in Australia (9).

Incidence of different seizures is portrayed in Table 4 (76.3% GTC (generalized tonic-clonic), 13.2% Juvenile Myoclonic Epilepsy (JME), and 2.6% Focal-Generalized, and 7.9% Complex Partial Seizures (CPS). In the 22 patients with active epilepsy, 5 cases had myoclonic jerks, and 17 cases did not. No myoclonic jerks was reported in patients with inactive epilepsy or those experiencing their first epileptic seizure in pregnancy. In Australia, in a study on 75 pregnant epileptic women, the majority of the cases

(82.7%) had GTC (9). The study in Canada reported most patients with GTC; two cases had absence, and 4 cases had focal or psychomotor epilepsy (27). In Italy, GTC was observed in 39.3% of the cases, localized in 47.1%, and unknown in the rest (28).

Etiology of Epilepsy in the Present Study: Only 5 out of our total 38 patients had abnormal neurological examination. According to the assessments, one case was caused by AVM, another case by head trauma, one case by tumor; epilepsy in 24 cases had unknown etiology. The causes of the first seizures in pregnancy were eclampsia in 7 cases, CVT in 3 cases, and TTP in one case. The English study reported the etiology of symptomatic epilepsy as including meningitis, brain abscess, encephalitis, meningioma, and head trauma, none of which was observed in the present study (29). Epilepsy in the study in Canada was caused by head trauma in 5 cases, and brain aneurysm in 4 cases (27). In a study done in Africa, prevalence of eclampsia was reported at 1.02% (31).

In this study, epileptic patients mostly used Carbamazepine, in addition to a few cases of Lamotrigine, Levetiracetam, and Sodium Valproate. Seven cases received multi-drug regimens (2 drugs), and 13 cases received single-drug regimens. Seizures were seen in 1 case of single-drug patients (14%), and 7 cases of multiple-drug cases (54%), almost four times the single-drug patients.

In Australia, 70.7% of pregnant women with a history of epilepsy received anti-epileptic medications prior to pregnancy. Epilepsy was controlled in 46 patients with only one or two drugs. The most common anti-epileptic medication was Phenytoin (81%), followed by Phenobarbital 29.3%, Primidone 20.7%, Carbamazepine 13.8%, and Sodium Valproate 5.2%. Out of the said patients, 39.6% received only one medication, 39.6% two medications, 17.4% three, and 3.4% more than three medications (9).

In Italy, recurrence of seizures, mostly GTC seizures, was higher in those receiving Lamotrigine (58.2%), and there was no seizure recurrence in 75% of Valproate users, 67.3% of Carbamazepine users, and 73.4% of Phenobarbital users (28).

Conclusion

More than 6 in 1,000 pregnant women have epilepsy. Though without a history of epilepsy, less than 4 in 1,000 pregnant women are afflicted with seizures, mostly caused by eclampsia. Seizures increased in 21% of epileptic pregnant patients, and declined in 21% of the cases.

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Studying the relation of quality work life with socio-economic status and general health among the employees of Tehran University of Medical Sciences (TUMS) in 2015

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Abstract

Introduction: The importance of socio-economic variables such as level of literacy, income and occupational status and their impact on the physical and psychological wellbeing of the people is clear for experts and policymakers. In much research, the root of increase in life expectancy and improvement in other indexes of health is considered to not only progress in medicine, but also improve in socio-economic indexes. Thus, the present study aims to determine the relation between socio-economic status and general health and the consequences of disease on the quality of work life of the employees of Tehran University of Medical Sciences (TUMS).

Methodology: The present cross-sectional research is of descriptive-analytical type, and was conducted in faculties of TUMS in 2015, and the population under study included all the 1,238 non-academic employees of the TUMS. The required data was collected by the Quality of Work life (QWL) questionnaire. This questionnaire was based on Walton components and Socio-economic Status (SES) questionnaire, and was designed in order to evaluate socio-economic status and has 4 components. The data on general health was collected by Goldberg and Hillier 28-Item General Health Questionnaire (GHQ-28) (1979) that has 4 subscales. Then, the collected data was recorded by SPSS version 18 software and was then analyzed by common methods of descriptive-analytical statistics.

Results: The results demonstrated that the frequency of socio-economic status of the employees under study were 179 persons (53.3 percent) for low level, 109 persons (35.5 percent) for moderate level, and 19 persons (6.2 percent) for high level, and the frequency of the quality of work life of the employees under study were 10 persons (3.3 percent) for low level, 108 persons (35.6 percent) for moderate level, and 185 persons (61.1 percent) for high level.

Conclusion: Considering the importance of quality of work life in socio-economic status, it is proposed that the following measures be taken into account: appropriateness of salary to economic factors such as inflation; demand and supply in fair and adequate payment; paying more attention to the physical conditions of workplace, e.g. light, cooling and heating facilities to prepare a secure and healthy workplace; preparing some possibilities for the employees so that they can further develop their personal talents and have opportunities for making progress in their specialized field by encouraging them to be creative and innovative to lead them to promotion in the organization; and providing continuous security and growth opportunities for the employees, allowing them to take initiatives, and provide them with any information or skill that they need in workplace to develop their human capabilities. In the present study no significant relationship between the quality of work life and general health, socio-economic status and quality of work life, and also general health and socio-economic status, was found.

Key words: Quality of Work Life (QWL), socio-economic status, general health, faculty employees.

Introduction

Nowadays organizations are considered as living creatures with an identity that is independent of their members (1), and by this new identity, they can affect the behavior of their employees. This personality and identity can be organizationally healthy or ill (2). Miles introduced the notion of "organizational health" in 1969. In his view, organizational health refers to the durability and persistence of an organization in its environment and adaptability to it, and also developing its own ability to be more adaptable to it (3). Wrong choice, misuse of skills, and lack of proper atmosphere for allowing creativity to flourish can endanger the health and promotion of the organization. When a position or office is proposed to the employees that is not commensurate with their dignity, it can lead to disobedience, absence from work, delays, and resignation. In an organization, if communication at all levels is not multilaterally and openly established, and full confidence does not exist between different parts, misunderstanding and disharmony will be created. When goals are not clear, they become vague, and as the result, the employees do not make a concerted effort to achieve the goals(4).

Recently the human factor has been considered as the most important and sensitive organizational element, and most of the new theories of organization and management have referred to this sensitive factor (5). One of the most important parameters affecting the performance of human resources is the role of individual health in improving the economy of a country. Therefore, any kind of planning or investment in human resources that leads to protect and promote the health of employees, can eventually lead to increased efficiency and return on investment (ROI) (6). Nowadays the notion of Quality of Work life has turned into a major social issue all around the world, while in the past the emphasis was only on personal life. From the 1970s onward, improving the employees' quality of work life has been considered as one of the most important issues in many organizations, including health care organizations (7). Due to the inevitability of some of the stress factors in health care organizations and the need to prevent psychological stress effects, one of the duties of managers in these organizations is taking some measures and actions to improve the quality of work life, and teaching coping techniques (8). Although there is no formal definition of quality of work life, however, Walton's theory has offered the most comprehensive components of quality of work life plan (9). He has offered the main components of quality of work life in four dimensions that are as follows: meaningfulness of work; organizational and social fit of work; provocativeness, richness, and fruitfulness of work; and security, developing skills, and continuous learning in work (10).

Quality of work life programs deal with various objective and subjective areas of employees' issues. Quality of work life is a process by which the organization's members can participate in making decisions that generally affect their job and particularly their work environment; in doing so,

they can use open and appropriate communication ways that have been designed for this purpose. As a result, their work-related stress will diminish and employees' satisfaction will increase. An organization that pays attention to its employees' quality of work life will benefit from having a competent workforce, the signs of which are willingness to cooperate with the management and improvement in the performance of the workforce (11).

General health is a subset of the health system and is defined as a set of important social activities and measures that are based primarily on prevention strategies (12). One of the characteristics of a healthy organization is that the physical and psychological health of the employees are as important and interesting as production and productivity for its managers (13). In recent decades various studies have been conducted on the relationship between work and stress and its consequences for health care workers. In these studies, some topics such as productivity, occupational accidents, absenteeism, and increase in physical and mental damage in various occupational groups have been scrutinized (14). The profession of the people is one of the main causes of stress in their life. There is more stress in professions in which human contact is important (15). Socio-economic determinants of health such as level of income, education, job, nutrition, and social class are far more important in catching diseases than the biological factors, and they play an important role in human health (16). In the social hierarchy, people take different positions based on their occupational status and level of education and income, and the position of the people in this system is defined by their socio-economic status. Although occupation and level of income and education all determine the position of an individual in the social hierarchy, and these factors are generally not separate from each other, they should be individually studied in order to realize their role in health. Level of education makes differences in terms of having access to information and level of expertise to take advantage of knowledge, while occupation entails differences in having access to scarce material goods. Occupational status includes both of these aspects, and also includes benefits of working in certain occupations such as dignity, privilege, and technical and social skills and power (17).

The present age organizations have a strategic approach to human resources and consider it as a smart and valuable asset, and desire to further improve the quality of life and job satisfaction of their employees (18). Workplace health and psychological health are created by improving quality of life indexes, and it is necessary to pay attention to this issue in all organizations in order to prevent job burnout and low efficiency. Measuring the understanding and sense of people about their own health in order to assess the status quo, investigating the efficacy of health interventions and health care, and implementing appropriate health services are of crucial importance (19). Socio-economic status is an important factor that affects the possibility of taking advantage of medical services, while the wealthy social groups, which in every respect are better equipped than the disadvantaged groups, can sooner and better convert

their need to demand, and hence, take more advantage (20). A survey of 17,000 employees in England showed that occupation rank itself plays a more important role in health than some risk factors combined, such as smoking and high blood pressure and cholesterol. Since healthy human is the axis of sustainable development, and also modern societies call for providing a proper environment for production and having the required speed to achieve comprehensive development, it is clearly the responsibility of health practitioners and researchers to investigate and explain all the social factors influencing health, and then give feedback to the macro policy-makers in the form of scientific and practical information. In this way, they can help a great deal in sustainable development (21).

The importance of socio-economic variables such as level of education, income, and occupational status, and their impact on physical and psychological health of the people, is clear for health experts and policy-makers. It has been suggested in many studies that increase in life expectancy and improvement in the other health indexes are not merely because of medical progress, but in many cases are due to the improvement in socio-economic indexes (22).

Global data show that environment, socio-economic status, housing, job security, access to health facilities, and human behavior are all crucial factors in securing or weakening health (23). Researches in many countries show extensive inequalities and differences in health conditions of various socio-economic, racial, ethnic, and geographical groups in society. This is indicative of the crucial impact of various factors on health that include reducing social exclusion, alleviating educational shortcomings, reducing insecurity and unemployment, and improving housing standards (24). Studies on the relationship between health and socio-economic status of a population have originally started from England. Gradually this type of research was of interest to researchers in other countries and useful data was collected in this field, all of which show that individuals and families who are in lower social groups, in comparison to higher and richer social groups, experience more and premature death, and diseases and defects are more common in this group; this inequality can be seen in all European countries, and is an undeniable fact that needs more attention (25). To this aim, this research has been conducted to determine the relationship between socio-economic status and general health, and show the consequences of disease that affects the quality of work life of TUMS's employees.

Methodology

This study is of descriptive-analytical type that has been conducted by cross-sectional method in faculties of TUMS in 2015, and the population under study included all the 1,238 non-academic employees of TUMS. The inclusion criterion for the study was being a non-academic employee in TUMS; data collection was conducted in 10 out of 11 faculties of TUMS, and one faculty was excluded from the study due to lack of cooperation. Quality of Work life (QWL) questionnaire was used to collect the required data.

This questionnaire was based on Walton's components, including fair and adequate payment (questions 1 to 5), safe and healthy working environment (questions 6 to 8), providing growth opportunities and continuous security (questions 9 to 11), having respect for the laws in the organization (questions 12 to 17), social dependence of work life (questions 18 to 20), the overall atmosphere of life (questions 21 to 25), social integrity and solidarity (questions 26 to 29), and developing human capabilities (questions 30 to 32). This questionnaire has been conducted by many researchers and contains 32 items, and is based on a Likert scale from very low (1 point) to very high (5 points).

Walton showed the reliability coefficient of the questionnaire to be 0.88 (26). Also in 2006 Rahimi reported the reliability coefficient of the test to be 0.85 (27). Furthermore, in this study, the Socio-economic Status (SES) questionnaire is implemented, which takes four components of income, economic class, education, and housing into account, and generally consists of 6 demographic questions and 5 key questions. The criterion scaling of questions in this questionnaire has 5 options and responses are graded on a continuum, from very low (1) to very high (5). Eslami et al. (28), by asking 12 sports experts, confirmed the face and content validity of this questionnaire. Also by applying Cronbach's alpha test, the reliability of the questionnaire was calculated as 0.83. General health data were collected by Goldberg and Hillier 28-Item General Health Questionnaire (GHQ-28) (1979). It has 4 subscales and each subscale contains 7 questions. These subscales include somatic symptoms, anxiety and insomnia, social dysfunction and severe depression. Of the 28 items of the questionnaire, questions 1 to 7 are about somatic symptoms, questions 8 to 14 ask about anxiety and insomnia, questions 15 to 21 assess social dysfunction, and finally, questions 22 to 28 are related to severe depression (29, 30).

In standardization of GHQ-28 questionnaire in Iran, Houman (1997) implemented Cronbach's alpha coefficient for the subscales to assess the internal consistency, and reported them to be 0.85, 0.87, 0.79, and 0.91, respectively. For the overall score, that demonstrates general health, he reported 0.85. Goldberg and Blackwell (1972), by using a clinical interview checklist for 200 surgery patients in England, concluded that more than 90% of the sample was correctly classified by the questionnaire as sick or healthy. Moreover, they reported the correlation coefficient between the scores of GHQ-28 questionnaire and the result of clinical evaluation of the results to be 0.80. Also they reported sensitivity and specificity as 0.84 and 0.82, respectively.

In order to assess the socio-economic status, the Socio-economic Status (SES) Questionnaire (Ghodratnama, 2013) was generally implemented. This questionnaire contains 4 components, namely income, economic class, education, and housing, and in total contains six demographic questions and 5 key questions. Criterion scaling in this questionnaire consisted of five responses, and the scoring method for each response was from very

low (1) to very high (5). Eslami et al. (28), by asking 12 sports experts, confirmed the face and content validity of this questionnaire. Also by applying Cronbach's alpha test, the reliability of the questionnaire was calculated as 0.83 (26). Thus, the collected data were recorded by SPSS version 18 software and then underwent statistical analysis. By using common methods in descriptive-analytical statistics, the results were demonstrated in the forms of tables, diagrams, etc.

Results

The results demonstrated that the frequency of socio-economic status of the studied employees were 179 for low status (58.3%), 109 for medium status (35.5%), and 19 for high status (6.2%).

Table 1: Socio-economic Status

Socio-economic status	Frequency	Percentage
low	179	58.3
medium	109	35.5
high	19	6.2
total	307	100

The results demonstrated that the frequency of QWL of studied employees were 10 for low status (3.3%), 108 for medium status (35.6%), and 185 for high status (61.1%).

Table 2: Frequency and percentage of Quality of Work life (QWL) status

QWL	Frequency	Percentage
low	10	3.3
medium	108	35.6
high	185	61.1
total	303	100

The results demonstrated that the mean and standard deviation of dimensions of quality of work life were 17.09 and 3.65 for fair and adequate payment, 8.44 and 2.95 for safe and healthy working environment, 9.62 and 2.61 for providing growth opportunities and continuous security, 19.76 and 6.39 for having respect for the laws of the organization, 9.12 and 4.30 for social dependence of work life, 15.41 and 5.04 for the overall atmosphere of life, 12.84 and 2.49 for social integrity and solidarity, and 9.08 and 2.83 for developing human capabilities.

Table 3: Status of QWL's dimensions

Dimensions of QWL	Mean	Standard Deviation
Fair and adequate payment	17.09	3.65
Safe and healthy working environment	8.44	2.95
Providing growth opportunities and continuous security	9.62	2.61
Having respect for the laws in the organization	19.76	6.39
Social dependence of work life	9.12	4.30
Overall atmosphere of life	15.41	5.04
Social integrity and solidarity	12.84	3.49
Developing human capabilities	9.08	2.83

The results demonstrated that in the somatic dimension of employee's general health, 135 persons were at very low level (43.4%), 120 persons were at slight level (38.6%), 43 persons were at medium level (13.8%), and 13 persons were at severe level (4.2%). In anxiety dimension, 108 persons were at very low level (35.3%), 125 persons were at slight level (40.8%), 60 persons at medium level (19.6), and 13 persons at severe level (4.2%). In social dimension,

101 persons were at very low level (32.5%), 171 persons at slight level (55.0%), 34 persons at medium level (10.9%), and 5 persons at severe level (1.6%). In depression dimension, 260 persons were at very low level (83.6%), 40 persons at slight level (12.9%), 7 persons at medium level (2.3%), and 4 persons at severe level (1.3%). In total, the number of employees at very low, slight, medium, and severe levels were 129 (41.5%), 138 (44.4%), 41 (13.2%), and 3 (1.0%), respectively.

Table 4: Status of general health and its dimensions

Dimensions of General health	Status				
	very low	slight	medium	severe	total
Somatic	135 (43.4%)	120 (38.6%)	43 (13.8%)	13 (4.2%)	311 (100%)
Anxiety	108 (35.3%)	125 (40.8%)	60 (19.6%)	13 (4.2%)	306 (100%)
Social	101 (32.5%)	171 (55%)	34 (10.9%)	5 (1.6%)	311 (100%)
Depression	260 (83.6%)	40 (12.9%)	7 (2.3%)	4 (1.3%)	311 (100%)

The results of the test show that among the employees that in terms of quality of work life those who were at a low level, 5 persons (50%) had slight general health. Also those of the employees that had medium quality of work life, 53 persons (49.5%) were at very low level of general health. 82 persons (44.3%) of the employees that experienced a high level quality of work life, had slight general health. The results of Fisher Test demonstrated that there is no significant relationship between quality of work life and general health (p=0.211).

Table 5: Quality of work life status in terms of general health

QWL	General health					probability
	very low	slight	medium	severe	total	
low	3 (30%)	5 (50%)	2 (20%)	0 (0%)	10 (100%)	
medium	53 (49.5%)	45 (42.1%)	8 (7.5%)	1 (0.9%)	107 (100%)	0.211
high	71 (38.4%)	82 (44.3%)	30 (16.2%)	2 (1.1%)	185 (100%)	

The results of the test demonstrate that among the employees in terms of socio-economic status those who were at a low level, 5 persons (50%) had low quality of life. Of those employees who had a medium socio-economic status, 59 persons (55.1%) had low quality of life. Also, 106 persons (59.2%) of the employees with high socio-economic status, had low quality of work life. The results of Chi-squared test show that there is no significant relationship between socio-economic status and quality of work life (p=0.106).

Table 6: QWL's Status in terms of socio-economic status

Socio-economic status	Quality of work life				probability
	low	medium	high	total	
low	5 (50%)	2 (20%)	3 (30%)	10 (100%)	
medium	59 (55.1%)	41 (38.3%)	7 (6.5%)	107 (100%)	0.106
high	106 (59.2%)	64 (35.8%)	9 (5.0%)	179 (100%)	

The results of the test show that among the employees with a very low level of general health, 71 persons (55.9%) had high quality of work life, while among the employees with slight general health, 82 persons (62.1%) had high quality of work life. Also among the employees with a medium general health, 30 persons (75.0%) had high quality of work life, and among the employees with severe general health, 3 persons (66.7%) had high quality of life. The results of Fisher test show that there is no significant relationship between general health and quality of work life (p=0.211).

Table 7: General health in terms of quality of work life

General health	Quality of work life				probability
	low	medium	high	total	
very low	3 (2.4%)	53 (41.7%)	71 (55.9%)	127 (100%)	
slight	5 (3.8%)	45 (34.1%)	82 (62.1%)	132 (100%)	
medium	2 (5%)	8 (20%)	30 (75.0%)	40 (100%)	0.211
severe	0 (0.0%)	1 (33.3%)	2 (66.7%)	3 (100%)	

The results of the test show that among the employees with a very low level of general health, 69 persons (54.8%) had a low socio-economic status, and among the employees with a slight level of general health, 78 persons (58.2%) had a low socio-economic status. Also among the employees with a medium level of general health, 29 persons (70.7%) had a low socio-economic status, and among the employees with severe general health, 2 persons (66.7%) had a low socio-economic status. The results of Fisher test show that there is no significant relationship between general health and socio-economic status (p=0.071).

Table 8: General health in terms of socio-economic status

General health	Socio-economic status				probability
	low	medium	high	total	
very low	69 (54.8%)	52 (41.3%)	5 (4%)	126 (100%)	
slight	78 (58.2%)	42 (31.3%)	14 (10.4%)	134 (100%)	0.071
medium	29 (70.7%)	12 (29.3%)	0 (0.0%)	41 (100%)	
severe	2 (66.7%)	1 (33.3%)	0 (0.0%)	3 (100%)	

Discussion and Conclusion

The results of the study show that the frequency of socio-economic status of the employees under study were 179 (53.3%) for low level, 109 (35.5%) for medium level, and 199 (6.2%) for high level. Also the frequency of employees quality of work life were 10 (3.3%) for low level, 108 (35.6%) for medium level, and 185 (61.1%) for high level.

The results also demonstrated that the mean and standard deviation of QWL's dimensions respectively are as follows: 17.09 and 3.65 for fair and adequate payment, 8.44 and 2.95 for safe and healthy working environment, 9.62 and 2.61 for providing growth opportunities and continuous security, 19.76 and 6.39 for having respect for the laws in the organization, 9.12 and 4.30 for social dependence of work life, 15.41 and 5.04 for the overall atmosphere of life, 12.84 and 3.49 for social integrity and solidarity, and 9.08 and 2.83 for developing human capabilities. In the physical dimension of employees' general health, 135 persons (43.4%) are at very low, 120 persons (36.6%) at slight, 43 persons (13.8%) at medium, and 13 persons (4.2%) at severe level. On the anxiety dimension, 108 persons (35.3%) are at very low, 125 persons (40.8%) at slight, 60 persons (19.6%) at medium, and 13 persons (4.2%) at severe level. On the social dimension, 101 persons (32.5%) are at very low, 171 persons (55%) at slight level, 34 persons (10.9%) at medium, and 5 persons (1.6%) at severe level. On the depression dimension, 206 persons (83.6%) are at very low level, 40 persons (12.9%) at slight, 7 persons (2.3%) at medium, and 4 persons (1.3%) at severe level. In total, the number of employees at very low, slight, medium, and severe levels are 129 (45.5%), 138 (44.4%), 41 (13.2%), and 3 (1%), respectively.

The results show that of those among the employees who were at a very low level of general health, 69 persons (54.8%) had a low socio-economic status. Among the employees who had slight general health, 78 persons (58.2%) were at a low socio-economic status. In the group with medium general health, 29 persons (70.7%) had a low socio-economic status, and in the group with a severe level of general health, 2 persons (66.7%) had a low level of socio-economic status. The results of Fisher test show that there is no significant relationship between general health and socio-economic status (p=0.071).

