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Short Communication(S)

Chronic Diseases Journal

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Inhibition of cell proliferation and increased-apoptosis of AGS and SNU-5 cancer cells following small interfering RNA (siRNA)-mediated down-regulation of vascular endothelial growth factor receptor 1 (VEGFR1)

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2 PhD Candidate, Department of Physiology, School of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Original Article

Abstract

BACKGROUND: Angiogenesis is vital for development of normal tissue and wound healing; but it play an important role in development of some diseases such as different types of cancer. Vascular endothelial growth factor (VEGF) and VEGF receptors (VEGFR) are two important key factors in this process. Previous studies have shown that down-regulation of VEGFR1 inhibits cell proliferation, migration, and vascular permeability of endothelial cells. So, blocking VEGF and VEGFR1 have been considered as a target to prevent the growth of tumors.

METHODS: In this study, VEGFR1 gene expression was suppressed in AGS and SNU5 cancer cells using RNA interference (RNAi) technology. Down-regulation of VEGFR1 was assessed at mRNA and protein levels using real-time polymerase chain reaction (PCR), and western blot methods. Moreover, the viability and apoptosis of these cells were analyzed using MTT and flow cytometry techniques.

RESULTS: VEGFR1 expression was significantly down-regulated both in mRNA and protein levels. MTT and flow cytometry results revealed that down-regulation of VEGFR1 inhibited cell proliferation, and induced apoptosis of these cancer cells.

CONCLUSION: Our findings suggest that VEGFR1 could play an important role in cell proliferation and tumor growth; and it could be considered as a valuable target for controlling tumor cells, and cancer therapies.

KEYWORDS: Vascular Endothelial Growth Factor, Small Interfering RNA, Down-Regulation, Cellular Proliferation, Apoptosis

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Introduction

After heart diseases, cancer is the second leading cause of morbidity and mortality worldwide,[1] and many efforts and extensive studies have been carried out in the field of cancer treatment and prevention to date.[2] Vascular endothelial growth factor (VEGF) and its receptors (VEGFR) are the key regulators of physiologic angiogenesis, during organ development, embryogenesis, and reproduction, and plays a major role in the pathobiology of cancer and inflammatory diseases.[3-6] They are structurally related members of the receptor tyrosine kinase (RTK) family, and secreted as glycoproteins that mediate critical signaling pathways for survival, proliferation, vascular permeability, and migration of endothelial cells by interaction of VEGF to its receptors, VEGFR1 (or FLT1), VEGFR2 (KDR), and VEGFR3.[7-9] VEGFR2 is dominantly found in endothelial cells, but VEGFR1 is widely expressed in normal and malignant cells such as endothelial, macrophages, hematopoietic stem

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cells, lung cancer, breast cancer, and pancreatic cancer and hematopoietic malignancies.[10,11] Some studies have shown that VEGFR1 plays an important role in malignant growth, and accelerate proliferation of transformed cells.[12,13] Furthermore, in-vivo and in-vitro studies on liver sinusoidal endothelial cells have revealed that VEGFR1 could induce expression of growth factors.[14,15] VEGFR1 is different from other VEGFRs; because it could also be expressed in soluble form.[13] Previous studies in some cancers such as breast cancer revealed that VEGFR1 was significantly upregulated in metastasis stage and was related to relapses, also was associated with shorter survival in resected breast cancer and early-stage non-small cell lung cancer.[13,16]

So, recent studies have considered VEGF and its receptors as crucial targets in inhibition of angiogenesis and growth of tumor cells.[17] Up-regulation of VEGF and its receptors such as VEGFR1 and VEGFR2 stimulates angiogenesis, while inhibition of these proteins using monoclonal antibodies or chemical inhibitors suppresses angiogenesis processes.[18-21] Previous studies such as clinical trials, using an aptamer[22] or an antibody fragment[23] that binds VEGF, have supported this ideal that VEGF pathway could be considered as a crucial therapeutic target for cancers therapy. Other studies used VEGFRs inhibition as an alternative strategy to antagonize VEGF.[5,11,19-21] This is a great strategy because of its potency to inhibit multiple members of VEGF family at once.[24]