In a study entitled "The relationship between socio-economic status and general health in single mothers", Shahram Mami, et al (2014) investigated the most important factors that have an influence on the general health of single mothers. This study was of cross-sectional-analytical type, the population under study was all the women covered by the State Welfare Organization of Iran-Ilam Branch, and the sample size was 750 people. The data was collected by using Socio-economic Status (SES) questionnaire and GHQ-28, and were recorded by SPSS version 16 software and then underwent various statistical analyses such as mean, standard deviation, and logistic regression analysis. The mean and standard deviation of the age of participants were 19.88 and ± 53.3, respectively. According to the results of this study, 79.8% of the participating women did not have good general health. In the logistic regression analysis, the most important predictors of general health for single mothers were age (p=0.004), extending the time of coverage (0.001), and having a diagnosed illness (p=0.001). Moreover, low literacy, undesirable economic status, and having chronic illnesses were the most important factors influencing the general health of single mothers. Therefore, paying more attention to this stratum of society, which in terms of general health is at a lower level than the other strata, requires planning and collective effort (24).

In his study entitled "Characteristics of economy, society, demography, and mental health in old age", Seifzadeh has implemented a survey method and questionnaire. The statistical population of the study was all the residents of Azarshahr 65 years old or more. In this study, stratified random sampling method (proportional) was implemented, and the sample size consisted of 312 persons. The results show that:
1- Men's mental health was more than that of women.
2- Mental health of participants who live with their spouse is more than those who have lost their spouse.
3- With aging, the health of the elderly deteriorates.
4- By increasing social support, the health of the elderly increases, and those of the elderly with higher social support, have better mental health than their peers with less social support.

5- There is a one-to-one relationship between socio-economic status and mental health, so that the elderly with a high socio-economic status are more healthy than other elderly. (25) Javadi, et al (2011) in a study entitled "Economic burden and health costs of chronic diseases in Iran and the World", investigated the economic burden and health costs of this world crisis and the challenges ahead, and proposed a number of prevention and control strategies. This study was a review of library resources and digital and printed literature from different scientific journals, and searching in valid websites such as Pubmed, SID, ISI, etc. Noncontagious diseases cause 35 million deaths annually, and are considered as a major obstacle to development in countries. These diseases have had extremely bad effects on the poor and vulnerable groups of the society, and have left many people in poverty (32).

In a study entitled "Predicting quality of life based on general health, social support, and self-efficacy in cardiovascular patients of Yasouj in 2014", Moghadam et al studied 70 cardiovascular patients going to medical centers and clinics of Yasouj. These patients were selected by convenience and purposive sampling methods. In this study, there was a significant relationship between quality of life, self-efficacy, general health, and social support (p<0.001). The results of the regression analysis show that all the predictor variables can predict 76% of the changes in the criterion variable (quality of life); furthermore, the results of stepwise regression analysis show that each one of the variables of general health, self-efficacy, and social support can respectively predict 69%, 4%, and 3% changes in criterion variable. By developing supportive social networks and educating self-efficacy skills, we can improve general health and quality of life of cardiovascular patients (33).

Rezghi Shirsavar et al conducted an applied research entitled "A survey of the relationship between occupational stress, general health, organizational intelligence, and job satisfaction with the performance of employees of Islamic Azad University – Shahre Qods Branch". The statistical population of this study consisted of all the employees of Islamic Azad University – Shahre Qods Branch that were in total 222 persons, and based on Morgan Table, 144 persons were selected as sample. In this study, GHQ-28 questionnaire, which explains people's cognitive, emotional, and behavioral performance, was used. The Standard 12-item Job Descriptive Index (JDI) questionnaire was used for investigating components of job satisfaction, and Alireza Faghihi's questionnaire (2009), which was reduced to 20 items, was used for investigating components of organizational intelligence. The results of this study show that the variables under study, namely general health, job satisfaction, and organizational intelligence have positive impact on the performance of the employees of Islamic Azad University – Shahre Qods Branch, but considering the provided data, there was a negative impact between occupational stress and performance (meaning the more occupational stress, the less score on performance). Generally, job satisfaction had the highest level of impact. Considering

the regression results, and in order to get the highest score on performance, it is suggested to managers of Islamic Azad University – Shahre Qods Branch to enhance the job satisfaction of the employees and at the same time reduce their occupational stress. (34) Bakhshayesh in a study entitled "Investigating the relation between general health and personality types and job satisfaction of employees working in Yazd Health Center", which investigated the relation between general health and personality types and job satisfaction of employees, 71 of the 21 to 56-year-old male and female employees working in Yazd Health Center were selected by consensus sampling method and studied by the use of GHQ-28 questionnaire, Standard 12-item Job Descriptive Index (JDI) questionnaire, and NEO Five-Factor Personality Inventory. The method of study was descriptive-correlational, and the data was analyzed by statistical tests of Pearson correlation coefficient, t-test, ANOVA, and stepwise regression. The results of the study showed that general health has a direct relationship with neurotic personality type (r=0.542), and has an inverse relationship to extroversion and favorability (r= -0.34 and r= -0.38, respectively), and has no relationship to flexibility and responsibility. There was an inverse relationship between general health and three components of job satisfaction (nature of work, job promotion, salary and total score of job satisfaction), and had no relationship to satisfaction of coworkers and supervisors. Low general health was consistent with neurotic personality type, and high general health was related to extrovert personality type and favorability. Low general health was consistent with low job satisfaction, and vice versa. In this study, in terms of personality types and job satisfaction, there was only a correlation (p=0.01) between satisfaction of the nature of work and extroversion. Therefore, we can conclude that any change in personality types or with any decrease or increase in general health, the level of job satisfaction changes (35).

The results of this study show that age, sex, and academic degree have a direct relationship with socio-economic status. In addition, it was noticed that age and academic degree have a positive relationship with general health, however, age, sex, and academic degree did not have a positive relationship to quality of work life. Among the various dimensions of quality of work life, socio-economic status had a significant relationship with fair and adequate payment, safe and healthy working environment, providing growth opportunities and continuous security, and developing human capabilities. As a result, considering the importance of quality of work life in socio-economic status, it is proposed that the following measures be taken into account: appropriateness of salary to the economic factors like inflation; demand and supply in fair and adequate payment; paying more attention to the physical conditions of workplace, e.g. light, cooling and heating facilities to prepare a secure and healthy workplace; preparing some possibilities for the employees so that they can further develop their personal talents and achieve the opportunities for making progress in their specialized field by encouraging them to be creative and innovative that leads to the promotion of the organization; and providing

continuous security and growth opportunities for the employees, allowing them to take initiatives, and provide any information or skill that they need in the workplace to develop their human capabilities.In investigating the relationship between general health and quality of work life, there was a significant relationship between physical and anxiety dimensions of general health and quality of work life. Therefore, by improving any component of general health, a positive impact on the quality of work life will be achieved. On the other hand, in this study, there was no significant relationship between quality of work life and general health, socio-economic status and quality of work life, and general health and socio-economic status.

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Factors that encourage early marriage and motherhood from the perspective of Iranian adolescent mothers: a qualitative study

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Abstract

Background: Early marriage and motherhood is one of the most important health challenges in developing countries and affects mothers, children, families and communities, thus their causes and predisposing factors must be explored. The aim of this study was to explore the factors that encourage early marriage and motherhood in Iranian culture.

Methods: Inductive Conventional Content Analysis approach was used in this qualitative study. Face to face in-depth semi-structured interview were conducted with 16 Iranian adolescent mothers in the Kerman province of Iran. Data collection continued until acquiring data saturation and MAX-QDA software was used for analysis of the data.

Results: Two main categories (external incentives and internal incentives) and 8 sub-categories (inappropriate economic condition, instability of family, desire and encouragement of parents, copying others, position (status), subjective beliefs, meeting inner needs and desires, insufficient awareness) were extracted from the data.

Conclusion: Various factors (personal, social, economic, cultural, spiritual and technological) encourage adolescents to early marriage and motherhood. Understanding of these factors can help health care providers, who work in the field of mother and child health, to provide appropriate assessment and interventions for improvement of the health of this group of society.

Key words: Adolescent Mothers, Marriage, Encourage, Iran, Qualitative

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Introduction

Marriage is one of the most important life events and is necessary for development of societies(1), but early marriage will be followed by unpleasant feelings if participants are not being prepared to take on new responsibilities(2). Early marriage which includes any legal or illegal marriage under the age of 18 (3, 4) is among the important challenges of the world, and it is estimated to reach 150 million cases by 2030 (5). Early marriages exist in many countries, especially developing countries, but most cases (46%) are related to South Asian countries(3). Early marriage and motherhood in Iranian culture has long been approved and the highest number of marriages has been seen among 15-19 year old girls(6, 7).

Although adulthood is one of the requirements for accepting mother's role, an increasing number of adolescent mothers are among serious challenges of many countries(8). According to the World Health Organization, more than 16 million adolescents become mothers each year(9). Such number is the lowest in South Korea and it is the highest in sub-Sahara Africa. Among 1,000 Iranian adolescent girls, 27 become mothers(10). Adolescent mothers, who must simultaneously go through two developmental crises (motherhood and adolescence), are not physically and emotionally ready to take the roles of mother, wife and their consequent responsibilities, and they are not able to overcome social and psychological challenges (11, 12).

Early motherhood has many consequences for girls, society, and the environment(8). It also causes financial problems for children's future and reduced social support(13). Child abuse, behavioral problems, shock, low self-esteem, depression and role conflict are seen in adolescent mothers(11). Low accountability, emotional fluctuations, lack of knowledge and experience, less desire to engage emotionally with the baby and breastfeeding, lack of attention to health and safety issues, the influence of peers and the probability of high risk behaviors during adolescence; highlight the importance of health care providers' role in dealing with such clients(14). In developed countries, there are several strategies for protect girls from early motherhood. In developed countries early motherhood is considered specially along with cardiovascular disease, cancer, and mental disorders (15), and it is studied by gynecologists, obstetricians, pediatricians, psychologists, sociologists and family physicians(16). Studies have indicated that many factors are effective on early marriage and motherhood including; economic factors (poverty, unemployment) (4, 6, 17, 18), social factors (gender discrimination, school dropout, social norms, mass media, migration from rural to urban areas, the influence of peers)(4, 15, 17, 19-21), cultural and religious factors (prevention from unrestrained sexual promiscuity, religious and cultural incentives, ethnicity and race) (19, 22), safety factors (war, rape, kidnapping)(3, 17, 22), psychological factors (low self-esteem, mental health problems, anti-social behavior, sense of emotional maturity)(19, 23, 24), political and legal factors (the national laws for marriage and sexual relations, legal gap)(23, 25), organizational factors (views of health care givers and access to services)(23), family factors (breakdown of family structures, the absence of father, family values, social and psychological problems of parents, parents demand)(3, 24), and individual factors (inability to continue education, love, desire to have children, sense of empowerment)(19).

Since, the provision of desirable healthcare services to adolescent mothers requires understanding of factors that encourage marriage and pregnancy through qualitative studies, this study was conducted to determine the factors that encourage early marriage and motherhood from the perspective of Iranian adolescent mothers. Findings of this study can lead healthcare teams to make proper decisions.

Materials and Methods

Design: This qualitative study was conducted through inductive conventional content analysis. Content analysis is a suitable method for obtaining valid and reliable results from textual data in order to create knowledge, new ideas, facts and a practical guide for performance, which extract concepts or descriptive themes from the phenomenon. This approach is recommended when there is not enough knowledge about the phenomenon or if this knowledge is fragmented (26).

Participants & Setting: This study was conducted in 2016 in Kerman province of Iran. Kerman is located in the south east of Iran, and has a high rate of adolescent mothers. A total of 16 adolescent mothers who met the inclusion criteria (having maximum of 19 years of age at the time of first birth, have a child or children up to 2 years of age, marriage of legal form, being able to speak Persian, being willing to share personal experiences and good cooperation with the researcher) participated in this study. Participants were selected purposefully with maximum variation in age, child's age, place of residence (urban or rural), financial situation (Table 1).

Data collection: Data were collected through in-depth semi-structured interviews conducted by first author (PhD candidate in nursing).The interviews were focused on the perspectives of the participants. Adolescents were asked to explain factors that have encouraged them towards early marriage and motherhood. Interviews began with a general question and progressed to specific questions. Time and place of the interviews were set with the agreement of the participants which were mainly at home. Interviews lasted for 45 to 60 minutes and during a 5-month period from March to August 2016. Entire interviews were recorded and transferred into audio files to be entered in the computer. Data collection continues until data saturation, when no new information was obtained from the interviews

Data Analysis: Analysis of the data was done by using the inductive conventional content analysis approach (Graneheim & Lundeman)(26). Predetermined categories were not used and categories emerge from the data. First audio files of interviews were listened to and recorded

interviews were immediately transcribed verbatim and then read several times to gain a general impression. The resulting text from the interviews was read line by line and broken down into meaning units (words or sentence or paragraphs), which were then condensed, abstracted, coded, and labeled. Then, the codes were re-read in order to be arranged into categories and sub-categories based on their similarities and differences. The first author performed data coding and all co-authors supervised the coding process. If there was a disagreement over the coding, the authors discussed and negotiated the codes until they achieved agreement. Data analysis was done continuously and simultaneously with data collection and the data and the generated codes were constantly compared. MAXQDA10 software was used also.

Trustworthiness: In this study, credibility increased through prolonged engagement with the researcher, spending sufficient time for data collection and analysis, favorite communication with participants, member check and peer check. To increase dependability, the baseline review of literature was limited at the beginning of the study and the opinion of an expert (outside the research team) was used. For confirmability, the research process was accurately recorded to make the follow-up possible. To ensure transferability, results of the study were checked with numbers of similar samples who were not among the participants.

Ethical considerations: The Kerman University of Medical Sciences Human Research Committee approved this study (ethics approval number: IR.KMU.REC.1394.591). Purpose of the study, how to publish results, and possible risks, dangers and benefits were explained to the participants. Participant anonymity, privacy and confidentiality were maintained. Interviews were conducted in a private and non-threatening environment and audio files were be kept anonymously in a secure place. Participants were ensured that their responses would remain confidential. Participants were also informed that participation in the study was voluntary and they could withdraw at any time. Written informed consent for participation in the study and recording of the interview was obtained. During the data collection, the first author was ready to provide help and support; if necessary.

Table1: Demographic characteristics of participants

Participants	Age at childbirth (year)	Age at marriage (year)	Children age (month)	Place of living	Current Education level	Education level of husband	Age difference with husband (year)	Job of husband
1	18.5	17	6	Rural	Diploma	Bachelor	4	Worker
2	15	14	24	Rural	Middle school	Diploma	11	Farmer
3	17	15	6	Urban	High school	Diploma	2	Self employed
4	18	16	13	Rural	High school	Diploma	14	Worker
5	14	12	14	Urban	Middle school	University Diploma	10	Engineer
6	17	14	8	Urban	Diploma	University Diploma	7	Jobholder
7	16	13	4	Rural	Middle school	Diploma	11	Self employed
8	17	14	18	Urban	Diploma	Diploma	10	Self employed
9	18	15	14	Urban	Diploma	Diploma	13	Engineer
10	17	14	23	Urban	University Diploma	Bachelor	10	Engineer
11	15	15	10	Rural	High school	High school	7	Self employed
12	17	15	13	Urban	High school	Diploma	11	Jobholder
13	15	14	24	Urban	Middle school	Middle school	24	Self employed
14	17	16	22	Rural	High school	High school	10	Clergyman
15	14	13	3	Urban	Middle school	Diploma	12	Worker
16	16	14	24	Urban	Diploma	Diploma	6	Self employed

Results

In total, factors that encouraged early marriage and motherhood were classified into two main categories and eight sub-categories (Table 2).

Table 2: Main categories and sub categories of factors that encourage early marriage and motherhood

Categories	Sub categories
External incentives	Inappropriate economic condition
	Instability of family
	Desire and encouragement of parents
	Influence of others
Internal incentives	Position
	Subjective beliefs
	Meeting inner needs and desires
	Insufficient awareness

1. External incentives

 External motivations related to family, life position and community had caused adolescents to get married and become mothers.

1-1: Inappropriate economic conditions: The financial problem was one of unpleasant situations for early marriage. Some adolescents were getting married to improve economic conditions for themselves and their families (Table 3. Quotation 1).

1-2: Instability of the family: Family breakdown, divorce or death of parents had caused adolescents to get married, and separation from family created a better position for them (Table 3. Quotation 2). Trying to resolve family disputes and helping strengthen families were also among reasons stated by adolescents for pregnancy (Table 3. Quotation 3).

1-3: Desire and encouragement of parents: Early marriage of some adolescents was due to urging of their parents. Financial problems, social norms, cultural and religious issues or their personal attitude were encouraged by parents to this desire (Table 3. Quotation 4, 5).

1-4: Copying from others: Excessive interest in friendship and the need to be approved by friends affected the decision of adolescents on marriage (Table 3. Quotation 6). Early marriage of sister or brother had also encouraged adolescents to get married in order to be similar to other family members (Table 3. Quotation7).

2 - Internal incentives

 Some factors that encouraged early marriage were related to adolescents 'desires', and were originated from their beliefs.

2-1: Position: Some adolescents were married in order not to lose such an opportunity. Adequate understanding of the suitor and detecting ideal features in him, were some of the reasons of early marriage (Table 3. Quotation 8). Some of the adolescents thought that, protection of marital relations depended on childbirth. Therefore they had decided to get pregnant (Table 3. Quotation 9).

2-2: Subjective beliefs that encourage the marriage & motherhood: Some adolescents selected marriage because of their subjective thoughts and beliefs. Some considered marriage as God's will and divine destiny and were not opposed to it (Table 3. Quotation 10). The belief "the situation will get better and more comfortable by childbirth", had caused adolescents to get pregnant (Table3. Quotation 11). Early puberty and gaining some abilities had caused adolescents to imagine that they were ready to get married (Table 3. Quotation 12). Facing cultural beliefs in consequences of contraception had encouraged adolescents to get pregnant and act based on their mentalities (Table 3. Quotation 13).

2-3: Meeting inner needs and desires: Feelings of loneliness and desires, love, respect, and independence had encouraged some adolescents to be married. Adolescents wanted independence and freedom in decision making and expected to be addressed as an influential person. They were tired of parental interferences and were married for love, soul-mate, and value acquirement (Table 3. Quotation 14). Most participants expressed that they wanted a child to get rid of loneliness. Some adolescents had become lonely after separating from previous dependencies such as; family, friend, school, etc… (Table 3. Quotation 15). Also having old parents who had not been able to be friendly with their children, had encouraged adolescent girls to get pregnant and close the age gap between themselves and their children (Table 3. Quotation 16). Love and desire towards baby, and satisfying the sense of possession which is one of the characteristics of adolescence were reflected in the statements of participants (Table 3. Quotation 17).

2-4: Insufficient awareness: Some of the adolescents thought marriage was simple and viewed it as a child play as they lacked sufficient knowledge about it, its meaning and philosophy. They were assuming the marriage only by its apparent applications and had not thought about it seriously (Table 3. Quotation 18). Some of them were presuming childbirth as a simple process, and were unaware of the possible difficulties of pregnancy and childbirth (Table 3. Quotation 19). Not having enough information about the possible mechanisms of pregnancy, unfamiliar with contraceptive methods, and they referred to their imperfect knowledge in this field as the cause of early pregnancy (Table 3. Quotation 20).

Table 3: Quotations of Participants

Quotation 1 "I saw my dad and my mom were struggling financially. They had difficult to covering our costs, so I was helping them as much as I could, I was working, then I thought that it was better to get married. I wanted to leave the home earlier so I could help my parents".p4

Quotation 2 "I was nine years old when my parents got divorced ... my mother married another man. I had a lot of problems with my stepfather and half-sisters and brothers. I could not accept my stepfather as my father.P6

Quotation 3 "My mother-in-law was angry with my mother. My mother said: if you have children, the hatred and resentment between the two families will be resolved".p7

Quotation 4 "When my sisters got married, my father said to me: if a good suitor comes for you, you have to accept him. My parents were satisfied with him so I accepted to get married" p15

Quotation 5 "A few months after our marriage my husband said: we must have a baby as I could not resist my parents' insistence anymore. I did not want to become pregnant too soon, but my husband's parents forced us".p3

Quotation 6 "I saw my friends who were married and also studying. They were satisfied. I thought I could do the same thing. I was always like them; we were buying the same clothes, and having fun together. I did not want to fall behind them. When the first suitor came, I got married". P5

Quotation 7 "Only one of my sisters married when she was 20 and my other sisters and brothers got married at 17 or 18 years. In our family, my siblings get married at early age".p12

Quotation 8 "I knew him very well. They were very nice people... he met my criteria. I was going to school that time, but I thought, if I got married I would be better off because my husband had a good condition. I did not want to miss the chance"p10

Quotation 9 "Three months had passed since our marriage but I was not pregnant yet. I told my husband: if I do not get pregnant we would get divorced, so you could marry again and have kids ... I was really scared".p4

Quotation 10 "It was God's will that we got married. It just happened. I said nothing, and did not oppose it. I let it happen".p1

Quotation 11 "My mother-in-law said; "if you have a baby, God will sort everything out and if there is a problem it will be solved".p6

Quotation 12 "I was fatter than my peers. I became menstruate very soon. I had to cook, clean and do housework. I had learned lots of things. My attitude was like older women, and I understood more than my age. I thought, I knew how to deal with husband and his family. My general knowledge was so high that older people were consulting with me."p8

Quotation 13 "My mother-in-law said; "if you use contraceptive pills, you may never get pregnant. Contraception is not good". She said: if I use contraceptive pills, my ovaries may stop working forever and I could never have children".p14

Quotation 14 "Before I was married, my parents decided for me. I wanted to be independent and I didn't like people interfere in my business. I wanted to get married as soon as possible, perhaps I would have more freedom. I wanted to get married to somebody that I love. Someone that we could make plan for our life together, and ask me what I like. We would have fun together and be together".p3

Quotation 15 "As I have no sister or brother, father, mother or friends, I decided to get pregnant, no one was beside me".p11

Quotation 16 "I like to have a grown up child when I am still young, because my parents were old and they could not understand me. I wished my parents were younger so we could talk with each other. I liked to get married early so my children wouldn't feel the same".p2

Quotation 17 "I like kids very much. I wanted to have children. When I saw other people's children, I wanted to have a baby too". P8.

Quotation 18 "My dad said: do you want to get married? Yeah, I like it very much I replied. I did not know what marriage means. I thought it was very good, I could put makeup whenever I wanted, and I could showoff my colored hair, my wedding ring and other stuff. Now I understand how playful and childish I was thinking".p9

Quotation 19 "I thought having a baby is very simple, I did not think it is hard. I did not think of childbirth and I was just thinking of having a baby".p16

Quotation 20 "I did not want to become pregnant. I was using contraception but I got pregnant. I did not think that getting pregnant happened so easily. I did not know how I can be pregnant. I wanted to do something in order not to get pregnant. I had heard there were ways to prevent or quit pregnancy but did not know them very well".p13

Discussion

In Iranian culture, being a mother is a predictable and ordinary event that happens after marriage and the reasons for early motherhood lay in early marriage. The minimum legal age of marriage in Iran is 13 for girls and 15 for boys, but there is no legal impediment to early marriage(6). Due to lack of laws or their implementation, there is no possibility to protect the girls from early marriage in many countries (18, 25, 27). In Iranian culture, women are expected to get pregnant as soon as they get married, and if this does not happen, people would assume there exists a problem and women should provide an explanation.

Early marriage and motherhood of the participants was in response to external and internal instincts.

A poor economic condition was among the causes of early marriage. Several studies indicated that poverty is one of the main causes of early marriage which is a survival strategy for cutting the costs for poor families (3, 4, 6, 7, 18-20, 22, 25, 28, 29).

Family breakdown was another incentive for early marriage. In Iran, offspring are highly dependent on family and the existence of parents who have special roles and responsibilities is essential. Divorce or death of a parent can change the normal process of family life. Coyne (2014) recognized the breakdown of family structure and the absence of the father as the reasons for early marriage and motherhood(24).

A group of adolescents were married due to the urge of their parents and relatives. Such a situation occurs mainly in traditional families. UNICEF identifies the most important reasons for early marriage as; the urge of parents, the need for self-esteem and social approval, relatives' pressure; preventing social stigma, staying unmarried in girls, and sex before marriage(3, 20). In Iranian culture, the most important reasons for parents' tendency towards early marriage of their daughters include; protect the girl and ensure her purity, security and safety. Of course, this is the parent's view and daughters may not agree. Worry of some parents from harassment has caused them to be interested in early marriage of their daughters. Most of the daughters in traditional Iranian culture accept decisions of parents without any disagreement. Thus sometimes parents don't consider desires of adolescents. Early marriage in many cultures is a way to avoid sin and sexual promiscuity (without legal marriage)(19). In these cultures, unmarried girl's sex is an odious sin and creates severe social stigma for family. The Muslims of Iran believe, marriage is the best way to meet the sexual needs even when a girl and boy are very young. In Islamic countries, because of religious beliefs in favor of early marriage and fear of pregnancy outside the marriage, parents agree with the marriage of their daughters at first opportunity(20, 22). Some adolescents decided to get pregnant to meet the demands of the relatives, especially the husband and his family. In Iranian culture, having children is fundamental and preservative of marital life and couples have children

to strengthen the relationship between themselves and their families. Kibretb (2014) stated that, one of the reasons for motherhood among adolescents is to help strengthen family relationships(4).

Some adolescents were married to be like their families or friends. Netsanet (2015) believes that, early marriage of mother increases the likelihood of her daughter to copy her(3). Most mothers prefer their daughters to get married at the same age as they did(7). This kind of mothers inculcate to their children that early marriage is a social value. Adolescents' tendency to emulate peers is also another reason for this copying behavior(30). Also, the media encourage adolescents to sexual relations.

Some of the adolescents were married to avoid losing the position. One of the social issues affecting early marriage is the fear of not finding a suitable partner. This belief exists in traditional Iranian culture, especially in rural areas. In some provinces of Iran, adolescent girls have the best suitors for marriage because the best men tend to marry girls who are at the peak of beauty. When the age of a girl increases, her opportunities for marriage diminish. Hence, families prefer early marriage of girls to prevent this problem. In some other cultures, any delay in marriage makes them believe that the girl does not have many options, so the girls get married when they have their first suitable opportunity(3). From the Muslims' point of view (including Iranians) some events are divine destinies, and will happen whether we want them or not, so must accept them. Marriage in adolescents was considered as such an event. In Iranian culture, there is this belief that marriage will happen, if God will. So the marriage time is at "hands of God". Existing religious beliefs of the society had caused adolescent mothers to see children as the reason for receiving God's blessing. They believed that, having children would make their life better so they had decided to get pregnant. Iranians believe, when a child is born, he/she brings many gifts for the family, and God paid more attention to family. Most adolescents believed they had enough physical preparation for marriage, and did not pay attention to mental social, financial, and spiritual preparation that are essential for marriage and making a family. Rapid physical growth during adolescence created the impression that they were prepared for marriage. Early marriage also is more common in adolescents who feel the emotional readiness for marriage. They believe they should offer their love and affection to another human(19). In Iran, marriage is legal and religious way of expressing love and Iranian culture supports adolescents who married to achieve love.

A group of adolescents were married to meet their inner needs and desires. Adolescents at this age are full of emotional instability and become interested in early marriage to get love and affection(19). Another encouraging factor for early marriage was gaining independence. Interference of people, especially parents were unpleasant for some adolescents, so they preferred getting married than obeying their parents. Being interested in having children and responding to inner desires such as getting rid of loneliness was causing adolescent mothers to get

pregnant. Some of the reasons that influence adolescents decision about pregnancy which included; an interest in having children, growing up (responsible, mature, independent), receiving love of the husband and getting rid of loneliness, having a sense of ownership (having a child) and increasing self-confidence (being a good mother)(31). Some of the adolescent mothers believed that, early motherhood depended on the energy and strength of the mother and having a small age gap with children can be beneficial for both mother and children.

Some others thought marriage was simple. Lack of sufficient information about the consequences of early marriage and suitable age for marriage had caused adolescents to believe marriage is simple(7, 29). Insufficient knowledge of adolescents about pregnancy, childbirth, and childrearing had also caused them to assume having children is a simple process, and they decided be pregnant. More participants in this study had been pregnant unintentionally. Majority of adolescents did not have adequate information about sex and pregnancy mechanism, and were using contraception incorrectly or did not have access to it (15, 16, 32, 33). Married adolescents are forced to have sex under the pressure of spouse, family and community that will ultimately lead to pregnancy(33, 34).

In Iranian culture, married women must be engaged in sex and married teens are also not excluded from this law.

In issue of early marriage and motherhood, the youth, mass media, schools, neighbors, religious centers, parents, researchers, health centers, and policy makers must be considered. Health providers can improve families' economy by introducing them to support centers. They could also help family disputes by providing appropriate counseling and advice. Providing appropriate education for adolescents, parents and other people involved can lead to appropriate and timely marriage. Identifying adolescent mothers' educational and caring needs and providing appropriate training and care can prevent unwanted pregnancy and its consequences. School nurses can use the influence of friends to promote optimum health behaviors in adolescents. All of these services must be done in accordance with the principles of counseling adolescents, in order to empower them in decision making and solving challenges. However, the sample size of this study was small and looked at only part of multiple cultures Iranian, so researchers suggest the need for similar research in the field.

Conclusion

The findings of this study showed that, decision for marriage and early motherhood is influenced by adolescents' external motivations (related to society and life situations) and internal motivations. Exploring the cultural context of different societies can guide healthcare policymakers in identifying high-risk groups and predict the consequences of this phenomenon with respect to different cultures' view, because achieving optimum health of mothers and child requires close examination of factors affecting marriage and motherhood. Adolescents, parents, teachers, and other influential people should be trained on the negative consequences of early marriage and motherhood. Health policymakers in Iran and other countries should protect girls against early marriage and motherhood, because adolescents need sufficient time to properly grow, and for development, and success.

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The Effectiveness of Cognitive-Existential Group Therapy on Reducing Existential Anxiety in the Elderly

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Abstract

Introduction and Objective: The elderly experience significant developmental changes due to the effects of aging; a common consequence is the activation of existential anxieties. In spite of the natural and constructive nature of existential anxiety, inappropriate response may lead to neuroticism. This study aims to investigate the effectiveness of cognitive-existential therapy on reducing existential anxiety in the elderly.

Method: The present study was carried out using a pretest-posttest semi-experimental design with control group and random assignment. The statistical population included all the elderly women in Yas Daily Rehabilitation Center. In this study, 20 people were selected through non-random sampling and after answering the Existential Anxiety Questionnaire (Masoudi Sani, Bahmani, 2015) and Cognitive Distortions Questionnaire (Abdollahzade et al. 2010 quoted from Farmani-Shahreza et al. 2016) were randomly assigned to experimental and control groups (each group included 10 people). The experimental group participated in 12 cognitive-emotional group therapy sessions (each session 90 minutes) once a week in, but the control group did not receive any intervention. The collected data were processed using SPSS-20 software to calculate covariance analysis.

Results: The results showed a significant reduction in the existential anxiety and cognitive distortions compared to the pretest. Also, in a two month follow-up session, existential anxiety and cognitive distortion scores were significantly reduced compared to pretest.

Conclusion: The findings of this research can be considered as a confirmation of the basic assumption of the cognitive-existential approach about the effect of correcting cognitive distortions that activate non-authentic responses to the existential anxieties.

Key words: cognitive-existential group therapy, existential anxiety, cognitive distortions, the elderly

Introduction

Elderliness is a phenomenon that is caused by changes in biology, physiology, biochemistry and anatomy in the cells of the body, these changes affect the function of the cells, and it begins at age 60. It is not a disease but a natural process of transformation that cannot be stopped or reversed (World Health Organization, 2001).

Iran is experiencing the establishment of aging phenomenon. Statistics show that in 2011, the population of the elderly over 60 was about 3.8% of the total population of the country (Iran Statistics Center, 2013), and it is expected that the number of elderly will reach 10 million people, that is about 10% of the total population (Malayeri & Jafari, 2004).

Elderly people experience different consequences in terms of physical, socio-economic, family, psychological, and (existential) being dimensions. In the physical aspect, the elderly experience several problems, including: 1. chronic physical illnesses such as high blood pressure and cardiovascular diseases and diabetes; 2. decreasing abilities such as vision and hearing; 3. Neuropsychological disorders, such as dementia, Alzheimer's and Depression (Duberstein et al., 2008).

In socioeconomic and family dimensions, problems such as declining financial status, loss of job and social status, death or immigration of close relatives, friends and peers (Wurtman, 1993), and loneliness due to physical weakness and reduced mobility (Mussen et al., 2005) have been reported. In the psychological aspect major problems include: depression (Stuart et al., 2005), feelings loneliness (Heravi Karimloo et al. 2007; Wurtman 1993), impatience, anger, feelings of emptiness, anxiety and concern, insomnia, tiredness and fatigue (Kaldi & Foroughan, 2004).

From other dimensions of aging, one can point out existential anxieties that are not necessarily clinical and illness but can be painful and annoying (Yalom, 1980). The increasing awareness of the elderly about the finiteness of life manifests itself with the emergence of the first signs of aging, and anxiety about the loss of control, t physical deterioration (Robbins, 1392) which indicates the arrival of the last stage of life. Diseases such as cancer and heart disease, among friends and acquaintances of the same age, inform the person they are entering this stage. One thinks that he has had limited time, while he has many unfinished projects (Wayne Saint, 2003). In the eyes of the elderly, loneliness is an unpleasant, negative, agonizing, hard, terrible and painful personal experience that creates a sense of impatience, uselessness, frustration, sadness, anxiety and hopelessness (Heravi Karimloo et al. 2007). Confronting existential issues including death, feelings of emptiness and meaninglessness, loneliness, uncertainty and unpredictability of the future, the elderly may face problems which provoke existential anxieties.

Existential anxiety is the result of awareness of the unstable characteristics of human situations. Indeed, since each of us desperately needs eternity, solidity, coexistence and purposefulness of life, and at the same time, all of us will end up with the inevitability of death, groundlessness of existence, loneliness, and absurdity, as a result of this conflict we experience existential anxiety (Yalom, 1980)

According to Kierkegaard, the main axes of anxiety are death, freedom, loneliness and meaning (Kierkegaard, 1848; Poiman, 1990; Yalom, 1980).

The fundamental conflict that causes the anxiety of death is the desire for survival, the continuation of life, and the awareness of mortality and the inevitability of death (Yalom, 1980, 2008; May and Yalom, 2000). According to Yalom, responsibility and choice are the attendants of freedom. The fundamental contradiction arises from the fact that human beings need to have a structural basis for life but there is no basis. The conflict between groundlessness and the desire to have a firm base leads to anxiety (Webb, 2008; Sand, 2008). The loneliness anxiety begins where one loves to be part of a whole; have an honest relationship with others and be protected by others, but in the real world he/she finds that none of these events are realizes and he/she is unmercifully lonely (Kierkegaard, 1848). Stager and Frasber (2006) considered the nature of man to find meaning in life. Because the basic human need is searching for meaning and achieving perfection this quest does not necessarily lead to a meaningful life (Kernan & Lepore, 2009). The existential conflict is created because we must find meaning for a universe that lacks any design and semantics by itself, and set goals for a future that is unpredictable (Yalom, 1980; Sand, 2008).

According to the existential view, genuine response to existential anxieties depend on our awareness and acceptance of such anxieties (Prochaska & Norcross, 1999). All people experience those anxieties but not all of them face personality and communication problems (Blinderman & Cherny., 2005). Misunderstanding of self as a human being and overlooking the givens of existence paves the way to neuroticism (Poiman, 1990).

Pathological anxiety is the product of an individual's quest for escaping and overcoming the inevitable givens of being, through the use of defense mechanisms, causing self-deceit, self-alienation, and getting away from the realities of existence. This type of anxiety is usually out of consciousness and prevents the individual from movement. Therefore contrary to the natural anxiety that is constructive, pathological anxiety is a destructive mental disorder (Corey, 2005).

Also in the elderly, this process can lead to the formation or intensification of psychological problems. The elderly need to have the ability to respond to fundamental existential problems and as they get older, responding to these issues can be a significant contribution to their inherent and fundamental concerns (Langle & Probst, 2000). If they cannot find genuine answers to their existential issues they will suffer pathological anxiety.

A range of psychological interventions have been used to reduce the psychological problems of the elderly, which indicates the need for psychological services for these elderly people. This range includes: cognitive-behavioral therapies (Hedayat, 2015; Barghi Irani, 2015), existential group therapy (Mooziri, 2013), spirituality-based cognitive therapy (Rahimi, 2014), group logo therapy (Poorebrahim, 2006; Fakhar, 2007, Yazdan Bakhsh, 2015); memory telling (Majzoobi, 2012), and hope therapy (Parvaneh, 2015). The literature indicates that existential group therapy and group logo therapy were not effective on the elderly (Mooziri, 2013; Poorebrahim, 2007; Fakhar, 2007).

Furthermore, the focus of most interventions for the elderly has been on the treatment of death anxiety, feelings of loneliness, depression, and enhancement of life expectancy, happiness, self-efficacy, mental health, quality of life and quality of sleep in the elderly. It seems essential to address the anxieties of being due to the prevalence, while less attention has been paid to existential anxieties in the elderly. Also the studies on existential anxiety in the elderly have just focused on one of the four factors of existential anxiety. Therefore, in this study, the Existential Anxiety Questionnaire (Masoudi Sani, Bahmani, 2015) has been used for the first time.

It would be beneficial to find the most effective and practical intervention method to reduce existential anxiety subsequent to aging due to the need to respect the human rights of the elderly and also to save time, effort and facilities. In cognitive-existential group therapy, it aims to use techniques of "cognitive therapy" to refine some schemas, negative automatic thoughts, and to correct the cognitive errors that contribute to the formation of psychological distress caused by the non-genuine response to existential anxiety. Moreover, this method pays attention to existential concerns such as death anxiety, uncertainty, meaninglessness, loneliness, and uncontrollability of the world that are intensified by the death threat in patients. In most intervention methods such concerns do not receive systematic attention. Therefore, it is expected that through this intervention, individuals will find their own unknown fears and conflicts over the issues of existence and will be able to cope with them in a genuine and effective way (Bahmani, 2010). Previous studies indicate that cognitive-existential therapy plays an effective role in reducing psychological distress in different populations (Bahmani, 2010; Naghyiaee, 2014, Farmani Shahreza, 2014; Eskandari, 2013; Paknia, 2015). In this regard, we seek to investigate the impact of this intervention on the elderly and to answer the question of "whether cognitive-existential group therapy can reduce existential anxieties in the elderly?"

Method

The study was carried out using a pretest-posttest semi-experimental design with control group and random assignment. The statistical population included all the elderly women in Yas Daily Rehabilitation Center. The sample included 20 people selected through a non-random sampling from among the elderly present in the center during the sampling period (summer 2016) who were prepared to participate in the group therapy and were eligible for inclusion criteria. The sample was divided into experimental and control groups in a random assignment (10 individuals in each group).

In this research, the dependent variable is measured before and after the presentation of the independent variable, and its design graph is as follows:

Experimental Group	G_1	T_1	X	T_2	T_3
Control Group	G_2	T_4	-	T_5	T_6

T1 and T¬4 represent the pretest, T2 and T5 the posttest, T3 and T6 show the follow-up and X is the Cognitive-Existential Group Therapy.

Instruments

In this research, Existential Anxiety Questionnaire, developed by Masoudi Sani and Bahmani (2015), was used to measure existential anxieties. This questionnaire has 29 statements and 4 subscales: 1- Death anxiety, 2- Responsibility anxiety, 3- Meaning Anxiety, and 4. Loneliness anxiety. The content validity of the instrument is based on the opinion of 10 experts, using the ICC method was 0.95 and the reliability of the instrument was 0.83 and 0.86, respectively, by Cronbach's alpha and test-retest method.

In order to measure cognitive distortions, the 20-item scale of Cognitive Distortions developed by Hassan Abdollahzadeh and Maryam Salar (2010) was used. The standardized Cronbach's alpha was 0.80. The questionnaire consists of 20 statements to measure the cognitive distortions proposed on the basis of Albert Ellis's theory and each irrational thought has 2 statements. Thus, statements 1 and 2 assess Polarized thinking; 3 and 4, Overgeneralization; 5 and 6, Filtering; 7 and 8, Disqualifying the positive; 9 and 10, Jumping to conclusions and fortune telling including mind reading and misconception; 11 and 14, Exaggeration and Minimization; 12 and 13, Emotional reasoning; 15 and 16, Should statements; 17 and 18, Labeling; and finally 19 and 20 assess Personalization. The Higher total score reflects a more positive thinking; however statement 1 is scored in reverse (Abdollahzade et al. 2010 quoted from Farmani-Shahreza et al. 2016).

Procedure

After preliminary studies and preparation of the protocol, and receiving a referral letter from the University of Welfare and Rehabilitation Sciences to the Welfare Organization of Tehran province, we got the necessary permissions and referred to the Yas Daily Rehabilitation Center. The research process began after permission was gained from the head of the Center. First, through broadcasting announcements and talks with the elderly in the Yas Daily Rehabilitation Center, they were informed of the study. Subsequently, describing the research goals and obtaining consent from the elderly and observing the ethical rules, the conditions for the participation in the research

were prepared. After interviewing the individuals and completing Existential Anxiety and Cognitive Distortions questionnaires, twenty elderly were selected according to inclusion and exclusion criteria and randomly assigned to the control and experimental groups. The inclusion criteria were: age of 60 and over, having the ability to speak, having no cognitive problems and a score of over 70 in the Existential Anxiety Questionnaire. Exclusion criteria included: having mind and brain disorders such as Parkinson's and dementia, having any psychiatric disorders based on the written contents of their file in the center and use of any psychotherapy and counseling services at the time of the research.

Subsequently, cognitive group therapy was performed for 12 sessions of 90 minutes and once a week for the experimental group (Table 1), while the control group received no intervention. In order to observe ethical issues, after group treatment with the experimental group, group therapy was also performed for the control group.

At the last session, the mentioned questionnaires were repeated on the participants of both groups. In order to ensure the durability of the therapeutic results, two months after the completion of the group therapy in the follow up phase, the participants again were assessed using questionnaires.

Data from pretest and posttest was entered in version 21 of SPSS software. After analyzing the assumptions of covariance analysis, this statistical method was used to analyze the data. Covariance analysis limits or eliminates the effect of the pretest variable and measures it using the regression equation. Among the important assumptions of this statistical method was the homogeneity of variances using Levene's test and Normality test by Kolmogorov–Smirnov test. These assumptions were checked and verified in the study.

The ethical considerations of this study included the following topics: 1) the participants in the research were assured that the information received would be confidential; 2) scores were given to those who would like to know their scores; 3) the planning of group counseling sessions was carried out in a way that would not interfere with the programs of the Yas Daily Rehabilitation Center; 4) The control group was assured that they would participate in eight sessions of Cognitive-Existential group therapy after the end of the research; 5) Any of the participants could freely leave the program at any time during the research.

Table 1: The protocol for cognitive-existential group

Sessions	Objectives
First	Setting goals and defining the process of cognitive-existential group therapy Explaining the outline of the sessions that are essential for creating group atmosphere in the sessions
Second	Continuation of the work for the desirable establishment of the group's forming traditions: accountability for themselves and others Introduction to the concept of existential anxiety and its difference from neurotic anxiety
Third	Investigating the concept of death anxiety and the related cognitive distortions
Forth	Helping to accept loneliness as a genuine experience to increase the desire and motivation for being with others and family members
Fifth	Challenging false beliefs about loneliness and social isolation, feelings of rejection, dependency, feelings of uselessness, hopelessness, fear of death and dying
Sixth	Helping the individuals to face the consequences of not accepting responsibility and ignoring the principle of freedom and choice
Seventh	Helping to reduce the fear of dependency and the sense of uselessness and hopelessness as sources of anxiety
Eighth	Challenging the concept of losing meaning in life Helping the elderly to find effective meaning and be free of cognitive distortions
Ninth	Continuing the process of reviewing goals and establishing new directions in life
Tenth	Facilitating continuous and consistent commitment to work in order to achieve new goals
Eleventh	Wrap-up session
Twelfth	Expressing the feelings of the participants about the group therapy Coordination for the follow-up meeting Post test

Results

The sample consisted of 20 elderly women with an average age of 70 who were randomly assigned into two groups of 10 in experimental and control groups (waiting list). According to the results of the Mann-Whitney U test, the two groups were homogeneous in demographic variables of age and education. In addition, the assumptions of the covariance test for the normality of the data distribution were confirmed by Kolmogorov-Smirnov test and homogeneity of variances were confirmed by Levin's test of two groups in dependent variables of existential anxiety and cognitive distortions.

Table 2: Mean and standard deviation of the existential anxiety scores and its subscales in the experimental and control groups in the pretest, posttest and follow-up

Variable	Test stage	Experimental group		Control group	
		Mean	standard deviation	Mean	standard deviation
Meaning anxiety	pretest	23.30	2.79	2350	2.99
	Posttest	18.90	3.69	23.70	2.90
	Follow up	19.20	3.85	24	2.98
Death anxiety	pretest	17.40	1.42	17.20	1.54
	Posttest	13.40	4.35	17.90	1.59
	Follow up	14.40	4.27	19.30	2.05
Loneliness anxiety	pretest	14.50	1.50	13.70	1.70
	Posttest	11.10	1.37	14.50	1.64
	Follow up	12.70	2.51	14.40	2.01
Responsibility anxiety	pretest	26.90	1.79	25.90	2.46
	Posttest	21.90	2.28	25.60	2.71
	Follow up	22.30	2.35	25.70	2.75
Existential anxiety	pretest	82.40	4.42	80.30	5.57
	Posttest	65.30	8.05	81.30	5.20
	Follow up	66.90	8.26	82.40	6.20

In Table 2, the comparison of mean scores in the pretest, posttest and the two-month follow up of the experimental group showed that the scores in the posttest and follow-up were reduced compared to the pretest.

Table 3: Mean and standard deviation of cognitive distortion scores in pretest, posttest and follow up

Variable	Test stage	Experimental group		Control group	
		Mean	standard deviation	Mean	standard deviation
Cognitive distortions	pretest	49.80	3.11	50.50	3.83
	Posttest	67.30	4.11	51.10	3.95
	Follow up	65.60	5.08	50.90	3.98

In Table 3, the comparison of mean scores of cognitive distortions in the pretest, posttest and follow-up tests showed that scores in post-test and follow-up were increased in comparison with the pretest. Considering that the higher the number of scores, the more positive the thinking is; the increase in scores shows that the cognitive distortions have been decreased.