RNA interference (RNAi) is a fundamental biological process of sequence-specific, post-transcriptional gene silencing, by which animal and plant cells regulate gene expression. This process is initiated by complementary base-pairing of RNAi with target RNA, which recruits cellular RNases that mediate RNA degradation.[25,26] These molecules are 19-23 double strand nucleotide, which is homologous in sequence to the silenced gene.[27] The strategy of RNAi to inhibit gene expression and function has developed rapidly as a research tool to a promising therapeutic approach.[28] This technology is now routinely used in scientific researches, and some biotechnology companies have reported the use of RNAi as therapeutic agents because of its potential to targeted gene silencing.[29] Small interfering RNAs (siRNAs) molecules are 19-23 double strand nucleotide sequences, which are homologous in sequence to the silenced genes, provide a useful means to selectively down-regulate mRNA transcripts and studying the function of gene products.[30]

In this study, the mRNA expression of VEGFR1 was down-regulated using synthetic siRNA in AGS and SNU-5 cells. We showed that suppression of VEGFR1 inhibited cell proliferation and growth, and stimulated apoptosis of these cells.

Materials and Methods

AGS and SNU-5 cells (from Pasteur Institute, Tehran, Iran) were grown in Roswell Park Memorial Institute (RPMI)-1640 medium (Inoclon, Iran) containing 10% fetal bovine serum (FBS) (Gibco), streptomycin (100 µg/ml), and penicillin (100 U/ml) (Life Technologies). Cells were incubated in a humidified 5% CO_2 incubator at 37 °C for 48 hours, and passaged using trypsinization. Up-regulate the expression of target gene was induced by hypoxic situation for 24 hours. Anti-VEGFR1 siRNA was designed with oligowalk online software. The siRNA sequenced designed to target VEGFR1 was GTGGCTACTCGTTAATTATCA. Working solution of siRNA was prepared according to manufacturer's protocol and stored at -20 °C.

AGS and SNU-5 cells were grown to ~80% confluency in RPMI-1640 medium for 24 hours before transfection. Lipofectamine 2000 (Invitrogen, USA) was used for transfection of anti-VEGFR1 siRNA according to manufacturer's instructions.

To assess the mRNA expression of target

genes, total RNA was extracted from the cells using TRIzol® Reagent (thermo fisher, US) according to the manufacturer's instructions. Agarose gel electrophoresis and spectrophotometry (NanoDrop™ 2000, thermo scientific) were used to measure RNA quality and quantity, respectively. 2 µg of total RNA was used for cDNA synthesis using 2-steps real-time polymerase chain reaction (RT-PCR) kit (Vivantis Technologies, Selangor, Malaysia), and OligodT and Random Hexamer primers, according to the manufacturer's instructions.

mRNA expression levels of genes were evaluated using quantitative real-time (qRT) PCR method. Appropriate primers were designed using Snap Gene and Oligo 7 software. The mRNA expression of VEGFR1 (forward: 5'-GGCTTCTGACCTGTGAAGCAAC-3', reverse: 5'- GAACTCTCGTGTTCAAGGGAGTG-3') was assessed and normalized to mRNA expression level of GAPDH (forward: 5'-GTGAACCATGAGAAGTATGACAA-3', and reverse: 5'-CATGAGTCCTTCCACGATAC -3') as an internal control gene.

qRT-PCR was performed using StepOne ABI system (Applied Biosystems, CA, USA). The final volume of reactions was 20 µl, which contained 20 ng of cDNA, 5X HOT FIREPol® EvaGreen® qPCR Mix Plus (ROX) (Solis BioDyne, Tartu, Estonia), and 200 nM of forward and reverse primers. The thermal reaction condition was as follows: denaturation of templates at 95 °C for 5 minutes, followed by 35 cycles of denaturation at 95 °C for 15 seconds, and annealing/extension at 60 °C for 30 seconds. Dissociation curve analysis and 2% agarose gel electrophoresis were used to verify the specificity of PCR products.