Table 4: The results of covariance analysis of the comparison of the experimental group and control group in existential anxiety and its subscales' post-test scores

Variable	Source of variance	Sum of squares	Degrees of freedom	Average squared	F	Sig	Effect size	Statistical power
Existential anxiety	Pretest	583/029	1	583/029	40/427	0/000		
	Group	1610/110	1	1610/110	111/644	0/000	0/868	1
	Error	245/171	17	14/422				
	Total	109566	20					
Meaning anxiety	Pretest	175/988	1	175/988	130/012	0/000		
	Group	104/917	1	104/917	77/508	0/000	0/820	1
	Error	23/012	17	1/354				
	Total	9388	20					
Death anxiety	Pretest	0/004	1	0/004	0/000	0/985		
	Group	100/657	1	100/657	8/853	0/008	0/342	0/801
	Error	193/296	17	11/370				
	Total	5193	20					
Loneliness anxiety	Pretest	2/597	1	2/596	1/138	0/301		
	Group	60/261	1	60/261	26/140	0/000	0/608	0/998
	Error	38/803	17	2/283				
	Total	3376	20					
Responsibility anxiety	Pretest	64/466	1	64/466	22/442	0/000		
	Group	98/815	1	98/815	34/412	0/0000	0/669	1
	Error	48/834	17	2873				
	Total	11463	20					

As shown in Table 4, participation in the cognitive-emotional group therapy has significantly decreased the existential anxiety and its subscales in the elderly. Also in the follow-up phase, a significant decrease was continued.

Discussion

The aim of this study was to investigate the effectiveness of interventions that are more appropriate to the specific needs of the elderly and to provide more effective helping methods for reducing the concerns and the existential crises of the elderly. In this regard we examined the general assumption that "cognitive-existential group therapy reduces the existential anxiety of the elderly".

As the findings in Table 4 show, the findings confirm the mentioned hypothesis. It seems that the cognitive-existential group therapy and the elements proposed in the treatment protocol, as well as the special way of relations in the sessions have been able to create a positive and significant change in reducing the existential anxiety and its subscales. It should be considered that the treatment atmosphere in the cognitive-existential group therapy is based on listening to the subject's stories considering the here and now, familiarity with the sufferings of others, the use of emotional support and receiving feedback from different people to reduce the feeling of being victim, the uniqueness of the problem, loneliness and helplessness, discrimination and oppression, feeling of security, secrecy, reflection and empathy, emotional release, self-disclosure, exposure, feedback, affection, acceptance and humour; this can be mentioned as a positive factor for this approach. In this method, the group continued the

sessions assuming that the confidence and sympathy between the group members persists and the psychological refinement was done every session.

Part of the content of the cognitive-existential group therapy helps understanding the phenomenological world of individuals using the prepared existential concepts. Using such concepts helps individuals to encounter their existential anxiety and to communicate with their original selves with all the inevitable existential anxieties and instead of denying and reprimanding their unpleasant feelings and emotions, experience them and take responsibility for their feelings, and most importantly, express these feelings and emotions. According to Kissan it is a useful intervention method that can deal with these fears fast and clear enough and can help reduce mental health problems (Kissan, et al., 2002; quoted from Bahmani et al., 2010).

During the treatment process, the elderly were involved with their existential questions. These questions caused them to activate and discharge their existential anxieties. In general, during the sessions, it became clear that feeling of lack of a worthwhile future and lack of self-efficacy to achieve it, inevitability and fear of death, lack of faith in the future, feeling of hopelessness, lack of meaning and purpose, and loneliness deprives the elderly from the motivation to try. Existential crisis and disturbances are developed as a result of fear of confrontation with

existential anxieties. So during the group process, we tried to help the elderly understand the unpredictability of the world and the uncertainty of the universe, assess their thoughts and assumptions about the uncontrollability of death and loss of opportunities in the past and the resulting anxieties, identify and challenge their cognitive distortions about the meaning of death anxiety (seeing death as the end of everything, unwillingness to track down their illnesses, fear of being forgotten after death, fear of painful death, disqualifying their efforts in their lives, fear of disability) and end their fears by accepting the anxiety of unpredictability and death. We also tried to introduce the concept of fundamental loneliness anxiety and help them identify and challenge their cognitive distortions about the meaning of loneliness (not being understood by close people, especially their spouse and children, the feeling of failing to understand others, the feeling of separation from children, attachment to other individuals to escape loneliness) and accept loneliness as a genuine experience to increase the desire and motivation to be with others and family members. They were also helped to challenge the meaning of their lives created by psychological disturbances and existential anxieties, and find a meaningful term for their lives, and change their attitudes toward problems and tolerance of difficulties, and through giving meaning to the sufferings and pains, change their focus from what has been lost, because the sense of the new meaning and purpose in life during the aging period (which includes the ability to combine and integrate the experiences and achieve an understanding of themselves and the world) is a protective factor against meaninglessness. Also, in the process of group therapy, elderly people tried to accept responsibility and freedom of choice, to identify and challenge their cognitive distortions about the anxiety of responsibility and freedom of choice (assigning responsibility for life events to others or social, cultural, economic, etc. circumstances, leaving the choice to others, believing in luck, trying to show oneself as victim) and to evaluate their priorities and decisions, and accept their own responsibility for their own destiny. In general, the group therapist tried to help the elderly to accept cognitive distortions that prevented them from experiencing existential anxieties and activated their defense mechanisms.

In general, according to previous studies, cognitive-existential group therapy can be considered as a suitable factor in reducing different types of mental disorders. Bahmani et al. (2010) in their research showed that cognitive-existential group therapy was more effective than cognitive therapy in reducing the mean of depression and increasing the mean of hopefulness.

Previous studies, consistent with the present study, Kissan et al. (1997) showed that using this method of treatment is helpful to reduce the amount of sadness and grief in patients with cancer, increase their problem solving ability and also create cognitive strategies. Breitbart (2001) suggested that existential therapies are one of the most appropriate approaches to reduce depression and increase hope in cancer patients. In addition Kissan et al. (2003) concluded that cognitive-existential therapy has a positive effect in reducing overall symptoms of psychological distress in

women with non-metastatic breast cancer. In another study, Kissan et al. (2004) concluded that this method would greatly reduce psychological distress and anxiety, and improve family relationships.

Therefore, according to the findings, the cognitive-existential therapy has been able to affect people with chronic conditions such as cancers, breast cancer, human immunodeficiency virus, and the elderly. This should be due to the main distinguishing feature of this intervention method, namely, paying attention to the existential anxieties and considering here and now during the treatment sessions as compared to other methods.

Also, the results of the two-month follow-up showed that cognitive-existential group therapy has a lasting and stable effect on the improvement of existential anxiety. In explaining this finding, it can be said that Cognitive-Existential psychotherapy can lead to long-term changes in terms of creating philosophical insights and changing attitudes in individuals.

Conclusions

In general, cognitive-existential group therapy due to addressing the existential concepts, especially for the elderly and deal with these concepts and working with the unreasonable beliefs of individuals and substituting logical beliefs can lead to the reduction of psychological factors and existential anxieties. Therefore, this method of intervention can be used in the treatment of the elderly, since the elderly need to continue their lives with meaning and purpose without fear of confrontation with death, loneliness, and existential concerns.

Limitations
The most important limitation of this study was the use of available sampling and, consequently, semi-experimental design, and that the research was conducted only on elderly women, which reduced the generalization power of the research.

Suggestions
Given that existential anxiety is activated in the elderly and addressing these anxieties in counseling and psychotherapy sessions can help to improve the existential crisis of the elderly, it is suggested that counselors of care centers, rehabilitation centers for the elderly and counseling and psychology clinics be trained based on the treatment plan presented in this study and take advantage of it to help the elderly. In addition, the results of this study can be used to improve the design of educational programs for health care and rehabilitation providers, as well as to plan for prevention of existential crises and to improve the health of the elderly and to prevent serious problems such as suicide in the elderly. Also, it is suggested that the effect of this therapeutic approach on other psychological variables be examined and the effectiveness of this treatment method be compared with other types of cognitive therapies in order to reduce the psychological problems of the elderly in order to achieve the most effective treatment method for this group.

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Post-mortem Distribution of Morphine in Cadavers' Body Fluids

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Abstract

Purpose: We aimed to compare morphine in urine and other body fluids, including cerebrospinal fluid (CSF), bile, pericardial fluid (PCF), and vitreous humor to determine the most reliable fluid for detection of postmortem morphine.

Methods: In this cross–sectional study on 87 cadavers of Kahrizak Forensic Autopsy Center of Iran, cadavers with a maximum of 72 hours after death with positive urine morphine rapid strip test were included. Morphine was evaluated with thin layer chromatography (TLC) test in urine, bile, CSF, PCF, and vitreous samples. The presence of morphine in these fluids was compared to urine samples. Data were analyzed by SPSS software, version 21.0.

Result: Mean±SD age of the cadavers was 44.5±4.1 (range: 22–67) years consisting of 85 (97.7%) men and 2 (2.29%) women. From 87 cadavers with positive urine morphine Rapid Strip Test, only 42 urine samples (48.3%) had positive TLC results, among which TLC was positive in 24 cases (27.6%) of bile, 9 cases (10.3%) of PCF, 5 cases (5.7%) of CSF, and 2 cases (2.3%) of vitreous sample. There was a statistically significant relationship between urinary and biliary morphine (Kappa=0.527, P<0.001), PCF (Kappa=0.22, P<0.001), and CSF morphine (Kappa=0.123, P=0.017), but the relationship between urinary and vitreous morphine was not statistically significant (P=0.139).

Conclusion: The moderate agreement between urine TLC and bile TLC reveals bile sample as the most reliable fluid for morphine detection, when a urine sample is not accessible.

Key words: Morphine; Bile; Cerebrospinal Fluid; Pericardial Fluid; Vitreous Body; thin layer Chromatography; Post-mortem

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Introduction

Opioids are frequently used as drug abuse and in clinical practice for acute and severe pain management (1). It alleviates pain at different levels, including raising the threshold at the spinal level, attenuating the perception of pain, and influencing the emotional and hormonal conditions at the limbic system; they act as full–agonists for μ receptor and a weak agonist for δ and κ receptors (2).

The major metabolites of morphine include morphine–3–glucuronide (M3G), and morphine–6–glucuronide (M6G), which are metabolized in different organs, such as liver, brain, and the kidneys (3). The ultimate aim of drug metabolism is to facilitate its urinary excretion (4); thus, urine samples are considered an appropriate method for measurement of drugs, like opioids (5). But the clinical measurements are different from postmortem methods, as the drug concentrations may be redistributed according to the anatomical site of sampling and time after death, known as postmortem redistribution (PMR) (6). As far as peripheral blood samples are suggested to have lower concentrations than the central samples and peripheral samples are not always available in cadavers after a few hours (7).

Thin layer chromatography (TLC) is an easy and inexpensive method to isolate or assess the purity of a compound in a mixture with high sensitivity and good reproducibility (8) that is used to detect drugs in biological materials, including measurement of urinary morphine (9). The distribution of drug metabolism and the PMR phenomenon make plasma, whole blood, urine, bile, and cerebrospinal fluid (CSF) as appropriate sampling sites for detection of morphine in cadavers (10). When central blood samples, like femoral vein samples, and urinary samples (as gold standard sampling sites) are not available, other body fluids can be used (11), yet, the difference in measurement accuracy of different sampling sites has to be further studied. We aimed to compare morphine in urine and other body fluids, including cerebrospinal fluid (CSF), bile, pericardial fluid (PCF), and vitreous humor (VH) to determine the most reliable fluid for detection of postmortem morphine.

Materials and Methods

Study design
In this cross–sectional study, 87 cadavers who referred to Kahrizak Forensic Autopsy Center, Tehran, Iran were recruited. The protocol of the study was approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran. Before recruitment of cadavers into the study, the design and objectives of the study were explained to their family and written informed consent was obtained. All principles of Helsinki's guideline were met throughout the whole steps of the present study.

The sample size was calculated to be 85 cases, based on the frequency of positive morphine in body fluids (12), with an accuracy of 10%, and α=0.05. The eligible cadavers were included using convenient sampling method. The inclusion criteria consisted of cadavers with a maximum of 72 hours after death with positive urinary morphine, documented by rapid strip test. Participants' age and sex were recorded and morphine was evaluated with thin layer chromatography (TLC) test in urine, bile, CSF, PCF, and vitreous samples. The presence of morphine in the fluids was compared to urine samples.

Statistical analysis
The results were reported by descriptive analysis, including mean±standard deviation (SD), and frequency (percentage) and inferential statistics, including independent sample T test and chi–square test. The associations of variables were tested by Kappa. For the statistical analysis, SPSS software, version 21.0 for Windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

Results

Mean±SD age of the cadavers was 44.5±4.1 (range: 22–67) years consisting of 85 (97.7%) men and 2 (2.29%) women. From 87 cadavers with positive urinary morphine (Rapid Strip Test), only 42 samples (48.3%) had positive TLC results, among which TLC was positive in 24 cases (27.6%) of bile, 9 cases (10.3%) of PCF, 5 cases (5.7%) of CSF, and 2 cases (2.3%) of vitreous sample. Comparison of positive and negative cases detected by urinary morphine than other fluids (sensitivity and specificity) are shown in (Table and Figure 1 - next page).

There was a statistically significant relationship between urinary and biliary morphine, PCF (P<0.001), and CSF morphine (P=0.017), but the relationship between urinary and vitreous morphine was not statistically significant (P=0.139). Measurement of agreement showed moderate correlation (Kappa=0.527) between urinary and biliary morphine, and weak agreement between urinary and PCF morphine (Kappa=0.22); also, there was a weak agreement between urinary and CSF morphine (Kappa=0.123).

Discussion

The results of the present cross–sectional study on 87 cadavers indicated the statistically significant association between urinary morphine and biliary morphine, PCF, and CSF morphine with moderate agreement between urinary morphine and biliary morphine, and a weak agreement between urinary morphine and PCF, and CSF morphine.

There are various reasons that a cadaver must be studied for the presence of drugs, for instance, toxicity of opioids and blood samples are the gold standard sampling site (13). But in cases where blood samples are not available or accessible, other specimens should be selected, including urine, bile, CSF, and VH (14).

Table 1. Comparison of positive and negative cases detected by urinary morphine than other fluids (sensitivity and specificity)

Urinary morphine	Biliary morphine		Pericardial morphine		CSF morphine		Vitreous morphine	
	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive
Negative	97.7%	2.3%	100%	0%	100%	0%	100%	0%
Positive	45.2%	54.8%	78%	22%	88.1%	11.9%	95.2%	4.8%
Total	72.1%	27.9%	89.2%	10.8%	94.3%	5.7%	97.7%	2.3%

Figure 1. Frequency of positive and negative cases detected by urinary morphine than other fluids
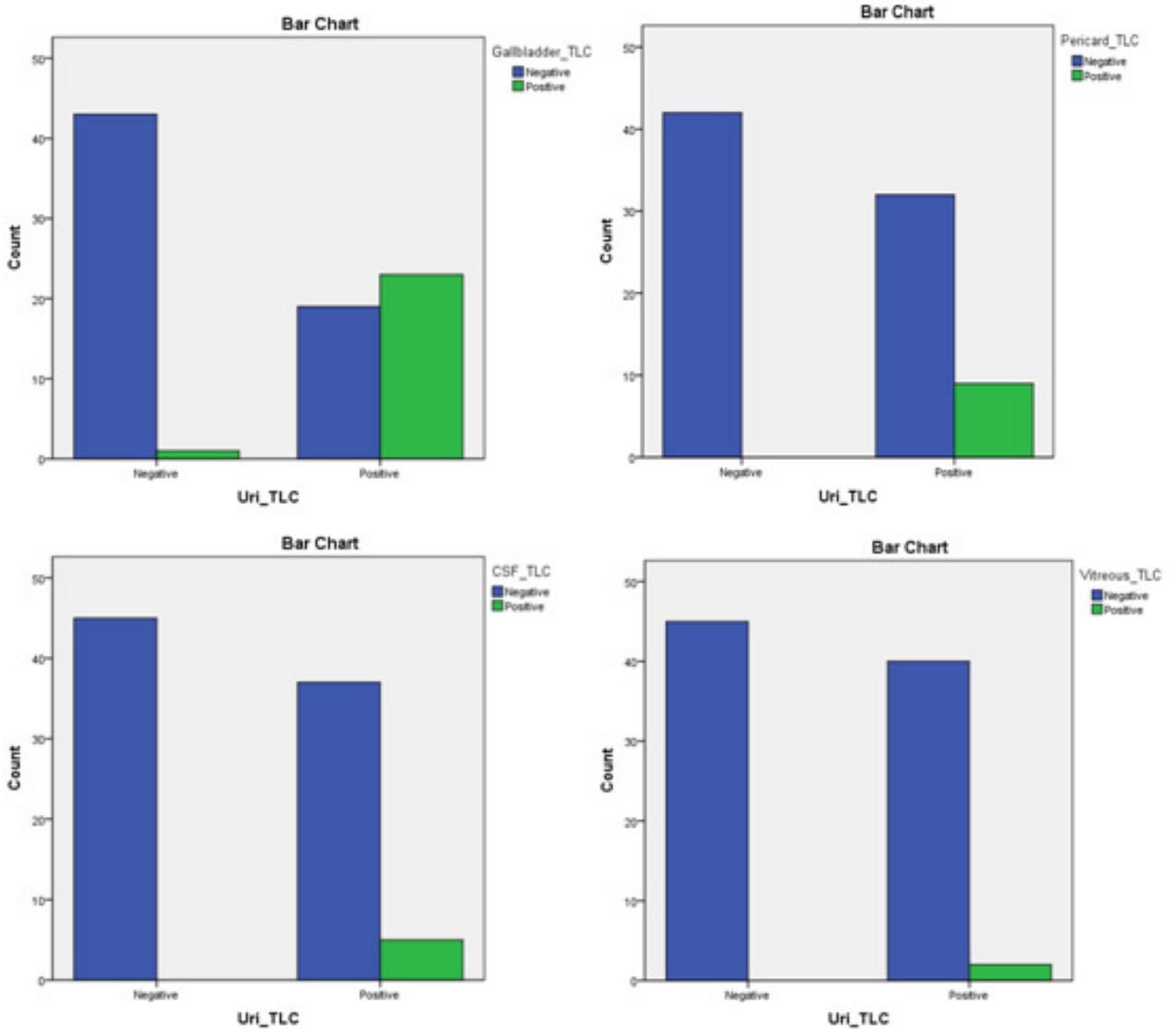
There are few studies that have evaluated the postmortem concentration of morphine in different body fluids and most studies have only focused on the comparison of one or two methods. One study showed higher drug concentrations in bile analysis than blood samples obtained from different sites (15), which is in line with the present study. Therefore, biliary specimens are an appropriate sample for assessment of morphine in cadavers. Also, other studies have indicated similar concentrations in PCF and blood samples for most drugs, especially morphine and its metabolites, and suggested PCF as a useful material for forensic toxicological assessment, when blood samples are not available (16, 17), which is consistent with the results of the present study, as there was a statistically significant association between PCF and urinary morphine, although the correlation was weak. Wyman and colleagues demonstrated highest morphine levels in liver, blood, CSF, and VH, respectively (12), which is similar to the results of the present study, indicating a statistically significant association between urinary and CSF samples, while this association was not statistically significant for VH. In another study, morphine and its metabolites was positive (>1 ng/ml) in 89% of urine samples, 68% of CSF samples, and 75% of VH cases (18), which was higher than the present study, indicating positive morphine in 48.3%, 5.7%, and 2.3% of urine, CSF, and VH samples. This difference can be due to the differences in the sampling technique, and measurement method. Holmgren and partners showed a significant difference between the concentrations in the VH and femoral blood for 23 substances and suggested VH an alternative specimen when blood samples are not available (19), while the results of the present study did not depict VH as an appropriate specimen, as there was no statistically significant association with urinary morphine, although in the study by Holmgren and colleagues, it was compared with blood sample, and was not specifically for morphine, which can justify the discrepancy between the results of the studies. The results of the present study on VH might be due to the inappropriateness of TLC method for analysis of morphine in VH, as studies have shown disposable pipette extraction (DPX) a fast, reliable, and easy to perform method for detection of drug abuse in VH with satisfactory sensitivity, precision, and accuracy (72–91%) (20), although TLC method, used in the present study, is an appropriate tool for forensic medical analysis of urinary opioids (21). In addition to the issues raised above, the interval between death and sampling also plays a significant role in the concentration of the drug, due to PMR phenomenon (6), which can justify the discrepancies among studies, as well. Thus, it is suggested that specimens should be selected individually for each case, based on the history and availability, while the procedures should be performed with proper quality (22), and post-mortem tissue/samples should be carefully selected, stored, preserved and utilized (23). Other studies have also assessed the tissue distribution of morphine and its metabolites in forensic medicine (24, 25), while the present research could suggest body fluids as an easy access method, especially bile, although further research is required on a comparison of the diagnostic accuracy of tissue versus fluids.

The main strength of the present study was a comparison of different sampling sites in one study in a referral Forensic Center that enables researchers with an appropriate spectrum, while most studies have only evaluated one or two methods (12, 16, 19). On the other hand, the present study had several limitations, such as limited sample size and cases of one Forensic Center that limits the generalizability of the results. In conclusion, the results of the present study showed that biliary measurement of morphine by TLC method could be an appropriate alternative for morphine detection in cadavers less than 72 hours after death when the urine sample is not accessible.

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Application of Social Networks to Support Students' Language Learning Skills in a Blended Approach

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Abstract

Introduction: The emergence of new technologies has created a potential educational environment where teachers can support second language learning. This study examines the effectiveness of the blended approach in learning English through the mobile social networks to enhance the level of listening and speaking skills of primary school students.

Method: The research design is an applied and semi-experimental method. Population included the students of primary school aged 7-9 with sampling selected randomly. Research tool was a researcher made test in English. In data analysis descriptive statistics (mean, standard deviation) and inferential statistics (covariance) were used.

Result: Gains in the scores of the final exam of the experimental group exposed to blended designing instruction compared to those in the control group taught through current face-to-face method, demonstrated a significant difference. The findings of the study support the idea that the use of the blended approach has affected the skills of the language learners for 1stgrade students (p<03), 2ndgrade (P<0/01), and third grade (P<0/02) positively.

Conclusion: The findings of the study bear some significant implications for curriculum designers, teachers and students and highlight the crucial role of using the technological devices and applications in promoting the learners' capabilities in listening/speaking.

Key words: Blended Approach, Primary School, English Language Teaching, social Networks

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Introduction

The Primary focus on computer use in language learning classrooms has improved to the point where technology is regarded as a part of the common teaching experience. While due to the limited time of the classrooms and abundance of students in primary schools, a solution is required to direct their individual language learning in a more effective way. Moreover children always need support during language learning and the intervention of parents or other family members with no expertise in the field of foreign language teaching will lead to irreparable harm to both teaching process and their motivation. These observations raised the question of how to design technology for digital natives to support second language learning in the classroom.

The concerns raised above are echoed by the blended learning approach in that the primary focus on computer use in language learning would be of a hybrid function i.e. in and out of classrooms.

The main focus of blended learning is on the learner involvement which could be better achieved with the help of the Internet and Information and Communication Technology (ICT). Garrison and Vaughan (2008) believe that the approach is fundamentally based on the thoughtful combination of face- to- face and online education, reconsideration of the design of the lessons for the highest possible learner involvement, and the reconstruction and replacement of the traditional classroom hours(1).