To examine the protein expression level of VEGFR1, total protein was extracted from cells by radio-immunoprecipitation assay (RIPA) lysis buffer (150 mmol/l NaCl, 50 mmol/l Tris-HCl, pH of 7.5, 1% Nonidet P-40, and 0.25% Na deoxycholate) containing protease inhibitors, and stored in -80 °C. Protein samples were separated by electrophoresis on 12% sodium dodecyl sulfate-polyacrylamide gel (SDS-PAGE), and then transferred to polyvinylidene fluoride (PVDF) membrane using Bio-Rad Trans-Blot® SD semi-dry system. Membranes were blocked with 5% (w/v) bovine serum albumin (BSA) in phosphate buffer saline (PBS) for 1 hour at room temperature, washed with PBS + 1% Tween20 (PBST), and then incubated with the following primary antibodies overnight at 4 °C; washed with PBST again, and incubated at room temperature with anti-rabbit secondary antibodies (Santa Cruz Biotechnology, CA, USA), goat polyclonal antibody actin (Cyto-Matin Gene, Iran) for 1 hour. Proteins were visualized with ECL Western Blotting kit (Cyto-Matin Gene, Iran).

Cells were seeded onto 96-well plates (10^3 cells/well), and were subsequently incubated for 24 hours. Cell viability was assessed by the colorimetric 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide, methyl-thiazol-tetrazolium (MTT) assay (Roche, Germany)[31] at 24, 48, and 72 hours post transfection with anti-VEGFR1 siRNA. Quant Universal Microplate Spectrophotometer (BioTek, Winooski, VT) was used to measure the absorbance at 570 nm.

Annexin-V-PI detection kit (Roche) was used to assess the number of apoptotic cells, according to manufacturer's instruction. AGS and SNU-5 cells were seeded in a 24-well flat-bottomed plate, and incubated for 24 hours at 37 °C, then transfected with anti-VEGFR1 siRNA. 48 hours post transfection, cells were collected and washed with PBS, then resuspended with PI and Annexin V in the binding buffer (10 mM HEPES, 140 mM NaCl, 2.5 mM CaCl2, and pH of 7.4). After 15 minutes of incubation at 37 °C, cells were analyzed by flow-cytometer (FACScan™ system, Becton Dickinson, NJ, USA).

T-test and one way ANOVA methods were

performed for analyzing data using Graphpad Prism 6 Demo and SPSS (version 22, IBM Corporation, Armonk, NY, USA). A P-value ≤ 0.05 was considered significant, and data were shown as mean ± standard deviation (SD).

Results

mRNA expression level of VEGFR1: mRNA expression level of VEGFR1 was analyzed using qRT-PCR technique 48 hours post transfection of anti-VEGFR1 siRNA in AGS and SNU-5 cells. mRNA expression levels of *VEGFR1* and *GAPDH* (as a reference gene) were assessed both in treated and untreated cells. T-test analysis of qRT-PCR results revealed that the mRNA expression level of *VEGFR1* gene decreased significantly in both cells transfected with siRNA compared to non-treat cells (Figure 1). This findings indicated that anti-VEGFR1 siRNA application successfully down-regulated the mRNA level of VEGFR1.

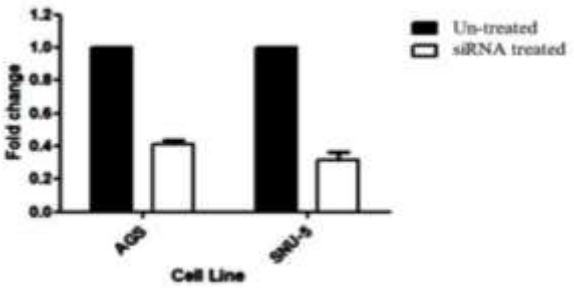

Figure 1. The quantitative analysis of expression level of VEGFR1 gene down-regulated in AGS and SNU-5 cells after treatment with anti-VEGFR1 siRNA. Each real-time PCR examination was carried out at least in triplicate. Data are shown as fold change in relative expression compared with GAPDH on the basis of Comparative Ct (2-ΔΔCt) method. Values are shown as mean ± SD.
siRNA: Small interfering RNA; VEGFR1: Vascular endothelial growth factor receptor 1; SD: Standard deviation

Western blot analysis: After analyzed on SDS-PAGE, protein were transferred to PVDF membrane using western blotting technique to analysis VEGFR1 protein level in AGS and SNU-5 cells. As shown in figure 2, cells treated with anti-VEGFR1 siRNA showed significant reduction of VEGFR1 protein level compared to untreated cells that expressed a 17kDa VEGFR1 band while. This shows that the use of anti-VEGFR1 siRNA targeted VEGFR1 mRNA specifically, and influenced its protein production. β-actin was used and expressed as a positive control in this experiment.

Figure 2. Analysis of siRNA effect on VEGFR1 protein expression in AGS and SNU-5 cells using western blot. β-actin was used as positive control. Negative control is without protein. As shown, a 19 KDa protein was expressed in cells transfected without siRNA, but transfection with anti-VEGFR1 siRNA has significantly reduced the level of VEGFR1 protein.
siRNA: small interfering RNA; VEGFR1: Vascular endothelial growth factor receptor 1

Cell viability assay: MTT assay was performed to evaluate the viability of AGS and SNU-5 cancer cells transfected with anti-VEGFR1 siRNA after 24, 48, and 72 hours. The results of MTT assay revealed that viability of AGS and SNU-5 cells treated with anti-VEGFR1 siRNA significantly reduced in a time-dependent manner compared to untreated cells (Figure 3). This results indicated the cytotoxicity of VEGFR1 suppression to these cancer cells.

Apoptosis assay: To evaluate the number of apoptosis AGS and SNU-5 cells, Annexin-V-PI kit was used. With regards to MTT assay results, 72 hours post transfection with anti-VEGFR1 siRNA, cells were collected and treated with Annexin V-FITC and PI, and analyzed by flow-cytometer, according to manufacturer's instruction.

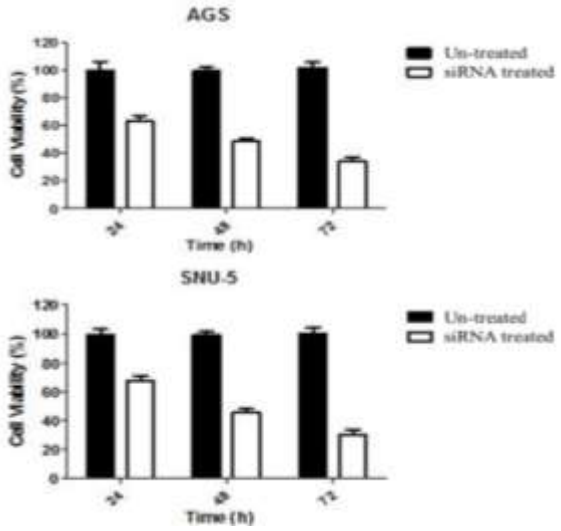

Figure 3. Survival ratios of AGS and SNU-5 cells treated with anti-VEGFR1 siRNA. The 80% confluence cell cultures were treated with siRNA. Cell viability was significantly reduced in a time-dependent manner. At 48h after treatment more than 50% of cells die. Results represented as means of three independent experiments by MTT assay (P ≤ 0.050)

siRNA: Small interfering RNA; VEGFR1: Vascular endothelial growth factor receptor 1; MTT: Methyl-thiazol-tetrazolium