To understand foreign language learning, it is necessary to examine not only the linguistic characteristics of the target language, but also the physical, psychological, and the social characteristics of the learner. As children play an active role in learning their native language, foreign language learners acquire through their skills, strategies, physical/ cognitive development, goals, attitudes, and certain motivations that are effective in their success. So with all these effective factors, learning will not be identical in different subjects. According to Uso-Juan and Martinez-Flor (2006), there has been a shift in our understanding of second language skills and the way they are learned/ taught over the past five decades. They maintain that there has been a big change in the paradigms of teaching language skills in three phases. They call the first phase the environmentalist approach where under the influence of the structural linguistics and behaviouristic psychology, the learning of the language skills were considered as a stimulus/response/reinforcement procedure. During the second phase (the 1960s) and after the publication of Chomsky's book Syntactic Structure (1957), the innatist view towards learning the four language skills was dominant. That is, learning language skills were considered as an active cognitive process where the learner and his mental abilities have a crucial role in active involvement in acquiring a second language skill. And the last phase or paradigm shift, as they further highlight, took place in 1970s where the interactionist approach and the functional/contextual aspects of language were of more

significance(2). Actually in learning the four language skills the interactional purposes of the learners were taken into consideration and not just the linguistic information or forms. In line with this very last approach towards learning the four language skills, the present study intends to use the social network framework as the main focus of the study and gear the learning procedure of the L2 skills and particularly listening and speaking, towards the interactional orientation of such educational technologies. Although many large-scale studies have been undertaken to identify the potential benefits of blended learning for primary school students, several researchers, as detailed in the following sections, have explored the concerns of this approach in language learning from different perspectives in a number of studies.

Kennedy and Levy (2008) conducted a study on Italian language learning using mobile phone. That is, in addition to classroom presentation, practice and feedback were also performed via mobile phone in their research. The results of the learners being taught through the mobile phone in Kennedy and Levy's study were more significant than those who were taught through current methods in classrooms. Meanwhile, each learner showed progress according to their learning speed(3).

Wong, et al.(2011) studied the blended approach in the development of the writing skills of primary school students in China. Writing problems of these students included incorrect use of words and writing rules. In their study the collaborative writing practice program was developed in the Wiki platform using a variety of tasks including paragraph writing, sentence building, summarizing or cataloguing. Based on the interaction between teacher and students and among students, the aim was to restore their writing skills. The results analysis indicated the improvement of writings kills of students in the experimental group. Blended approach had, indeed, a positive effect on the improvement of the students' writing skills(4).

In a study by Sandberg, et al. (2011), the effect of learning English via the mobile phone was evaluated on the fifth grade students of a primary school in three groups. To the first group, English lesson was presented in the class room with the subject of wild animals. In the second group, in addition to class room teaching, children visited the zoo and were given the mobile phone in order to perform some related activities. The third group, like the second one, learned their lessons as the other groups, but they took their mobile phone home. The pre-test and post-test were performed for all the three groups. The results showed that the group who took their mobile phone home had more learning progress. The study showed that the use of the mobile phone in language learning increased the students' motivation and ultimately led to more effective learning providing efficient learning experiences(5). In effect, in addition to the formal English teaching at school, it has become more possible to practice in an informal environment outside the classroom context by using mobile phones at home.

Although the studies reviewed in this section intended to enhance the language learning phenomenon by the use of such ubiquitous technological devices as mobile phones, they did not take the role of the social network tools on the mobile phones into much consideration. Another point worth noting is that even those research studies which investigated the impact of the social network tools in learning mainly focused on the skills other than listening and speaking. As an example Sugie (2012) intended to develop an appropriate blended social learning model for Chinese language education in Japan. The point was how to increase the motivation and learning speed of the high school students and include this motivation in real-life events. The main purpose of Sugie's study was to make opportunities to increase students' relationship with native Chinese speakers through the use of information technology and communications in order to improve their writing skills and thereby increase their motivation and satisfaction from learning Chinese. The participants in the experimental group were novice learners undergoing presence training and presence grammatical exercises, web-based training and having interaction with the native Chinese speakers through the use of a white board. Qualitative analysis of students' evaluation showed that the level of satisfaction increased in Japanese learners and the experience of online speaking with native speakers had a good impact on Chinese learning improvement(6). Based on the appropriate analysis of the students' needs, the educational systems stakeholders can design technological models in such a way that both the learners' reaction to the new learning environment and the possible effects on the process of learning /acquisition are promising.

The literature shows that there have been some studies which considered the role of social networks in boosting the learners' language acquisition procedure and the type of interactions. Despite the growing body of research on the use of the technological platforms in language learning, a gap is still felt to exist in elaborating the social network potentiality in supporting the learners and their cognitive learning development (7).

Motivated by the issues raised above from both the pedagogical and theoretical perspectives, the researchers conducted an action research to further examine the application of social networks technology in language learning. Hence, the purpose of this research study was to explore the effect of blended approach in a supportive environment on the listening and speaking skills of the children aged 8-10 in a real context. Thus, the formulated hypothesis of this study was that the English learning gains in the first, second and third grade students through the blended approach were greater than those not exposed to the same method.

Method

1. Study design and population
The present study was applied and interventional research. The population of the study included all male elementary school students in Tehran, District 3, South-west of Iran, of whom 90 students were selected randomly as the sample of the study. Students ranged in age from 8 to 10 in first, second and third grade, respectively.

2. Methods
The study design is quasi-experimental.

3. Measuring tools: validity and reliability
To measure the student's achievements in listening and speaking skills, a researcher-made test (Oral test was developed for the pre-test and post-test phases of the study). Since one of the researchers was indeed the teacher of the experimental group, before administering the test and to assure the validity of the test, a panel of experts with 15 years of relevant experience provided some comments in 3 rounds and their opinions were taken into account in revising the test items. The test-retest technique was utilized in determining the test reliability (0.70).

4. Intervention
In each of the control and experimental groups there were 14 first grade students, 16 second grade students, and 15 third grade students. At the beginning of the training phase, the pre-test was performed to both the experimental and control groups according to the determined objectives. For each session of implementation, an appropriate lesson plan was developed consistent with the class teaching methodology and available technology facilities. The students' performance was reported by the teacher at the end of each class and the contents required for the next session were sent to them through their parents' mobile phone using What's App software for the experimental group but for the control group the activities were carried out through the usual notebooks or in class practices. The parents were briefed and trained on how the assignments were sent and how they should check. In fact, a survey questionnaire was administered among the students' parents asking who would like to cooperate with the researchers in the project and could contribute to the sending and receiving procedure of their children's assignments via their mobile phones, with the support teacher who provided the main teacher and the students with some help where necessary. Some of the sent activities were assessed during the class or the related feedback was provided for the students. The students were sometimes required to do some activities, report on them and send the recorded assignment through the mobile phones. As an example, when some audio files were sent to the students, they could send the answer as audio, picture or movie files. In one of the activities, for instance, one question was posed as: 'Where are you sitting, what is your mother doing, and what are you having for dinner tonight?'… One month after the complete implementation of the program along with attending the classes two days a week for four weeks, the post-test was carried out on the students in both groups. The score 70 out of 100 was regarded as the passing grade. In the meantime, parents and their children had some interactive activities with the support and guidelines of the teacher and looked

for their probable problems through the intervention or non-intervention educational /language practices of their children.

In fact, according to the expected performance of the children group, the primary presentation was conducted in the classroom with regard to the network-based real and tangible medium, drawing and presentation medium, or multimedia. Also the second round of presentations were carried out with the appropriate feedback and guidance from the teacher for each student in different groups or individual groups using a diverse range of activities. A variety of small and large group games was carried out with the help of audio files or repeating of the same files by students for their performance in both classes of each grade. However for productive performance, it was attempted to create an opportunity outside the classroom and in real-life environments for students to express their thoughts and send them to support teachers in the form of audio and video files or movies. But for the control group they should have imagined and talked about the same situation as the experimental group.

In the control group the feedback was given inside the classroom to the students but for the experimental group it depended on their mistakes or errors i.e. sometimes the support teacher provided each student with direct feedback and sometimes the teacher herself talked about it inside the classroom providing some clues for the correct answer, and finally they came up with the final correct form together and decided on the best answer.

5. Ethical consideration
The ethical considerations necessary to satisfy the participants were observed, so a survey questionnaire was administered among the students' parents showing who liked to cooperate with the researchers in the project and could contribute to the sending and receiving procedure of their children's assignments via their mobile phones with the support teacher who provided the main teacher and the students with some help where necessary.

6. Inclusion and exclusion criteria
Inclusion criteria included having written consent on behalf of the parents in order to implement the social network activity in learning English language.

Exclusion criteria included unwillingness to participate in the study and the absence in sessions or transfer of a student from school.

7. Data Analyses:
Data of study were analysed using descriptive statistics (frequency, percentage, mean, standard deviation) and inferential statistics (Kolmogorov - Smirnov test and Levin analysis, Covariance) usingSPSS- 21 software to examine the hypothesis of study.

Results

Descriptive statistics data in the two groups are presented in Tables 1-3 opposite :

Table 1.Descriptive statistics data in experimental and control groups of 1st(n=28), 2nd(n=32) and 3rd(n=30) grade primary school.

In order to test the hypothesis of research homogeneity of variance and normality of distribution in the analysis of data. They were examined through the Kolmogorov–Smirnov and Levine tests. Test results are presented below in Tables 2 and 3.

As the results in Table 2 show, the probability of random difference between sample distribution and normal distribution is higher than 0.05.

As the results in Table 3 show, the significance level was higher than 0.05, and thus the hypothesis of homogeneity of variance was confirmed in sample groups.

The first row of Table 4 (page 94)showed the effect of the pre-test significance (0.04). That is, the pre-test and post-test were correlated and it was required to select it to control primary differences between the two groups in each grade. The second rows show the performance between the two groups after the test, which was significantly different (0.03, 0.01, 0.02). Thus, as indicated in the table of descriptive data, the group who learned language through the blended pattern had a higher mean than the group who underwent conventional training. The ubiquitous technological tool of mobile phone has the potentiality of presenting so many learning features and its ease of use, convertibility into a language learning device and capability of creating new software enabled all teachers and students to work with them.

Discussion

To answer the research hypothesis (English learning in first, second and third grade students through the blended approach were greater than the students not exposed to blended approach), language program with a blended approach using mobile phone was designed and was tested on the first, second and third grade students. The results of analysis of covariance showed that the blended approach had a positive impact on the learning process and the difference between the experimental and control groups were statistically significant for the primary first-grade students (0.03), second grade (0.01) and third grade (0.02) at the level of 0.05. In other words, the approach has been able to facilitate a kind of personalized learning by developing a flexible environment. The study results are consistent with that of Ghaffari et al.(8), Sandberge et al. (5), Sugie (6), De Silva Soares & Weissheimer (9) , Lai et al. (10), and Ferreira et al. (11), Fahimi et.al(12).

Table 1: Descriptive statistics data in experimental and control groups of 1st(n=28), 2nd(n=32) and 3rd(n=30) grade primary school

	Mean			Standard deviation			Maximum value			Minimum value		
	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
Pretest	51.5	59.8	63	8.7	13	8.5	73	78	78	40	37	45
Posttest	88	87.3	90	9.3	9	8.7	100	100	100	66	69	74

Table 2: Kolmogorov–Smirnov test results of 1st, 2nd, 3rd grade primary school

Variable	Statistic			Significance		
	1st	2nd	3rd	1st	2nd	3rd
Pretest	0.83	0.8	0.5	0.83	0.7	0.9
Posttest	0.85	0.8	0.8	0.85	0.6	0.5

Table 3: Levine test for homogeneity of variances of 1st, 2nd, 3rd grade primary school

	Statistic			First degrees of freedom			Second degrees of freedom			Significance		
	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
Pretest	0.03	2.0	0.04	1	1	1	26	30	28	.80	0.1	0.8
Posttest	1.6	0.4	1.8	1	1	1	26	30	28	0.2	0.5	0.1

The students and their parents expressed positive feelings regarding working through the blended approach using mobile phone. As the support teacher was aware of the specific interests and needs of the students they felt a sense of obligation to further their students' learning and correct their common mistakes. The students expressed some surprise about the feedback provided because it did not resemble the type of feedback they had had before. Drawing from the results discussed above, the researchers developed a visual model to better illustrate the instructional design of the learning environments in different models of blended approach.

According to researchers in the field of Computer Assisted Language Learning (CALL), some of the existing shortcomings in the foreign language learning contexts can be overcome using the appropriate technology and innovative medium of instruction. This is in part due to the fact that there is limited access to the natural environment of native language in foreign language education and in many cases; it is confined to a few minutes of listening to/ watching the audio/video materials inside the classroom through the implementation techniques which are also impaired. As Jonassen, et al.(2008) point out; technology includes the design of various types of learning environments which involve the learner(13) Facilitating the role of the teacher and learner is useful in this type of exercise. The most significant perceived merits of blended learning were related to the combination of the elements and the amount of support provided by teachers and the institute's infrastructure. Creating the blended learning environments that are informative and interactive without sacrificing the flexibility of the individualized instruction requires much greater effort and creativity on the side of teachers. What seems to be necessary is developing a bank of learning activities relying on various types of game and non-game software based on the fixed or portable technologies that are becoming more popular day by day among children. It can provide a lifelong learning route for them in a way that in more advanced levels of productive performance, students will be able to show their creativity and linguistic competence by writing a variety of interesting topics in group blogs or Wikis as some forms of blended learning platforms which can be the foundation for some useful learning models.

It also turned out that the techniques and methods of blended approaches and the use of media or technology in children's language learning has caused some confusion for teachers. As Ozdamli and Uzunboylu, (2015) assert, teachers' and students' perceptions to use technology are positive but their technology learning adequacy levels are not sufficient (14). Therefore, some educational courses should be provided for teachers in the context of this approach and its methods so that they can adapt themselves to the demands of new learning opportunities.

Conclusion

In summary, even though the findings of the present study and a large number of other research projects have supported the positive role of technology, it should be borne in mind that the key to the success in using the blended approach in teaching language is to integrate it wisely in educational contexts. Since technology as Saeedi and Sajjadi (2014) have asserted, has a double face(15). That is, much care should be taken in designing a practical and fruitful blended classroom by the use of the technological platform through which the maximum learning outcome is achieved.

Source	Sum of squares			Degrees of freedom			Mean square			Statistic			Significance		
	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
Pretest	316	275	263	1	1	1	316	275	263	4.6	4.2	4.2	0.04	0.04	0.04
Group	337	468	334	1	1	1	337	468	334	4.9	7.2	5.3	0.03	0.01	0.02
Error	1704	1884	1671	25	29	27	68	65	62						
Total	219182	246685	245230	28	32	30	316								

Table 4: The results from examination of the impact of pretest on posttest through analysis of covariance of 1st, 2nd, 3rd grade primary school

The present study made an attempt to develop a model of blended classroom for children at different proficiency levels in a way that they enjoy learning and are supported positively within a face-to-face and virtual environment. The finding of the study can be of benefit to curriculum designing stakeholders and teachers to be more active in using the technological tools in enhancing the learning phenomenon in primary school contexts.

Limitation:
Even though this study unravelled some issues related to blended learning in the context of Iran, further research should be conducted on this approach, especially in the field of language learning. Furthermore most studies focused on one aspect of technology and were mostly case studies. Moreover, articles were not so much concerning language blended learning on children and the study population were boys and for girls the results may not be applicable.

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Figure 1: A model to illustrate the instructional design of learning environment in a blended approach
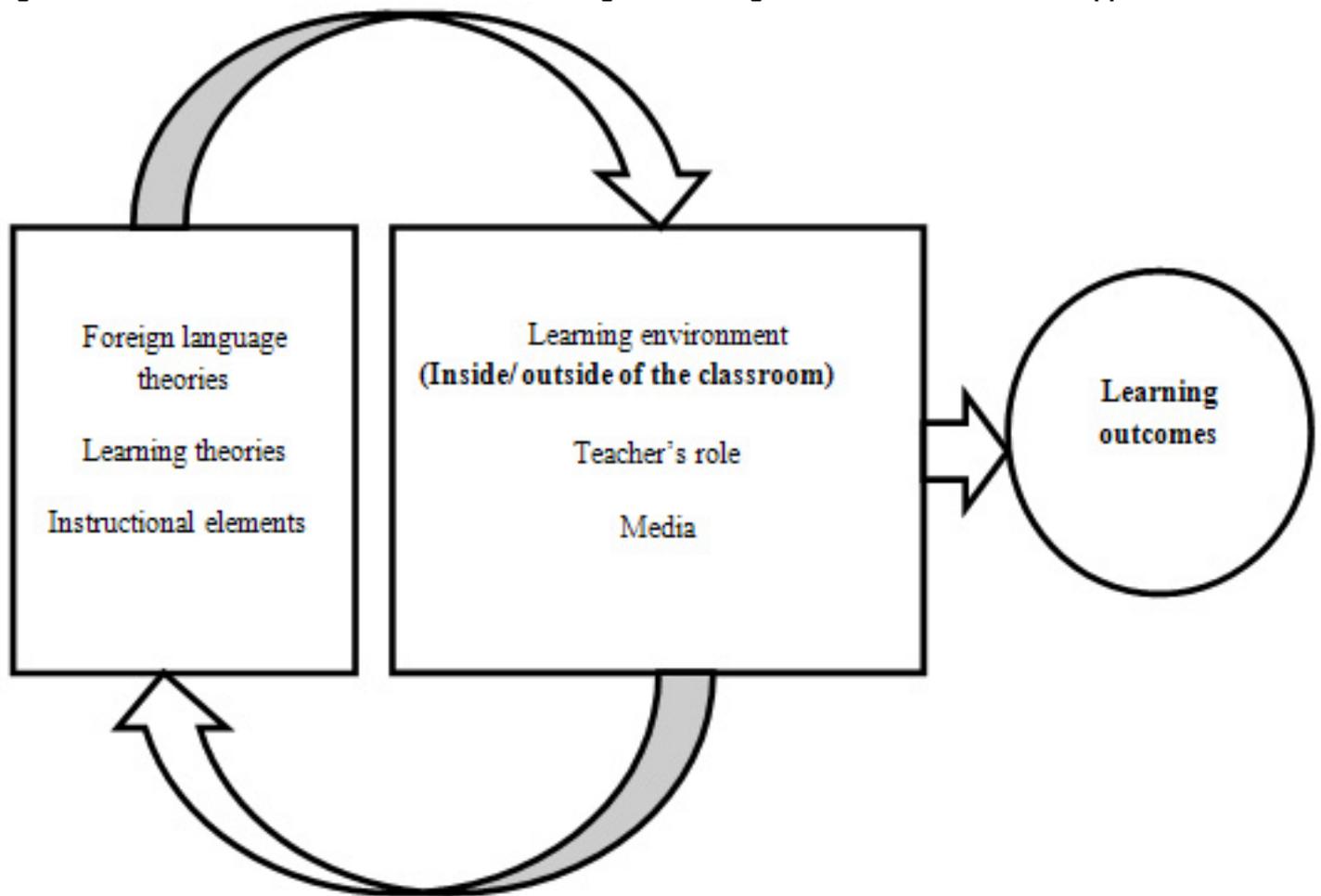
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The Relationship between Chronic Pain and Obesity: The Mediating Role of Anxiety

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Abstract

Obesity is nowadays considered as one of the problems impairing functioning and quality of life. Obesity is defined by body mass index (BMI), and most studies on the association between psychiatric disorders and obesity have exclusively studied depression. But there are just a few researchers that have studied the association between obesity and anxiety, and the mechanism of this association remains unclear. This study aims to evaluate the extent to which the association between chronic pain and obesity are mediated by anxiety and moderated by coping strategies. The study population comprised 200 participants (100 male and 100 female) aged between 20 and 70 (M=45) years old. All participants completed the Pain Self-Management Checklist, Beck Anxiety Inventory-II, and Lazarus Coping Skills Scale. The statistically significant paths were anxiety-pain, pain-obesity, and anxiety-emotional coping strategies (p<0/005). In summary, chronic pain predicted obesity directly, and specific coping strategies (emotional coping strategies) did not moderate the relationship between chronic pain, obesity and anxiety, but anxiety mediated this relationship.

Key words: Obesity, Anxiety, Chronic pain, coping strategies

Introduction

In the coming decades, global health will be faced with enormous challenges with several public health problems such as Obesity, major depressive disorder (MDD), and anxiety (Kelly, Yang, Chen, Reynolds, & He, 2008; Kessler et al., 2003). Obesity and Major depressive disorder and/or anxiety disorders impose a large cost on individuals, health care services and society and are associated with long-term disabilities, morbidity and mortality (Müller-Riemenschneider, Reinhold, Berghöfer, & Willich, 2008; Pi-Sunyer, 2009). Several studies have suggested bilateral relationship between obesity and MDD and/or anxiety disorders and also the possibility of their comorbidity (Afari et al., 2010; Luppino et al., 2010).

Pain is the most common physical symptom-based condition reported in both the general population and in primary care (Kroenke, 2003) and it causes several functional and work-related disabilities (Greenberg et al., 1999; Institute of Medicine, 2011). Additionally, several studies have proved additive and adverse effects of different kinds of pain such as osteoarthritis pain, chronic headaches (Bigal et al., 2007) and neuropathic pain (Miscio et al., 2005). In obese people the impact of pain on the functional status and health-related quality of life is greater than people with normal weight (Marcus, 2004; Ray, Lipton, Zimmerman, Katz, & Derby, 2011).

The underlying mechanisms of the pain and obesity relationship is still unclear (Rossi, Luu, DeVilbiss, & Recober, 2013). In some literature obesity has been defined as a pro-inflammatory state and inflammatory mechanisms are involved in the development of pain, so inflammation can be considered as a part of the causal pathway. Additionally, evidence suggested a causal relationship between acute pain and transient insulin resistance (Greisen et al., 2001; Ray et al., 2011). Eventually, there is an association between depression and both obesity and chronic pain, and obsessive patients with comorbidity of depression and anxiety have worse experience of pain (Ray et al., 2011; Tietjen et al., 2007). A potential unifying mechanism may be found in the metabolic syndrome, which is known to be associated with chronic pain (Loevinger, Muller, Alonso, & Coe, 2007; Ray et al., 2011), inflammation (Lee, Lee, Huang, & Sheu, 2007), insulin resistance (Lann & LeRoith, 2007) and mood disorders (Räikkönen, Matthews, & Kuller, 2007).

There are several ways and strategies to cope with chronic pain which has been examined by various studies (Büssing, Ostermann, Neugebauer, & Heusser, 2010). Pain-related coping may be defined as individuals' attempts to manage problems associated with their pain state (DeGood & Tait, 2011) and according to their ability to effect symptoms, coping strategies has been divided into two categories: adaptive and maladaptive. Often, adaptive and maladaptive coping responses have been known as active and passive responses, respectively. For instance, adaptive coping appears in the form of staying active and pacing problem solving, while maladaptive

coping tends to present passive strategies such as resting and avoiding (Jensen, Turner, Romano, & Nielson, 2008). It's assumed that the role of maladaptive coping strategies in chronic pain consequences is more important than adaptive coping strategies (Geisser, Robinson, & Riley, 2000). This assumption has been examined frequently in different studies. For instance, the increased use of passive coping responses after multidisciplinary pain treatment has been associated with increased disabilities and depression (Jensen, Turner, & Romano, 2007). In a study on 106 military veterans who suffered from chronic pain, there was a strong association among maladaptive responses, pain interference and depression, while the relation of adaptive coping styles and pain intensity was considerable (Tan, Teo, Anderson, & Jensen, 2011). It is hypothesized in the present study that coping strategies and anxiety would impact the relationship between chronic pain symptoms and obesity.

Materials and Methods

This study explores the mediating role of anxiety and moderating role of coping strategies in the relationship between chronic pain and obesity. As one of the inclusion criteria, participants had to meet the criteria for chronic pain and obesity (BMI >30). Additional inclusion criteria for this study were being at least 18 years of age, current self-report of chronic pain (of more than 6 months' duration) confirmed by medical record and diagnosis, obesity, and having received treatment for a painful condition within the last 5 years (recorded in their medical records). Participants were excluded if they were older than 70 years old. All participants (N=200) signed informed consent and completed study-related tasks. Participants were selected through accessible sampling from the general population.

Data collection
Demographic characteristics, such as participants' age, gender and educational level, were gathered with relevant self-report questions.

Measures
Symptoms of anxiety were assessed by Beck anxiety inventory (BAI-II). The 31-item self-report Chronic Pain Inventory (CPI) was used for assessment of pain severity. Coping strategies were evaluated by Coping Questionnaire, developed by Lazarus and Folkman, (1984), containing 66 items (16 distractors and 50 main items) that assess direct confrontation, distancing, self-control, seeking social support, accepting responsibility, evasion and avoidance, solving planned problems and positive re-evaluation (Sadeghi & Niknam, 2015). Lazarus reported the reliability of each subscale from 0.66 to 0.79 and the reliability of the coping skills was estimated 0.84 (Rajabi Damavandi, Poushne, & Ghobari Banab, 2009). These values reflect the desirable reliability of the test (Sadeghi & Niknam, 2015).

Asghari-moghaddam et al (2008, 2011, 2008, 2002) assessed chronic pain using Chronic Pain Inventory (CPI) (Asghari-moghaddam, Abedi Ghelich Gheshlaghi,

(Asghari-moghaddam, Abedi Ghelich Gheshlaghi, & Khalil-zade Poshtgol, 2008; Asghari Moghadam, 2011; Asghari Moghadam & Golak, 2008; Asghari Moghadam & Najarian, 2002). This inventory, which contains 31 items, assesses pain severity, the start time of pain, pain intensity six months after pain start time, influence of pain on the social and family relationships, and the number of operations because of pain.

Statistical analysis
Table 1 shows the mean and standard values of research variables: the scores mean for emotional coping and problem solving coping were 39.80 and 36.87, respectively. Furthermore, the means for anxiety, pain and obesity were 14.76, 33.01 and 32.34, respectively.

Table 1: Descriptive statistics of variables

Variables name		N	Mean	Std.
Coping styles	Emotional	200	39.80	11.84
	Problem solving	200	36.87	9.69
Anxiety		200	14.76	11.06
Pain		200	33.01	15.12
Obesity		200	32.34	3.22

Results

Path analysis was used for analysis of research data. As per the obtained results, anxiety proved to be a mediating variable in the present study and, based on literature review, pain and coping styles have effects on obesity after they have been affected by anxiety; therefore, the following model was tested (Figures 1 & 2)**):**

Three paths from anxiety to pain, emotional coping and problem solving coping; one direct path from anxiety to obesity; and three direct paths from pain, emotional coping and problem solving coping to obesity can be observed on the path diagram. Analysis results show that standardized regression weight from anxiety to emotional coping is 0.23 and p<0.001; anxiety to problem solving coping is 0.12 and p>0.08; anxiety to pain is 0.32 and p<0.001; emotional coping to pain is 0.08 and p>0.23; problem solving coping to pain is -0.18 and p<0,01; pain to obesity is 0.25 and p<0.001; emotional coping to obesity is-0.05 and p>0.50; problem solving coping to obesity is-0.04 and p>0.58; and anxiety to obesity is 0.005 and p<0.94. Table 2 shows the foregoing results completely. Fitness indexes did not confirm the fitness of conceptual model with observed data. Chi-square stood at 141, 983, the degree of freedom at 1, and Probability level at 0.001. Chi-square index shows the significant difference between conceptual model and observed model. As many references have suggested that chi-square is dependent upon sample size, it is thus more desirable to use other fitness indices for model fit test. Therefore, CFI, NFI and RMSEA indices were used. As shown in Table 3, these indices do not confirm the models.

Table 2: Regression Weights (Default Model)

			Regression Weights		S.E.	C.R.	P
			Unstandardized	Standardized			
Emotional coping strategies	<---	anxiety	.246	.230	.074	3.330	•••
Problem solving coping strategies	<---	anxiety	.107	.122	.062	1.734	.083
Pain	<---	anxiety	.451	.327	.094	4.805	•••
Pain	<---	Emotional defence	.103	.080	.087	1.178	.239
Pain	<---	Problem solving defence	-.275	-.175	.104	-2.639	.008
Obesity	<---	pain	.052	.248	.016	3.339	•••
Obesity	<---	Emotional defence	-.013	-.047	.019	-.669	.503
Obesity	<---	Problem solving defence	.013	.039	.023	.551	.582
Obesity	<---	anxiety	-.001	-.005	.022	-.065	.948

Figure1: Unstandardized estimated
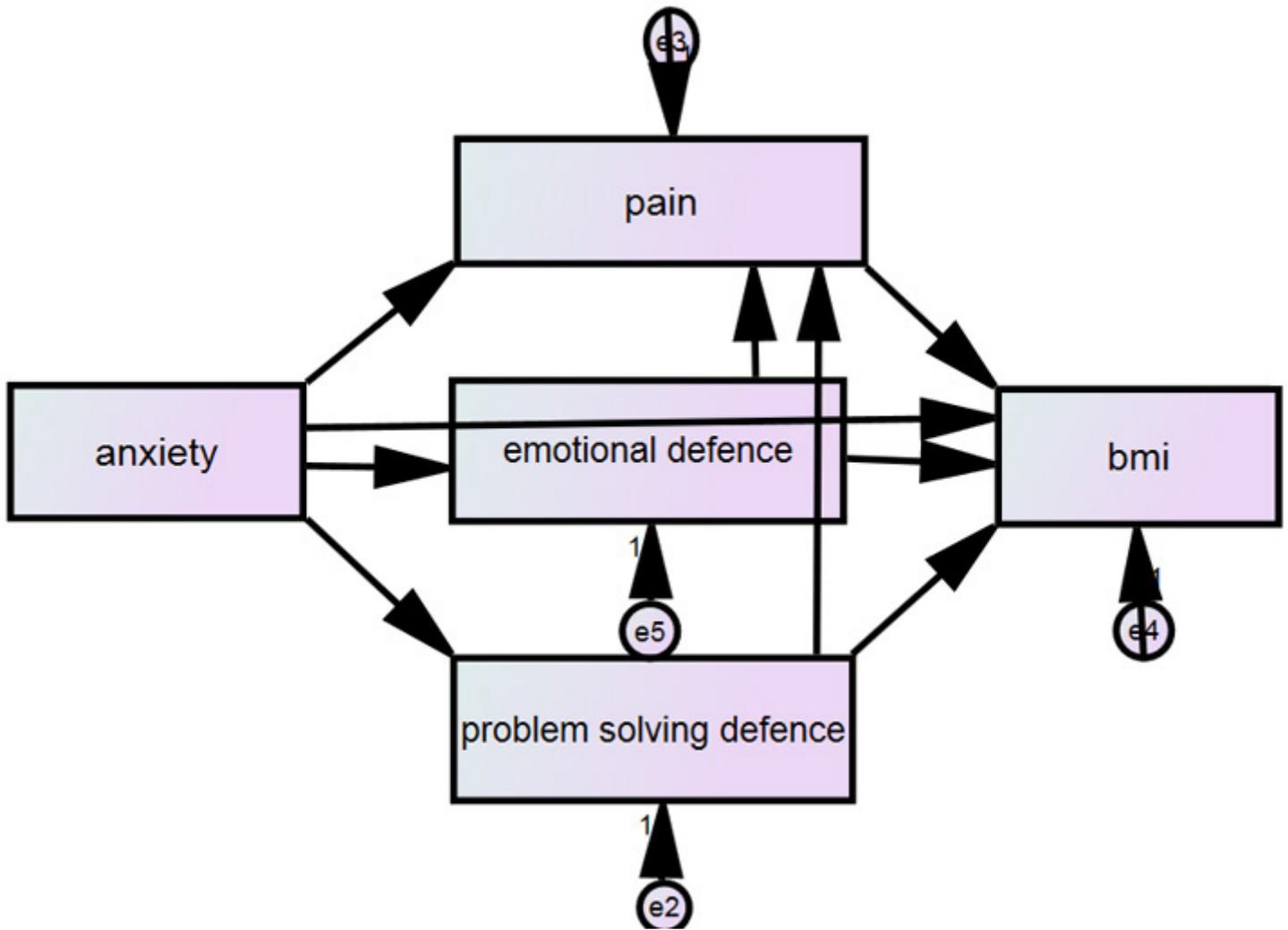
Table 3: Indices of fitness

Index Name	Observed Value	Excepted Value
$\dfrac{\chi 2}{df}$	141.983	Below 3
RMSEA	0.84	Below 0.1
CFI	0.23	More than 0.9
NFI	0.27	More than 0.9
IFI	0.27	More than 0.9

Figure 2: Standardized estimated
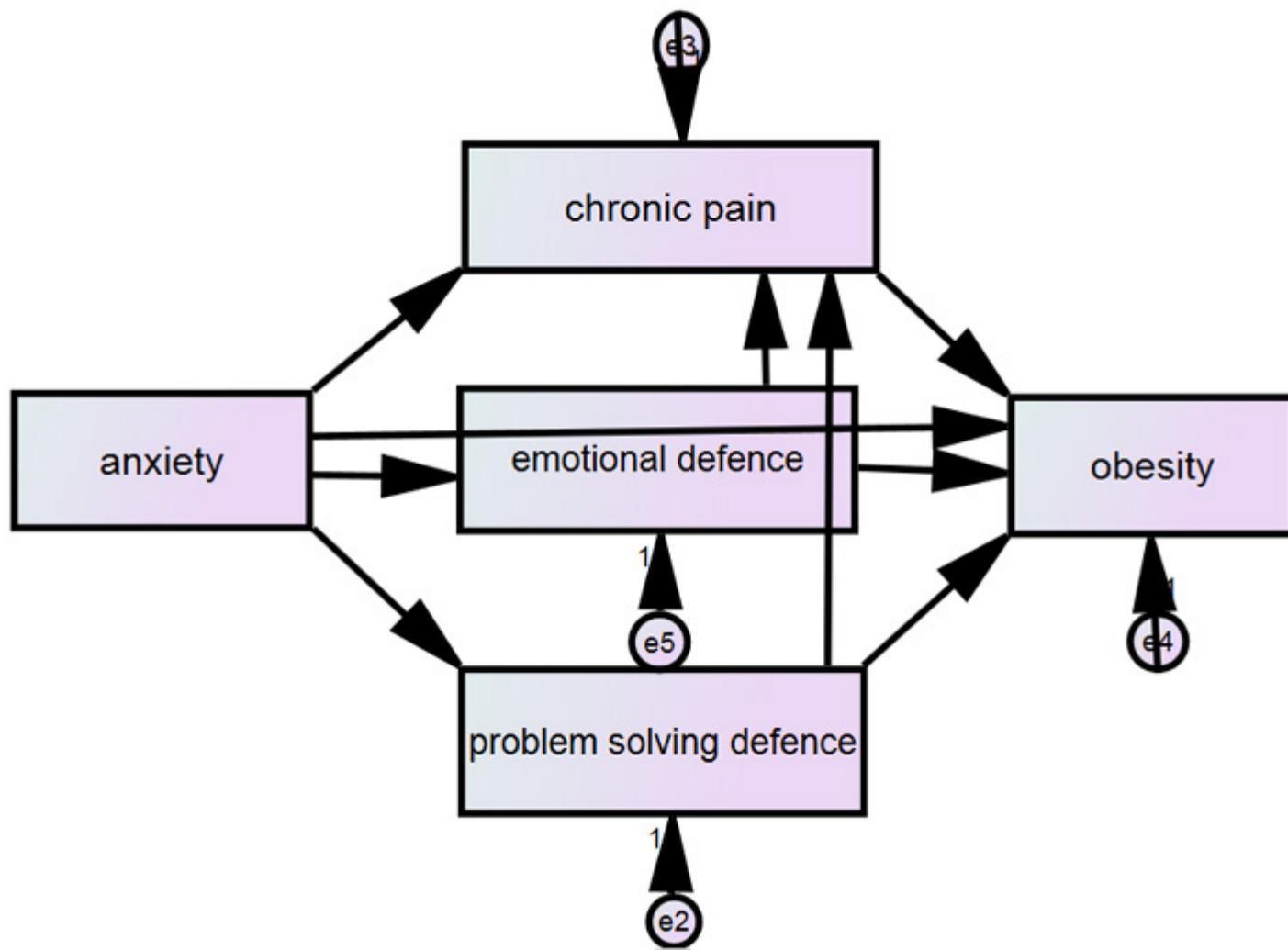
Discussion

The present study explored the relationship between chronic pain and obesity with the mediating role of anxiety and moderating role of coping strategies. Personal resources play an important role in reduction and prevention of anxiety. The results obtained by the present study show that anxiety predicts emotional coping strategies. In other words, greater anxiety correlates with greater emotional coping strategies. The result is consistent with the findings of similar studies. For example, the importance of dysfunctional coping strategies in predicting anxiety and its helpful role in managing anxiety were indicated by researchers (Cooper, Katona, Orrell, & Livingston, 2006). There is a relationship between psychological distress and different coping strategies. There are negative relations between the problem-focused coping and anxiety, stress and depressive symptoms, while this relation in case of the avoidant coping is positive (van Berkel, Boot, Proper, Bongers, & van der Beek, 2014). Problem-focused coping helps to manage the stress causing the problem, and emotional-focused coping diminishes the negative emotions associated with the stressor (Folkman, Lazarus, Dunkel-Schetter, DeLongis,

& Gruen, 1986). However, avoidance coping, as a type of passive coping, is highly related to psychological outcomes due to minimizing, denying or ignoring to deal with a stressful situation (Holahan, Moos, Holahan, Brennan, & Schutte, 2005; Snow, Swan, Raghavan, Connell, & Klein, 2003).

Based on the results obtained in this study, there is a significant prediction between anxiety and chronic pain. In other words, anxiety increases the severity of pain. Additionally, pain, depression and anxiety frequently co-occur and have additive and adverse effects on health-related quality of life (HRQL), functional impairment and treatment response (Bair, Robinson, Katon, & Kroenke, 2003; Bair, Wu, Damush, Sutherland, & Kroenke, 2008). A study on 500 primary care patients with chronic pain discovered negative association between anxiety severity and pain severity (Bair et al., 2008). There are some findings that claim chronic pain substantially increases the likelihood of anxiety disorder (McWilliams, Cox, & Enns, 2003). In other research, it was concluded that the presence of any of the five common pain complaints increased the likelihood of having an anxiety disorder significantly (Kroenke & Price, 1993).

The other finding of the current study is related to the prediction of obesity by chronic pain. The findings demonstrate that obesity is strongly associated with chronic regional pain (CRP) as well as reporting of musculoskeletal pain at specific members such as the knees. Furthermore, obesity is associated with more severe pain (Deere et al., 2012). Obesity is also associated with an increased risk of pain at any members, as well as a range of musculoskeletal pain phenotypes. The strongest associations, as observed in analyses on boys and girls combined, were between obesity, risk of CRP, and knee pain. Whereas CRP also comprised pain at shoulders, lower back, and hips, all of which showed weak evidence of an association with obesity, the relationship between obesity and CRP may have been driven by that with knee pain. Obesity was also associated with pain severity, as reflected by higher average pain scores in obese participants reporting CRP and knee pain (Deere et al., 2012). However, the findings of the present study are in contrast with those of other researchers that claim obesity influences the pain. It was found that pain predicts obesity. In general, the path analysis (as shown above) shows that anxiety is a predictor of chronic pain and chronic pain can predict obesity. On the other hand, anxiety can predict the emotional coping strategies, but the emotional coping strategies are not able to predict obesity.

Limitations

The present research was faced with some limitations, such as a small study population. The population of the present research being 200 individuals can be one of the reasons for Indices of fitness not confirming any fitness between conceptual model and observed data. Another limitation was the cross-sectional design, and the authors of the present study recommend that this research be repeated in a longitudinal prospective design.

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Implementation status of moral codes among nurses

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Abstract

Background and objective: Nurses should have an appropriate level of ethical development to perform their daily care. Ethical codes should be understood by nurses and used in each dimension of nursing practice. Therefore, this study aimed to investigate the implementation status of nurses' ethical codes.

Methods: This descriptive-analytic study was carried out on 202 nurses working in internal and surgical wards using easy sampling in educational hospitals of the Faculty of Medical Sciences, Abadan. The implementation status of ethical codes was investigated using a researcher-made questionnaire and the obtained data were analyzed using SPSS ver. 16.

Results: There was a statistically significant difference between the level of ethical performance of nurses with cases such as organizational positions, work shift, academic education, and ethics retraining courses and work experience (p< 0.005). This difference was not observed in relation to gender, marital status, educational degree, history of presenting complaints and job satisfaction and the workplace (p>0.005).

Conclusion: Results of this study showed that nurses should firstly recognize the dimensions and ethical issues in their profession for the ethical performance of professional nursing; therefore, it is recommended to maximize the efficiency and quality of health care by educating the medical staff and raising their awareness of professional ethics.

Key words: Professional Ethics, Code of Ethics, Nurses

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Introduction

The health care system consists of a variety of components, each of which plays its role in some way. Among the components of this system, nursing is one of the most important pillars, so that the services provided by this component directly affect health and disease related indicators and related outcomes (1). Although observance of professional ethics is necessary in all occupations, this factor is more necessary in the nursing profession because spiritual behavior along with the responsibility of nurses with patients plays an effective role in their health improvement and recovery. Therefore, the nursing profession is based on ethics (2-3). Nursing ethics refers to the observance of professional ethics in providing nursing cares (4) which leads to conscientiousness towards the patient and the health organization (2-3). Any problem in observing nursing ethics can affect the most scientific and best nursing care (5). Although nursing knowledge has been significantly expanded and great emphasis has been placed on nursing technical competencies as well, the issue of ethical competence in care or care ethics has been some times neglected (6). With increasing attention to ethical issues and challenges in care settings, health care providers have been facing complex situations due to ethical issues (7). The working environment of nurses and their daily exposure to death lead to ethical tension among them (8). In fact, ethical tension occurs when a person knows what is right but the work constraints hinder proper work (9). According to existing studies, about 11% of and 36% of nurses face ethical challenges and problems every day and every few days, respectively (10-11). In the clinical environment, the ethical action factor, which means thinking, practicing, and accepting the responsibility of the performed act, may be confused with the contradictory values existing in it (12). There is also the fact that it seems nursing ethical values are not always clear (13), and the health services providing working environment undergo constant changing affecting the ethics factor (14). This issue leads to more complexity of the subject. The evident fact in recent years is that although nurses are trained on ethical issues, one of their major concerns is that they do not know how to deal with different ethical situations and problems (15). The results of studies in the ethics field indicate weakness in nursing ethical decision making (16). According to the studies, the mean score of ethical reasoning was reported to be 51.74 and 16.42 among nurses in other countries and Iran, respectively (17). Many investigations in different societies have led to the recognition of different aspects of ethical sensitivity (18). However, there are limited studies on ethical sensitivity, and this issue has not been adequately addressed by the researchers as to the importance it has in clinical practice. Kim et al. believe that the outcomes of previous research on the subject of ethical sensitivity are limited and of little depth (19). Therefore, it seems that a comprehensive view of this important issue can be valuable. Given the inadequate studies on nursing ethics, and since one of the important achievements of observance of ethical codes is to facilitate the implementation of clinical governance, which includes cases such as taking steps to minimize the risk to employees and patients, paying attention to patients' complaints and use of the best evidence in clinical decision making (20), this study aimed to investigate the implementation status of ethical codes in nurses.

Method

The present research is a descriptive-analytic study which was conducted in 2016. The research population consisted of nurses working in hospitals affiliated to the Abadan Faculty of Medical Sciences who were selected using convenience sampling method. Inclusion criteria included having a bachelor's degree in nursing and above, employment in one of the internal and surgical wards, having at least six months of work experience and informed consent for participation in the study. After obtaining permission from the Research Ethics Committee of Abadan Faculty of Medical Sciences, and presenting an introduction letter from Research Management to the head of target hospitals, the questionnaires were distributed by the researcher after repeated referring to the wards at the right time, explaining the research objectives, the method of filling in the questionnaire and obtaining informed consent. It should be noted that the samples completed the questionnaire freely and without direct supervision of the researcher, then the completed questionnaires were collected by the researcher. Two questionnaires were used to collect information.

A) Demographic information questionnaire including age, sex, marital status, educational level, organizational post, work shift, ethics education, retraining courses during recruitment, the history of a patient's legal complaint from a nurse, professional satisfaction, work experience and the workplace.
B) To investigate the nurses' performance to the nursing ethics of Iran, a researcher-made questionnaire, by Mohajl Moghadam et al. (5), was used. In this questionnaire, according to Iran's Nursing Ethics, ethical guidelines have been developed in five areas of nurses and community, nurses and professional commitment, nurses and cares provision, nurses and the therapeutic team colleagues, nurse and education, and have 35 statements per area. Options, including Always, Often, Occasionally, Rarely, Never, and not experienced were considered in each statement. Cronbach's alpha coefficient for the reliability and internal consistency of the questionnaire was calculated 0.79 by Mohajl Moghadam et al (5). Face and content validity of the questionnaires were also evaluated in this study (5) by the professors of medical ethics, social medicine, Islamic education and nursing. SPSS ver. 16 is used in this research. For statistical analysis of data, descriptive statistics were used for obtaining basic information such as frequency, frequency percentage, mean, minimum and maximum, number of data and standard deviation. In inferential statistics, the Kolmogorov Smirnov test was used for normality of variables and independent t-test, Mann-Whitney U test, Kruskal-Wallis and Pearson correlation were also used. It should be noted that all ethical considerations, including obtaining the code of ethics (IR. ABADANUMS.REC. 1395. 133), obtaining

informed consent from the participants, confidentiality of information, the possibility of withdrawal from the continued participation of nurses if desired and the publication of the results as a group study were considered.

Findings

69.3% of the participants in this study were women and 52% were married. 93.6% had ethical education and 86.6% had passed retraining courses in this field. Moreover, 86.6% had no history of making complaints, 67.3% of them are satisfied with their professions, and the average age is 32.396±7.335. Other information on demographic variables is presented in Table 1.