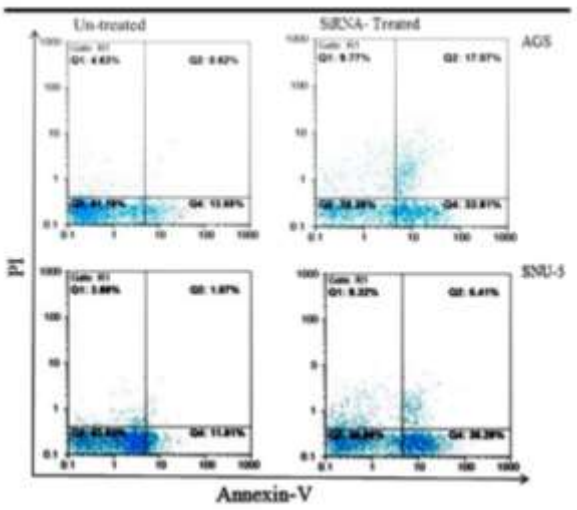

Figure 4. Flow Cytometry analysis of AGS and SNU-5 cells stained with Annexin V-FITC and PI. (A) Cells without treatment were used as controls. (B) Cells underwent apoptosis induced by anti-VEGFR1 siRNA. Diagram Q1 to Q4 represents necrotic, early apoptotic, late apoptotic and live cells, respectively. Treated cells showed significantly increased in the rate of early and late apoptosis compared with control.

siRNA: Small interfering RNA; VEGFR1: Vascular endothelial growth factor receptor 1

Results of apoptosis assay revealed that the number of apoptotic cells had notably increased following transfection with anti-VEGFR1 siRNA in comparison to non-transfected cells. Total apoptosis had elevated 3.7 and 3.2 times in treated group compared to control group in AGS and SNU-5 cells, respectively (Figure 4).

Discussion

VEGF and its receptors play a key role in the process of angiogenesis, which is an important factor in tumor growth and metastasis. Due to the increasing use of therapeutic inhibitors of VEGF signaling pathway in recent years, understanding the mechanisms underlying this pathway has become more important.[32,33] Previous studies had shown that of VEGFR-2 activation can activate downstream signaling pathways including ERK, JNK, PI3K, AKT, P70S6K, and p38MAPK.[32,34]

In other hand, the function of VEGFR1 is not well established.[35,36] Research on different kind of cancers including breast cancer, lung cancer, and gastric cancer has revealed that up-regulation of VEGFR1 is associated with tumor growth, tumor cell activation, and metastasis,[37-41] and its soluble form has been up-regulated in serum of patients with gastric cancer.[42] Blocking the function of VEGF signaling pathway is an important therapeutic approach to control angiogenesis, tumor growth, and metastasis. Previous studies have reported co-expression of VEGF and VEGFR1 in gastric cancer cell lines such as MGC803, AGS-1, RF-1, and RF-48, as well as specimens of gastric cancer.[41]

Many different agents have been reported including chemical compounds and antibodies to block or suppress VEGF signaling pathways in goal of control angiogenesis, tumor growth, and metastasis.[9] Another strategy is to

suppress VEGF receptors to antagonize VEGF. In this strategy, several VEGF family members could be blocked at once. So, VEGF receptors have been considered as therapeutic targets for cancer therapy.[43,44] Currently, about 44 VEGFR inhibitors such as novartis, axitinib, motesanib, sunitinib, and sorafenib are in clinical phase development, and some of them have been used for cancer therapy.[45,46] Hwang et al. have reported that concomitant inhibition of VEGFR1 and VEGFR-2 with paclitaxel increase the TUBB3 expressing cancer cell line cytotoxicity, and their inhibition with paclitaxel, anti-VEGFR1, and anti-VEGFR-2 in AGS cell was more cytotoxic.[42] Moreover, Zhang et al. reported that VEGFR1 was the dominant receptor in tumor microenvironment.[6] Due to these findings, we have postulated that AGS and SNU-5 gastric cancer cell lines express VEGFR1.