Table 1: Descriptive statistics of demographic variables

		Frequency	Frequency percentage
Degree	BA	196	0.97
	MA	6	0.3
Organizational position	Nurse	194	0.96
	Head nurse	8	0.4
Work shift	Morning	26	12.9
	Afternoon	2	0.1
	Night	15	7.4
	Circulating shifts	159	78.7
Work experience	Less than 5 years	92	45.5
	5-10years	56	27.7
	11-15 years	30	14.9
	More than 15 years	24	11.9

Comparison of the nurses' performance to the Iranian nursing ethics in each of the demographic variables is presented in Table 2. Considering the normality or non-normality of distribution of the sample, the appropriate test has been used. There was no statistically significant difference between the distribution of performance to Iran's nursing ethics with gender, marital status, educational level, complaints history and having job satisfaction and workplace ($p > 0.005$).

Table 2: The relationship between the socio-demographic characteristics of nurse with their performance to the nursing ethics of Iran

Variable	Classification	Mean	Standard deviation	Statistics	Degrees of freedom	Significance level
Organizational position**	Nurse	5.256	0.527	0.457	-	0.049
	Head nurse	5.589	0.304			
Work shift ***	Afternoon	4.928	0.020	Only two cases do not participate in the test 10.021	2	0.007
	Morning	5.374	0.369			
	Night	4.870	0.567			
	Circulating shifts	5.294	0.529			
University education **	Yes	5.297	0.503	0.693	-	0.009
	No	4.874	0.669			
Retraining course **	Yes	5.299	0.511	1320.500	-	0.022
	No	5.012	0.575			
Work experience***	Less than 5 years	5.159	0.575	9.888	3	0.02
	5-10 years	5.426	0.3977			
	11-15 years	5.311	0.499			
	More than 15 years	5.276	0.534			

* Both groups are normal and the independent T test is used.
** At least one group is not normal and Mann-Whitney U is used.
*** At least one group is not normal and the Kruskal-Wallis test is used.

Table 3 shows the frequency percentage of distribution of nurses' performance to the nursing ethics of Iran from their point

Table 3: Frequency percentage of distribution of nurses' performance to the nursing ethics of Iran from their point of view

	Statements on Nursing Ethics in Iran	Not experienced	Never	Rarely	Sometimes	Mostly	Always
1	I attempt to reduce pain, prevent diseases and improve public health.	0	0	20	5	19.3	73.8
2	I carry out nursing care with respect for human rights, social values and religious beliefs of the patient.	0	2.5	1	2	18.3	76.2
3	I paid special attention to vulnerable groups such as the elderly, people with disabilities and physical disabilities	0	1	0.5	3.5	21.8	73.3
4	In crises, natural disasters and epidemics, I carry out my duties with caution.	2.5	1	1	5	23.3	67.3
5	When considering nursing interventions and clinical decisions, I will also take ethical responsibilities.	0	0	1	2	14.4	82.7
6	Within the range of my duties and authority, I try to provide a safe and healthy environment for the patient.	0	0	0.5	2.5	18.3	78.7
7	I secure patient safety with timely attendance, performing professional tasks and recording care provided.	0	0.5	1	1.5	24.3	72.8
8	I provide the best care to the patient, based on professional standards from valid research findings.	0	0	0.5	8.4	27.2	63.9
9	I carry out all nursing interventions by maintaining human dignity and respect for the patient and his or her family.	0.5	0.5	1	3	20.3	74.8
10	I attempt to protect patient's secrets, privacy, respect for individual autonomy and obtain informed consent.	0	0	0.5	3	21.3	75.2
11	I prevent possible injuries to the patient by identifying and reporting possible professional errors made by my colleagues.	0.5	0	0	6.9	26.7	65.8

12	In the event of an error in nursing interventions, I honestly explain it to the patient and observe honesty and fairness.	2.5	2.5	4.5	10.4	30.2	50
13	I maintain and promote my physical, mental, social and spiritual abilities.	0	0	4.5	5.4	28.7	64.4
14	To maintain professional competence, I keep my knowledge and skills up to date.	0.5	0.5	3	8.4	28.2	59.4
15	I have the knowledge and ability to take care of the patient, without direct supervision of the authorities, and I am responsive to my duties.	0	1.5	0	9.9	22.8	65.8
16	I refrain from accepting any gift or privilege from a patient or relatives	7.4	3.5	0.5	2.5	11.9	74.3
17	I introduce myself to the patient by naming my name, title and professional role.	0.5	2	1.5	6.9	16.8	72.3
18	I establish a relationship of mutual trust with the patient so I can understand his/her needs and concerns.	0	0.5	0	74.5	35.1	56.9
19	Prior to nursing interventions, I will provide the patient with sufficient information to accept or reject the interventions.	0	0	2.5	5.9	37.6	54
20	In order to empower the patient to improve her/his self-care, the patient and their family are being trained upon discharge	0.5	0.5	1	3	28.2	66.8
21	In emergency situations outside of the work environment, I also provide care for the patient or injured person.	5.4	2.5	7.9	13.4	30.7	40.1
22	I use patient information only for health-related purposes (treatment, research) and for the benefit of the patient.	0	0	2	5	27.7	65.3

23	I adopt precautions to ensure the safety of nursing interventions and consult with colleagues.	0	0	1	5.4	27.2	66.3
24	I will report any complaints and problems to the department in charge.	0.5	0	0.5	6.4	25.2	67/3
25	I will abstain from taking actions that violate ethical and legal principles, even with the patient's request.	0.5	0.5	0.5	2	19.8	76.7
26	I work to accept reality and meet the patient's wishes in the final days of her/his life.	0.5	1	1.5	8.4	19.8	64.4
27	Different levels of professionalism, other nurses, masters and behavioral students are honored with respect.	1	0.5	2	3	15.8	77.7
28	I consult with the Ethics Committee of the Hospital in the face of any ethical challenge.	10.9	2	5.9	20	29.2	42.1
29	In case of patient participation in research projects, I will observe patient rights and ethical considerations.	2.5	1	3.5	6.4	28.7	57.9
30	I use my professional position to persuade the patient to participate in research and education of students	9.4	2.5	5	12.4	27.2	43.6
31	If the patient and his/her family do not cooperate in teaching the students, it will not affect the delivery of the services.	5	2.5	1	11.4	25.7	54.5
32	As a clinical nurse, I attempt to improve the skills and capacities of nursing students.	3.5	0.5	4.5	11.9	25.7	54
33	I decide on the donation of patients with brain death or vegetable life.	32.7	22.8	3.5	5.4	12.9	22.8

34	I decide regarding the quality and quantity of the survival of coma patients.	30.2	24.8	5	5.4	8.9	25.7
35	I hide the prognosis of malignant diseases like cancer from the patient or his/her family.	25.7	18.3	11.9	9.9	13.9	20.3

Discussion and Conclusion

Based on the findings of this study, the variables such as age, sex, level and type of education have no effect on the ethical development of nurses and this has been emphasized by Zirk et al. (21) and Ghoorchiani et al. (22); however, Dehghani et al. (23) and Sokhanvar et al. (24) opposed to the lack of correlation between these variables. Also, there was no significant statistical difference between married and non-married nurses in terms of ethical performance, which was also emphasized in other studies (23, 25). The organizational position of nurses has had a significant effect on their ethical performance in this study, so that head nurses who often have a better a history of work and a sense of responsibility towards their work, had best performance, though it is not confirmed in some studies (23 and 25). Since the ethical principles in human encounters with patients and ethical laws are the same, in this research, the service area has not had an effect on the level of ethical development of nurses, which is consistent with the study by conducted by Zirk et al. (21). There was a significant relationship between the shift work of nurses and the quality of professional ethics performance and other studies achieved similar results (23). Morning nurses have had a better ethical performance than working shift nurses. The work environment and various shifts lead to nursing burnout, which in turn leads to a decrease in the ethical development level in nurses. Therefore, it seems necessary to make some changes in nurses' work shifts in order to reduce the effect of fatigue due to long working hours. Variables of passing the retraining course and university education were significantly related with the level of ethical development. Individuals with both trained ethics as well as in-service training were more likely to use ethical resources and institute ethical performance. In an environment where this training is not given much importance, ethical issues are overlooked over time and individuals only consider themselves to be bound to comply with institutional policies and clinical considerations. Since the studies of other researchers (26, 21, 23, 5) have also confirmed the effect of this training, it is necessary to pay close attention to educating ethical concepts, especially using new teaching methods in nursing education programs and in-service nursing programs. Hundert points out that there is a small probability that students who are not familiar with ethical theories before being in a clinical position can identify ethical problems (27). Erdil and KorkMazz agree with this idea (28). Their undesirable performance requires a change in the content of the curriculum and the method of teaching professional ethics in the nursing baccalaureate and before entering the clinical field (29).

Perhaps one of the challenges facing ethics education is the provision of qualified instructors in the teaching of ethical issues that have been referred to in research (30), because learning situational ethics has a considerable impact in increasing the internal motivation of individuals for ethical performance. Also, it was shown in this study that as the clinical experience of nurses increases, the ethical development of nurses decreases, which is consistent with the results of the Ham and Dean Mohammadi (31-33). However, there are obstacles to implementing these codes, which should be addressed first, so that they can be expected to be implemented well in the clinical field. Implementation of these codes requires the coordination and cooperation of all nursing practitioners and authorities such as the Ministry of Health, the Nursing Organization, the National Medical Sciences Universities, the Nursing Board and other nursing organizations, which must, with the participation of each other, eliminate structural barriers to the implementation of nursing ethical codes so that it will be turned into a charter applicable to hospitals. One of the limitations of this research is the fact that only nurses' views have been investigated, but it seems that a more comprehensive view on solving ethical problems in a clinical setting can be achieved by investigating the viewpoints of patients and nursing students. Data were also collected by self-reporting questionnaire, in which participants may not report their actual data.

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The comparison of quality of life, self-efficacy and resiliency in infertile and fertile women

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Abstract

Background: Pregnancy and infertility are important life events that are associated with specific psycho-social aspects, and infertility is usually regarded as a stressful and threatening event that is influenced by psychological factors.

Objective: The purpose of this study was to evaluate and compare the quality of life, self-efficacy and resiliency in infertile and fertile women.

Method: This causal comparative study, included all fertile and infertile women referred to Arash Hospital and Mirza Kuchak Khan Hospital in Tehran; 60 infertile women and 60 fertile women were selected using convenience sampling method. To collect data, the quality of life questionnaire (WHOQOL-BREF), Sherer's self-efficacy Questionnaire, and Conner and Davidson's Resilience Questionnaire were used. Descriptive statistics (mean and standard deviation) and inferential statistics (correlation test and regression analysis) were used to analyze the data.

Results: The results showed that mean (standard deviation) of quality of life, self-efficacy and resiliency in fertile women was 86.62 (11.162), 64.40 (9.048), and 71.40 (11.640), respectively. The mean (standard deviation) of quality of life, self-efficacy and resiliency for fertile women was 79.13 (10.829), 58.05 (7.688), and 66.92 (10.339), respectively. The results of t-test showed that between fertile and infertile women, in terms of quality of life, self-efficacy and resiliency there is a significant difference.

Discussion and Conclusion: The results showed that the level of quality of life, self-efficacy and resiliency in infertile women is less than in fertile women. Based on these results, it can be said that considering the importance of psychological factors in exacerbating the physical and mental damage associated with infertility, psychological interventions focused on quality of life, self-efficacy and resiliency with the aim of improving the mental health of the infertile people, is necessary.

Key words Fertility, Infertility, Quality of Life, Self-efficacy, Resiliency

Introduction

In many countries of the world, including Iran, pregnancy and having a child are generally a positive and welcome event and an important factor in gaining social status and strength of marital life, and infertility is often a great stigma, leading to psychological and social harm. Infertility is defined as lack of pregnancy following one year of intercourse without the use of contraceptive methods (Richard et al., 2014). The World Health Organization (WHO, 2004) estimates that 60-80 million couples experience infertility around the world. In recent years, infertility has risen (Jisha & Thomas, 2016).

In this way, it is estimated that in the world, 8-15 percent of couples may experience infertility (El Kissi et al., 2013). The prevalence of primary infertility in Iran was reported at 24.9% in 2004 (Vahidi et al., 2004; quoted by Jamshidimanesh et al., 2015). Infertility is considered one of the most important stressful events in life and a negative event for couples, which causes interpersonal distress in marital relationships (Rashidi et al., 2008; El Kissi et al. 2013), a serious threat to marriage and the continuation of marital life (Khetarpal &Colleagues, 2012), and in some cases, separates couples (Galhardo et al., 2011).

It seems that the impact of infertility is not limited to marital and sexual relationships, but it affects all dimensions of the individual's life and its effects are imposed on other psychosocial aspects of the infertile people (Chachamovich et al., 2010). Psychological problems are the consequences of infertility (Cwikle, Gidron & Sheiner, 2004). Research on the consequences of infertility has shown that infertility causes emotional disturbances in both women and men and their spouses (Greil, et al., 2011; Faramarzi et al., 2013; Takaki & Hibino, 2014). Infertility is linked to the prevalence of psychological and psychiatric problems, and numerous studies have reported the prevalence of these problems in infertile couples (De Berardis et al., 2014). Anxiety, depression and other psychiatric disorders are reported in couples and people with infertility, and studies report the prevalence of psychiatric problems from 6 to 68 percent (Sule, Gupte & De Sousa, 2017).

In several studies, it has been shown that infertility leads to reduced mental (subjective) well-being (Tovliat & Tamannaeifar, 2015), reduced mental health and marital adjustment (Tamannaeifar, 2011), decreased quality of life (Xiaoli et al., 2016; Chachamovich et al. 2010; Lau et al, 2008), decreased sexual function (Hassanin et al., 2010; Monga et al., 2004), anxiety, depression and decreased quality of marital life (Matsubayashi et al., 2004), feeling of helplessness and experience of negative emotions (Chandra et al., 2014).

Infertility due to its unfortunate consequences affects people's attitudes about themselves, toward life and the quality of life (Chachamovich et al., 2010) and causes a loss in quality of life (Hassanin et al., 2010; Drosdzol&Skrzypulec, 2008).

Quality of life is one of the most important health components that has received considerable attention in recent years. The concept of quality of life has been defined in various ways. The World Health Organization (WHO) defines quality of life as "the individual's perception of one's position in life, according to the cultural context and the value system of the community in which he/she lives," and considers this concept as a combination of physical health, state of Psychological health, level of independence, social relations, individual beliefs of these factors with environmental characteristics (Ghafari et al., 2012). Several studies have shown that quality of life in infertile women is lower than that of fertile women (Trent et al., 2002; Coffey, Bano & Mason, 2006; Nilfrooshan et al., 2006). It has been shown that the quality of life in infertile people with mental disorders is lower (Van der Akker, 2005; Chachamovich et al., 2010). It has been widely demonstrated that clinical symptoms of depression are related to the outcomes of quality of life (Schweikert et al., 2008; Ohaeri, Awadalla, & Gado, 2009).

Some studies have shown that demographic variables such as age, educational level, weak marital relationships, and the length of lifetime attempts to treat infertility are predictive of the quality of life in infertile people (Fekkes et al., 2003; Ragni et al., 2005; Lau et al. 2008). The study of Chachamovich et al. (2010) has shown that anxiety and depression are associated with a low level of quality of life in the infertile and the effect of depression is greater than anxiety and other clinical variables and socio-demographic factors.

Although numerous studies have shown the negative effect of infertility on the quality of life in infertile women (Fekkes et al., 2003), some studies have reported that there is no difference in the quality of life of the infertile population compared to the healthy population (Hearn et al., 1987). Even some studies have shown that quality of life and marital adjustment of infertile women are higher than fertile women (Onat&Beji, 2012). The attitude towards women's infertility is often influenced by racial differences and religion and culture undoubtedly affect quality of life in some aspects, such as infertility (Inhorn& Buss, 1994).

Another factor that has been addressed in women's infertility is self-efficacy of infertile people. In the case of infertile people, self-efficacy is the perception of patients of their ability to use cognitive skills to control emotions. An infertile person with high self-efficacy has more emotional (affective) stability and more insistence on treatment (Cousineau et al., 2006). Self-efficacy is an indicator of the individual's ability to use stress coping skills and the use of personal resources necessary to meet situational demands. There is some evidence that self-efficacy plays a role in managing illness, symptoms, and functional limitations (Banik et al., 2017). Hence, infertile people with high self-efficacy can maintain calmness. High self-efficacy enhances health behaviors and improves health status, and may even lead to an increased probability of pregnancy (Cousineau et al., 2006). Jamshidimanesh et al. (2015) showed that self-efficacy training for infertile

women had a positive effect and training programs that include familiarity with the reproductive system, definition of infertility, prevalence, causes, diagnostic methods, treatment protocol, and the necessary tests will increase the self-efficacy of infertile women. Sami and Tazeen (2012) reported that the increase in infertile women's information about the causes and treatments of infertility and ways to reduce stress and self-efficacy training can have positive effects and will lead to better healthcare of infertility and to avoid traditional and insecure methods.

Considering that studies have shown that infertility is associated with a lot of stress, the issue of resiliency has also been of particular importance, because resiliency is considered as one of the personality traits that play a protective role against life-threatening factors including diseases. Resiliency is the process or ability to adapt to the challenges and threats of life and to overcome them (Newman, 2003). Resiliency is the ability to resist against difficult living conditions and a dynamic process in adapting to important disasters; therefore, resiliency is considered as a positive symmetry of vulnerability (Herrmann et al., 2011). Resiliency focuses on groups exposed to risk factors, but who are faced with few negative consequences and may even have positive outcomes (Tiet& Huizinga, 2002).

Studies have shown that infertile people's resiliency is less than fertile people (Sexton, Byrd & Kluge, 2010; Kagan et al., 2011; Lee et al., 2012). Rezaie et al's (2013) study showed that with increasing resiliency, patients are helped to better deal with harsh conditions. A study conducted by Lee et al. (2012) shows that resiliency can lead to optimism, spirituality, psychic calm and an increase in the quality of life of infertile women. Abbasi et al. (2014) showed that considering the fact that resiliency causes people to reasonably and positively deal with life stresses, they can positively evaluate life events. Therefore, low levels of resiliency in infertile women can reduce their psychological well-being.

Researchers believe that infertility is a life crisis for the couples involved, and others consider it as the most stressful event after a divorce and the death of a dear one (Herrmann et al., 2011). Even if most couples with infertility show that infertility does not have a long-term effect on their life satisfaction, at the time of diagnosis and subsequent treatment, the level of satisfaction is reduced (Verhaak et al., 2007) and can affect many aspects of life including the quality of life. Therefore, the present study was conducted to compare the quality of life, self-efficacy and resiliency in infertile and fertile women.

Method

This study is a causal comparative study. The statistical population of this study consisted of all fertile and infertile women referring to Arash Hospital and Mirza Kuchak Khan Hospital in Tehran. 60 infertile women and 60 fertile women were selected using convenience sampling method. After expressing the research aim for the subjects, they were asked to respond to the questionnaires if they wished.

Subjects were told that the data of the questionnaires were completely confidential. To collect data, Quality of Life Inventory (WHOQOL-BREF), Sherer's Self- efficacy Questionnaire, and Connor & Davidson's Resilience Questionnaire were used.

Quality of life questionnaire
The Quality of Life Questionnaire (WHOQOL-BREF) assesses the quality of life totally and in general, and has four areas of physical health, mental health, social relationships and environmental health. This questionnaire has 24 questions, each of the areas has 3. 6, 7 and 8 questions, respectively. The questionnaire has two other questions that do not belong to any of the areas and that generally assess health status and quality of life. Nejat et al. (2006) have reported the reliability of this scale by Cronbach's alpha method in areas of physical, psychological, social and environmental health, respectively, 0.70, 0.73, 0.55 and 0.84, and after two weeks using test-retest method a coefficient of 0.70. In the study of Kiaei et al. (2016), Cronbach's alpha in all areas was above 0.70 and only in the social relationships was 0.55.

Self-efficacy questionnaire
Sherer's Self- efficacy Questionnaire has 17 items. Sherer (1982) argues that this questionnaire measures three aspects of behavior, including the desire to initiate behavior, the desire to expand efforts to complete a task and being different in confronting obstacles. The scoring of this scale is on a Likert scale from absolutely disagree (1) to absolutely agree (5). Sherer (1982) reported the Cronbach's alpha of this scale 0.76. In the study of Behrozian et al. (2013), the coefficient of reliability of this test was 0.80.

Resilience questionnaire
This questionnaire was developed by Connor and Davidson (2003) to measure the power of coping with stress and threat, and has 25 questions. This questionnaire is scored on the Likert scale from zero (completely false) to 4 (completely true). The average score of this scale is 25, and the higher score indicates the more resiliency. In the research by Samani, Jokar and Sahragard (2006), the reliability of this tool using Cronbach's alpha coefficient was reported to be 0.87. In another study by Bavali et al. (2013), Cronbach's alpha coefficient was 0.83.

Results

Table 1 shows the mean and standard deviation of quality of life, self-efficacy and resiliency in infertile and fertile women, and tables 2, 3 and 4 show the results of t-tests.

Data in Table 1 show that the mean (SD) of quality of life, self-efficacy and resiliency in fertile women are 86.62 (11.162), 64.40 (9.048), and 71.40 (11.640), respectively. The mean (standard deviation) of quality of life, self-efficacy and resiliency for infertile women are 79.13 (10.829), 58.05 (7.688), and 66.92 (10.339), respectively.

Table 1: Mean and standard deviation of quality of life, self-efficacy and resiliency in infertile and fertile women

Variable	Group	Minimum	Maximum	Mean	SD
Quality of life	Infertile	55	103	79.13	10.829
	Fertile	70	114	86.62	11.162
Self-efficacy	Infertile	43	77	58.05	7.688
	Fertile	44	85	64.40	9.048
Resiliency	Infertile	48	89	66.92	10.339
	Fertile	57	100	71.40	11.640

Table 2: T-test results for comparing infertile and fertile women in the quality of life variable

	Levene test for homogeneity of variances		T-test for equality of means				Confidence interval 95%	
	F	Significance level	T statistics	df	Significance level	Mean difference	Low	High
Assuming the equality of variances	0.008	0.931	-3.727	118	0.0001	-7.483	-11.459	-3.508
Assuming the inequality of variances	-	-	-3.727	117.892	0.0001	- 7.483	- 11.459	- 3.508

Table 3: T-test results for comparing infertile and fertile women in the self-efficacy variable

	Levene test for homogeneity of variances		T-test for equality of means				Confidence interval 95%	
	F	Significance level	T statistics	df	Significance level	Mean difference	Low	High
Assuming the equality of variances	1.656	0.201	-4.143	118	0.0001	-6.350	-9.385	-3.315
Assuming the inequality of variances	-	-	-4.143	114.992	0.0001	- 6.350	- 9.386	- 3.314

Table 4 T-test results for comparing infertile and fertile women in the resiliency variable

	Levene test for homogeneity of variances		T-test for equality of means				Confidence interval 95%	
	F	Significance level	T statistics	df	Significance level	Mean difference	Low	High
Assuming the equality of variances	0.954	0.331	-2.231	118	0.028	-4.483	-8.464	-0.503
Assuming the inequality of variances	-	-	-2.231	116.379	0.028	- 4.483	- 8.464	-0.503

Data from Tables 2, 3 and 4 show that there is a significant difference between infertile and fertile women in terms of quality of life, self-efficacy and resiliency, and the level of quality of life, self-efficacy and resiliency in infertile women is lower.

Discussion and Conclusion

Infertility is not just a gynecological illness, but also a bio-psycho-social problem that includes psychiatric problems, reduced quality of life, marital conflicts and sexual disturbances (Onat & Beji 2012). Therefore, the present study aimed to compare the quality of life, self-efficacy and resiliency in infertile and fertile women.

The present study showed that quality of life in infertile women is lower than in fertile women. This finding is in line with the results of the research by Xiaoli and others (2016), Chachamovich et al. (2010), Drosdzol and Skrzypulec (2008), Lau et al. (2008), Fekkes et al. (2003) and Alami et al. (2009). In explaining the difference in the quality of life of infertile women and fertile women, it can be said that the quality of life in infertile women is related to the amount of pressure of people around for giving birth, the intensity of desire for having a child, the burden of infertility treatment costs, an individual's assessment of the household's economic situation and irrational thoughts related to having a child and the duration and cause of infertility. Infertile women also suffer more stress and with increasing stress, their therapeutic response decreases and leads to a decline in quality of life. Attitudes toward the issue of women's infertility are often affected by racial and cultural differences, and on this basis, culture affects the quality of life of the infertile people (Inhorn & Buss, 1994). Because of the problems and consequences of infertility and a decrease in quality of life, most researchers state that the primary objective of psychosocial counseling should be the promotion of the quality of life in infertile people, regardless of their wish to have a child is fulfilled or not (Van den Broeck et al., 2010).

Another result of this study was that self-efficacy in infertile women is weaker than in fertile women. This finding is in line with the results of research by Pahlavani et al. (2002), Alizadeh et al. (2005), Nene, Coyaji and Apte (2009) and Faramarzi et al. (2014). It has been reported that self-efficacy plays a role in predicting health behaviors and quality of life. When dealing with a chronic disease, it is necessary to carry out behaviors and activities that reduce the effect of the disease on the quality of life; self-efficacy can play an important role in this regard and affect the physical, emotional and social dimensions of quality of life (Cramm et al. , 2013). A study by Van der Slot et al. (2010) showed that high levels of self-efficacy in patients are associated with their better quality of life. Self-efficacy contributes to individual adaptation to symptoms of illness, and one's beliefs about controlling disease and dealing with it, prevent quality of life from being reduced (Motl & Snook, 2008).

People who see themselves as inefficient individuals avoid difficult assignments and suffer when faced with discomfort. Therefore, self-efficacy is critical to understanding the health status and quality of life. Hence, patients with higher self-efficacy report fewer effects of illnesses and better quality of life (Astrid et al., 2005). Jamshidimanesh et al. (2015) found that self-efficacy training for infertile

women had a positive effect, and a training program that included familiarity with the reproductive system, definition of infertility, prevalence, causes, diagnostic methods, treatment protocol, necessary tests, and fertility methods, enhances the self-efficacy of infertile women. People who have high self-efficacy take part in the health care program, and participation in these programs increases the quality of life of patients (Rafii, Naseh & Yadegary, 2012).

Also, the present study showed that the resiliency level in infertile women is lower than in fertile women. Some other studies have also shown that the resiliency rate in infertile people is lower than in fertile individuals (Sexton, Byrd & Kluge, 2010; Kagan et al., 2011; Lee et al., 2012). Infertility causes tension in infertile women reduces self-esteem, physical health and increases depression, stress and anxiety (Greil, Slauson-Blevins & McQuillan, 2010) and by reducing an individual's coping resources leads to low levels of resiliency (Jebraeili, Hashemi, & Nazemi , 2016). The study by Sexton, Byrd & Kluge (2010) showed that infertility reduces people's resistance to life problems, such that these people have less hardiness and resilience facing problems compared to other people. Resiliency, on the other hand, causes a logical and positive coping with the stresses and leads to a positive reassessment of events (Abbasi et al., 2014). Resilient people have self-esteem, self-efficacy, problem-solving skills, and satisfactory interpersonal relationships (Wagnild & Young, 1993). If we transfer this concept into infertile patients, it means that these patients have a good quality of life despite the fact that infertility has severe stress for them (Ridenour, Yorgason & Peterson, 2009).

According to the findings of this research and previous studies, it can be said that infertility as a gynecologic illness is associated with negative consequences such as psychopathology, loss of quality of life and marital dissatisfaction. Therefore, in addition to the medical treatment process, psychological interventions aimed at improving the mental health of infertile women is necessary.

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Brain MRI Findings in Children (2-4 years old) with Autism

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Abstract

Autism is a neurodevelopmental disorder with a range of clinical presentations, from mild to severe, that is now classified in a broader class of disease called "autism spectrum disorders" (ASD). The aim of this study was to investigate Brain MRI findings in children (2-4 years old) with autism. The sample of the study included 40 autistic children aged 2 to 4 years whose disease was confirmed by a fellow psychiatrist based on the diagnostic criteria of autism spectrum disorders DSM IV-R. Having explained the study to parents and after obtaining their consent, a questionnaire was completed and a three-dimensional brain MRI was performed for each patient in the radiology department of Ghaem or Imam Reza hospitals. From among the 40 patients, 25 patients had a history of convulsion. Among the other patients, 4 patients (10%) suffered from simple febrile convulsion (simple FC), 2 cases from complex febrile convulsion (complex FC), 6 cases (15%) from TCG and 3 (7.5%) from Landau–Kleffner syndrome (LKS). Of the 15 patients with a history of convulsion disorders, 5 patients (12.5%) used phenobarbital, 4 patients (10%) took valproate and 2 patients (5%) were treated with multi-drug regimen. Although, we did not measure white matter connections, lesions in such neuroanatomic pathways may be causal factors of behavioral and emotional dysfunctions in autistic patients. Finally, it is also important to understand how WMH severity changes over time.

Key words: MRI, Brain, Children, Autism

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Introduction

Autism is neurodevelopmental disorder with a range of clinical presentations, from mild to severe, that is now classified in a broader class of disease called "autism spectrum disorders" (ASD). The most common clinical ASD sign is impaired social interaction, which is associated with verbal and non-verbal communication deficits and stereotyped behaviors [2]. In most cases, it is not presently possible to detect a known or specific etiology; these are referred to as non-syndromic autism [1]. The clinical relevance of MR scanning in children with ASD is still an open question and must be considered in light of the evolution of this technology. In 2000, MRI was judged to be of insufficient value to be included in the standard clinical evaluation of autism according to the guidelines of the American Academy of Neurology and Child Neurology Society [1]. This consensus stated that the prevalence of lesions detected by MRI in children with autism has been reported to be similar to normal control subjects [2]. However, this statement was based on results obtained from small samples of patients and, more importantly, included mostly insufficient MRI sequences. An adequate brain MRI interpretation must include at least three different sequences (T1, T2, FLAIR) in three different planes. Yet, there are few clinical radiological studies with complete clinical MRI examinations in children with ASD. For example, in some small groups of children with ASD, some radiological MRI anomalies were described, such as accentuated Virchow–Robin space [3], acrocallosal syndrome [3], pachygyria [3] macrogyria and polymicrogyria [3]. However, until now, no reliable data has been available regarding the prevalence of MRI abnormalities in a large sample of patients with non-syndromic ASD.

In addition, in order to determine if the MRI abnormalities detected in the present population of children with non-syndromic AD could be also observed in a normal population of children. The aim of this study was to investigate Brain MRI findings in children (2-4 years old) with autism.

Methods

The sample of the study included 40 autistic children aged 2 to 4 years whose disease was confirmed by a fellow psychiatrist based on the diagnostic criteria of autism spectrum disorders DSM IV-R. Having explained the study to the parents and obtained their consent, a questionnaire was completed and a three-dimensional brain MRI was performed for each patient in the radiology department of Ghaem or Imam Reza hospitals. Then brain MRIs were studied by fellow radiologist and the executor of the project. Brain MRIs of each patient were compared with the brain MRI of a child of the same age who did not have autism spectrum disorders and was under imaging for any other reason (trauma, infection, headache, etc.). The volume of frontal lobes and amygdala in each side were specified and then analyzed.

Quantitative analysis (Statistical Parametric Mapping = SPM) was employed for volumetry. In this method,

quantitative analysis was Voxel-based analysis, i.e. Voxels situated in the same spatial location were compared with each other, and the value of each voxel represented the probability of belonging to GM, WM or CSF. The method was implemented in a toolbox with the same name, SPM version 8.0. A very important step in quantitative analysis method of SPM was Normalization. On the basis of the existing atlases in SPM, MRI images of healthy and diseased individuals were normalized in such a way that all images of this stage were overlapped in terms of spatial coordinates. To do this step, SPM used Affine transformation matrix that was specific to each person under study (healthy and diseased) (44).

Software WFU_PickAtlas version 3.0 and software Easy Volume were of the features available in the toolbox SPM. This software was applied for creating standard mask images based on Talairach and Tournoux Atlases and calculating the volume of gas. Among the areas in WFU_PickAtlas, it could be referred to the areas considered in the study that included: Amygdala, Frontal Lobe and whole brain. The atlas was based on MRI images of a mature and healthy adult. In this study, the population under study was 2-4 years old children. That was why the Hammers Atlas was used here, because it was applied for 2-4 years old children and was available in NIHPD database (NIH Pediatric MRI Database). Using the Atlas, indexes of the intended areas were extracted and standard mask images were created using image processing toolbox in MATLAB. Changes in the shape and size (deformation) of the standard masks had to be so that it could be specifically used for volumetric of MRI images of patients under study. For this purpose, affine transformation matrix described earlier was employed for reverse conversion. In other words, this matrix that was specific for each person in the study was implemented on standard masks to create specific masks. When these steps were completed, the software Easy Volume was used to determine the volume of specific masks.

All children were evaluated by a pediatric neurologist, a clinical geneticist and a child psychiatrist. In addition, the recommended biological and medical screenings for ASD were performed, including high-resolution karyotyping, DNA analysis of FRA-X and normal standard metabolic testing (plasma and urine amino and organic acid analysis, urine glycosaminoglycans (GAG) quantitation, urine oligosaccharide, purine and pyrimidine analysis, and creative guanidoacetate urine analysis).

MRI was performed with a 1.5 Tesla (Sigma General Electric) scanner using the following sequences: 3D T1-weighted FSPGR sequence (TR/TE/TI/NEX: 10.5/2.2/600/1, flip angle 10u, matrix size 2566192, yielding 124 axial slices and a thickness of 1.2 mm, field of view 22 cm), axial and coronal FSE T2-weighted imaging (TR/TE: 6000/120, 4 mm slices, 0.5 mm gap, field of view 22 cm) and coronal FLAIR sequences (TR/TETI: 10000/150/2250, 4 mm slices, 1 mm gap, field of view 24 cm). MRI studies were performed during sleep induced by premedication (7 mg/kg of sodium pentobarbital) for all AD children to obtain immobility during scans. Signal intensities on T1, T2, and

proton density-weighted images relate to specific tissue characteristics. For example, the changing chemistry and physical structure of hematomas over time directly affects the signal intensity on MR images, providing information about the age of the haemorrhage. The most common pulse sequences are the T1- weighted and T2-weighted spin-echo sequences. The T1-weighted sequence uses a short TR and short TE (TR, 1000msec, TE, 30msec). The T2-weighted sequence uses a long TR and long TE (TR. 2000msec, TE. 80msec). The T2-weighted sequence can be employed as a dual echo sequence. The first or shorter echo (TE, 30msec) is proton density (PD) weighted or a mixture of T1 and T2. This image is very helpful for evaluating periventricular pathology, such as multiple sclerosis, because the hyperintense plaques are contrasted against the lower signal CSF. More recently, the FLAIR (Fluid Attenuated Inversion Recovery) sequence has replaced the PD image. FLAIR images are T2-weighted with the CSF signal suppressed. When reviewing an MR image, the easiest way to determine which pulse sequence was used, or the "weighting" of the image, is to look at the cerebrospinal fluid (CSF). If the CSF is bright (high signal), then it must be a T2-weighted imaged. If the CSF is dark, it is a T1- weighted or FLAIR image. Pathologic lesions can be separated into 4 major groups (solid mass, cyst, blood, fat) by their specific signal characteristics on the three basic images: T2- weighted, FLAIR, and T1-weighted. Since studies have shown that T2- weighted images are most sensitive for detecting brain pathology, patients with suspected intracranial disease should be screened with T2-weighted spin-echo and FLAIR images. T1-weighted images are needed only if the preliminary scans suggest hemorrhage, lipoma, or dermoid. The axial plane is commonly used because of the familiarity with the anatomy from CT. Coronal views are good for parasagittal lesions near the vertex and lesions immediately above or below the lateral ventricles, temporal lobes, sella, and internal auditory canals. The coronal plane can be used as the primary plane of imaging in patients with temporal lobe seizures. Sagittal views are useful for midline lesions (sella, third ventricle, corpus callosum, pineal region), and for the brainstem and cerebellar vermis.

Results

Table 1

Variable	Patient group (mean)			Control group (mean)
	Boys	Girls	Total	
Age (month)	45.21±12.99	41.41±13.69	44.07±13.15	44.97±12.95
Age of first symptoms (months)	23.07±6.99	21.58±5.48	22.62±6.54	
Age of diagnosis (month)	36.25±9.22	29.83±5.49	34.32±8.73	
Percentage of round head (%)	76.14±16.54	78.17±11.91	76.75±8.73	49.95±21.41
Frontal Lobe Size (Cc)	599.09±72.17	564.71±77.38	588.77±74.49	466.99±56.73
Amygdala volume (cc)	3.56±0.55	3.17±0.73	3.44±0.63	3.59±0.66
Total brain volume	1418.52±135.58	1398±99.01	1412.46±123.31	1183.04±123.42
Frontal volume ratio to total brain (%)	42.19±2.62	40.33±4.27	41.63±3.26	39.51±2.80
Amygdala Amount to Brain Total Amount (%)	0.25±0.038	0.230±0.054	0.24±0.044	0.300±0.039

Age at the onset of symptoms and age of diagnosis
Age at the onset of autism symptoms was between 12 and 42 months with an average of 6.54 ± 22.62 months. Age at the onset of symptoms in autistic boys was between 12 and 42 months with an average of 6.99 ± 23.07 months and in autistic girls, between 16 and 36 months with average of 5.48 ± 21.58 months.

Mann-Whitney nonparametric test revealed a statistically significant difference (p=.422) in average age at the onset of symptoms between girls and boys with autism.

Recent studies have shown that autistic boys and girls exhibit different behaviors so this could be the reason.

Age at diagnosis of autism was between 22 to 59 months with an average 73.8 ± 32.34 months. Age of diagnosis of autism among boys realized to be 24 to 59 months with an average of 9.22 ± 36.25 months and among girls, between 22 to 36 months with an average 5.49 ± 29.83 months.

Comparison of average age at diagnosis between girls and boys with autism using the Mann-Whitney nonparametric test demonstrated a statistically significant difference between the two groups (p = .039). On average, the age of diagnosis in girls was lower.

History of prenatal problems
Out of the 40 patients, 26 patients (65%) had a history of prenatal complications. From among other patients, 2 patients (5%) had a history of neonatal jaundice, 1 patient (5.2%) of preterm birth, 2 patients (5%) of low Apgar score, three patients (% 5.7) of labor problems and six others (15%) of several simultaneous problems.

In the control group, 32 out of 40 patients (80%) had a history of prenatal complications. From among the other patients, 5 cases (12.5%) had a history of neonatal jaundice, 2 cases (5%) of preterm birth, and one patient (2.5%) of low Apgar score at birth.

Comparing the two groups in terms of the history of peripartum problems using chi-square test showed a statistically significant difference between them (p = .021).

Family history
Out of the 40 patients, 10 patients (25%) had a family history of autism spectrum disorders, while in the control group, only 3 (7.5%) had a positive family history of autism spectrum disorders. A comparison between two groups in terms of family history of autism spectrum disorders using the chi-square test indicated a statistically significant difference between the two groups (p = .034).

Speech disorders and echolalia
In the group of patients, a total of 40 patients showed a range of speech disorders. 20 out of 40 patients (50%) suffered from echolalia. In the control group, 4 patients (10%) had a speech disorder that was associated with hearing impairment. None of the control group had echolalia.

Comparing the two groups in terms of speech disorders and echolalia using chi-square test showed a statistically significant difference (p <.001).

Head circumference
The investigation of the two groups in terms of head circumference percentiles showed that head circumference percentile was between 46 and 99 percentiles with an average of 15.17 ± 76.75 percentile in the experimental group and between 12 to 96 percentiles with an average of 21.41 ± 49.95 in the control group, respectively.

Independent t-test indicated that mean head circumference percentiles between the two groups was significantly different (p <.001).

The mean head circumference percentile was equal to 16.54 ± 76.14 and in the range of 46 to 99 and to 11.91 ± 78.17 and in the range of 60 to 98 among autistic boys and girls, respectively.

Comparison of mean head circumference percentile of autistic girls and boys with autism using independent t-test showed a statistically significant difference (p = .704).
As a result of the comparison of mean head circumference percentile between autistic and normal boys using independent t-test, it was found that there is a statistically significant difference between them (p <.001).

Comparison of mean head circumference percentile among girls with autism and normal girls using independent t-test indicated a statistically significant difference (p <.001).

The amygdala
Investigation of the two groups in terms of the volume of the amygdala revealed that the volume of the amygdala was between 1.13 to 4.21 ml with an average of 0.63 ± 3.44 ml in the experimental group and between 55.2 to 47.5 ml with an average of 0.66 ± 3.59 ml in the control group.

Comparison of mean amygdala volume between the two groups using independent t-test showed a statistically significant difference between them (p = .322).

The mean volume of the amygdala in autistic boys was 0.55 ± 3.56 ml in the range of 1.23 to 4.21 ml and in autistic girls equal to 0.73 ± 3.17 ml in the range of 1.13 to 3.70 ml.

Comparing the mean volume of amygdala between autistic girls and boys using Mann-Whitney test showed statistically significant difference between the two groups (p = .049).

Comparing the mean volume of the amygdala between autistic patients with non-verbal disorder and other autistic patients using the Mann-Whitney test demonstrated a statistically significant difference between the two groups (p = .049).

Mann-Whitney test showed that there was a statistically significant difference (p = .018) in the mean volume of the amygdala between autistic patients with echolilia and other autistic patients.

Independent t-test revealed a statistically significant difference (p = .697) in the mean volume of the amygdala between autistic and normal boys.

Comparison of the mean volume of the amygdala between autistic and normal girls using independent t-test showed a statistically significant difference between the two groups (p = .153).

Conclusion

From among the 40 patients, 25 patients had a history of convulsion. Among the other patients, 4 patients (10%) suffered from simple febrile convulsion (simple FC), 2 cases from complex febrile convulsion (complex FC), 6 cases (15%) from TCG and 3 ones (7.5%) from Landau–Kleffner syndrome (LKS). Of the 15 patients with a history of convulsion disorders, 5 patients (12.5%) used phenobarbital, 4 patients (10%) took valproate and 2 patients (5%) were treated with multi-drug regimen (4).

Only 8 cases (20%) of the 40 patients in the control group had complex FC. Of these, only one was using phenobarbital. Comparison between the two groups in terms of convulsion disorders using chi-square test showed a statistically significant difference between them ($p < .001$)(5)

To our knowledge, the present retrospective study reports the largest series of systematic visual analyses of MRI from patients with non-syndromic AD. These patients have been carefully screened to exclude known medical disorders associated with autism. We observed an unexpectedly high prevalence of brain abnormalities (48%). This unexpectedly high level of anomalies contrasts with the generally accepted view that MRI is close to normal in children with AD [6]. This could be explained by methodological improvement, including here, of considering MRIs containing all the acquisitions necessary to detect brain abnormalities. We found three types of brain anomalies, including white matter hyperintensity on T2.FLAIR sequences, temporal lobe signal abnormalities and dilated Virchow-Robin spaces (7). Such abnormalities were not found in any child in the comparison group, which is in agreement with a recent MR study in a large group of normal children [8]. These abnormalities cannot be detected when only a T1 sequence is acquired. It is important to note that this high prevalence of abnormalities was found despite a stringent definition for an abnormal MRI. Indeed, all minor anomalies or normal variants (ventricular dilatation, accentuated Virchow-Robin spaces, abnormal hippocampal shape, arachnoid cysts, cerebellar atrophy, etc.) were not considered as abnormal. Similar results were found in a recent study that included a smaller sample of children with developmental disorders, including ASD, with abnormal MRI being reported in 49% of patients [9]. In addition, Taber et al. have also described high incidence of abnormal Virchow-Robin spaces in children and adolescents with ASD and normal IQ [10]. Our study was subject to a number of limitations. One intrinsic limitation is that the comparison group was not matched for IQ with the AD group, which was largely composed of children with AD and mental retardation. Therefore, we cannot say whether these MRI abnormalities are specific to autism. Nevertheless, in our series, the 23 patients with normal IQ had the same types of MRI abnormalities as did patients with AD and mental retardation. In idiopathic mentally retarded children, the most frequently reported MRI abnormalities are ventricular dilatation, arachnoid cysts, moderate subarachnoid space enlargement, cerebellar atrophy and/or cortical atrophy, partially opened septum pellucidum and/or cavum vergae and corpus callosum anomalies [11]. These types of abnormalities are often considered to be minor MRI findings and were not reported as abnormal in the present study. Nevertheless, they were rarely observed in the AD group (3%). Another limitation is that our findings cannot be extended to persons with high-functioning AD or to the full spectrum of ASD, which covers very heterogeneous disorders. Therefore, further clinical MRI investigations are necessary in these sub-groups of patients. Finally, another important issue will be to further characterize putative clinico-radiological sub-groups in AD and future studies need to be performed. Certainly, the MRI abnormalities recognized in the present study are not specific to AD, since they have been previously reported in other neurological, metabolic or genetic childhood disorders. Posterior periventricular hyperintensity was found as a white matter signal abnormality in 18.77% of the patients. Classically, this abnormality can be found in periventricular leukomalacia, metabolic disorders, viral infections or vascular disorders [12]. White matter MRI abnormalities were recently described in a large series of patients with cerebral palsy and were categorized into three levels of severity from mild to severe; in this study the abnormalities were always linked to motor deficits [13]. The white matter abnormalities that we have found in children with autism are comparable to the mild to moderate levels described in cerebral palsy, but no motor deficits were observed in our AD patients. Isolated or associated white matter abnormalities were found in 30.77% children with autism in our series. They could represent injury to the brain parenchyma and resultant disruption of neural circuitry. The main question is which different mechanisms may be involved in the emergence of such white matter abnormalities (14). It is highly possible that these white matter hyperintensities (WMH) might simply represent the 'tip of the iceberg' in terms of structural white matter lesions. Thus, the presence and severity of white-matter hyperintensities associated with autism might be understood as an extreme consequence of underlying microstructural processes that affect brain connectivity and which may be more specifically investigated using diffusion tensor imaging methods. WMH, depending on the localization, are commonly classified as periventricular hyperintensities (PVH) or deep white matter hyperintensities (DWMH)(15). Deep white matter hyperintensities were identified as having mainly a vascular etiology, and periventricular hyperintensities could be due to ependymal loss, differing degrees of myelination and cerebral ischemia. WMH are reported to be commonly associated with older age, and cardiovascular risk factors such as hypertension and diabetes. Lesions in one specific part or disruption of interconnections among areas regulating social and communication cognition could trigger the onset of autistic symptoms. Furthermore, posterior white matter connections with the temporal regions could be of particular importance to social disturbances in autism. Although, we did not measure white matter connections, lesions in such neuroanatomic pathways may be causal factors of behavioral and emotional dysfunctions in autistic patients. Finally, it is also important to understand how WMH severity changes over time.

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