Here, we used anti-VEGFR1 siRNA to block VEGFR1 expression in AGS and SNU-5 cell lines. Our results revealed that mRNA and protein expression levels of VEGFR1 significantly decreased in AGS and SNU-5 cells 72 hours post transfection with siRNA compared to control group. These results demonstrated the efficiency of anti-VEGFR1 siRNA to block VEGFR1 function. These findings are consistent with previous studies which demonstrated blockade of VEGFR1 using anti-VEGFR1 antibodies or synthetic compounds, suppressed tumor growth and metastasis in vivo and in vitro.[47,48] In addition, the results of MTT and apoptosis assays demonstrated down-regulation of VEGFR1 could significantly inhibit cell growth and increase apoptosis of AGS and SNU-5 cells. Although, some studies have reported that blockade of VEGFR1 is not adequate without combined suppression of VEGFR-2 to inhibit tumor growth and cell proliferation,[49,50] but other studies demonstrated that suppression of VEGFR1 signaling could inhibit the growth and survival of several mouse tumor models, and increase apoptosis of many cell lines.[41,51,52] A study by Szabo et al. on glioblastoma have revealed that shRNA down-regulation or blocking the phosphorylation of VEGFR1 in vitro and in nude mice could reduce tumor cells growth.[53] Moreover, another research on tumor cell lines such as pancreatic and colorectal cancer cells have demonstrated a possible role for VEGFR1 in cell growth and survival.[54] Furthermore, the inhibition of VEGFR1 signaling in CAKI1 and SKUT1b cells using siRNA oligonucleotides inhibited tumor growth, and decreased survival of cancer cells.[41] These previous works support our findings, and indicate that blocking VEGFR1 using RNAi mechanism suppresses cell proliferation and tumor growth, as well as induction of cancer cells apoptosis.

Conclusion

Our results showed that using specific siRNAs, to down-regulate the expression of VEGFR1 and suppression of its function, can inhibit cell proliferation, and drive apoptosis of tumor cells. As previously proposed, and according to our findings, blocking of VEGFR1 can be considered as a therapeutic target to inhibit tumor growth.

Conflict of Interests

Authors have no conflict of interests.

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Students' mental health status and its related factors in Sanandaj City Universities, Iran, 2016

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Original Article

Abstract

BACKGROUND: Mental health is considered as one of the most important factors in the promotion and development of people. This is very important, especially in students. This study aimed to determine the students' mental health status in Sanandaj City universities, Iran, during the year 2016.

METHODS: In this cross-sectional study, the samples were 1100 students in Kurdistan University, Islamic Azad University of Sanandaj, and Kurdistan University of Medical Sciences. The samples were selected using stratified random sampling method with proportional allocation. The data were collected using General Health Questionnaire (GHQ) including 28 questions to assess mental health status.

RESULTS: The average score of mental health among the students was 32.10 ± 12.00. The highest and the lowest frequency of mental disorders were related to aspects of social functioning (11.24 ± 3.62) and depression (5.53 ± 5.24), respectively. The students of Kurdistan University of Medical Sciences had better mental health than the other students in all aspects of mental health. There was a significant relationship between mental health with gender (P = 0.060), and marital status (P = 0.010).

CONCLUSION: The findings of the study showed that parents, educational environment, economic situation of families, and students' current home have important role in their mental health.

KEYWORDS: Mental Health, Universities, Students, Major Depressive Disorder

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Introduction

One of the important factors affecting youth, which creates major changes in their social, family, and personal life, is entry to university. Students' life is a very important and critical part of their life. In this period of time, one of the most important components of public health, which is mental health issue, must be given special attention.[1-3] Mental health is considered as one of the most important factors in development of human beings. This is especially important for students. Although students are considered to be the preferred community, various studies indicated that students are also suffering from a variety of emotional disorders.[4,5] These disorders begin with mild anxiety, and end in various disorders of psychosomatic, neurotic, and even psychotic.[6] Based on World Health Organization (WHO) report, more than 450 million people around the world live with a kind of mental disorders.[7] More than 15% of all recognized diseases around the world are mental health disorders.[8]

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Mental health is one of the most important components of public health that provides a balance in life, and resistance against the problems for people. Psychosocial problems impose a significant pressure on individuals; as predicted, in 2020 depression has the highest cost for community health systems after heart diseases.[1,9] Failure of having mental health impairs development of individual, and causes some problems for his/her ability to perform his/her duties, which leads to a lack of community development and consequences of it.[10] It is important to pay attention to the mental health of students, because they are considered as the main and important pillars of universities. One of the important components of creating mental health among students is their attitude and satisfaction with the field of study, which itself is also considered as a strong and important stimulus to motivate them, which improves the quality of education and academic achievement.[11]

The conducted researches in Iran revealed that university students have different mental and emotional disorders. In creating these problems, factors such as lack of social support, students' unfamiliarity with the university environment at the time of their entry to university, separation and distance from the family, lack of interest in the field of study, incompatibility with the dormitory environment and his/her roommates, lack of amenities, and economics can play a role.[12-15] Gallagher[16] and Mackean[17] conducted that university students had increased mental health problems such as depression, suicidal thoughts, psychosis, anxiety, addictions, risk for suicide, use of psychiatric medications, and other chronic psychiatric disorders compared to general population. In the study of Movlazadeh et al., 69.7% of the students had mental health problems, and there was a significant and inverse relationship between the mean score of the previous semester with depression and social function.[18] In another study, Anbari et al. concluded that the students were not in good health status, and had a mild impairment.[10]

This study was designed to determine mental health status among the students in Kurdistan University, Islamic Azad University, and Kurdistan University of Medical Sciences, in Sanandaj City, Iran, in year 2016.

Materials and Methods

The present research was a cross-sectional study. Study population consisted of students in Kurdistan University, Islamic Azad University of Sanandaj, and Kurdistan University of Medical Sciences. The study population in 3 surveyed universities was about 12000 students. Based on cluster random sampling method, 1100 cases of them were selected. Among 3000, 4500, and 5500 students in Kurdistan University of Medical Sciences, Kurdistan University, and Islamic Azad University, 250, 400, and 450 cases, were selected and surveyed, respectively. Each university was considered as a cluster; in each university, several colleges, and in each college, several classes were randomly selected and finally, students of those selected classes were surveyed. Inclusion criteria included being student in Universities of Kurdistan, Medical Sciences, and Islamic Azad, willing to participate in the study, and having spent at least two semesters. Not having of any inclusion criteria was considered as exclusion criterion.

To examine the mental health status of the surveyed students, the Goldberg's General Health Questionnaire was used. The questionnaire has 28 questions, known as the GHQ28, and was made by Goldberg in 1972 to examine the general health status of individuals.[19] The Persian version of this questionnaire has been used in several studies, and its validity and reliability have been verified from 0.79 to 0.85.[10,20,21] In this study,

the Persian version of the questionnaire was used. The questionnaire contains 28 questions in 4 dimensions including physical symptoms, anxiety and sleep disorders, social function disorders, and depression. Each of the fields has 7 questions.

The scale of the questionnaire has 4 points; 0 (no), 1 (a little), 2 (much), and 3 (very much). Therefore, the score for each domain is 0 to 21 and the total score of the questionnaire will vary from 0 to 84 for each person. Scores from 0-22 are considered as the lack of mental disorders, 23-40 indicate a mild mental disorder, 41-60 indicate a moderate mental disorder, and scores from 61 to 84 are considered to be severe mental disorders. The remarkable point in this questionnaire is that achieving a high score on a scale indicates more symptoms of mental health disorders, in other words lower general health. Getting lower score in this research, represents the least symptoms of mental health disorders, and indicates more and higher general health.

For data collection from the studied individuals, the researchers went to the selected classes. Before the study, explanations were given to the students about the importance of the study. We requested the samples to complete the questionnaires carefully. Participation in the study was optional for the students, and they were not forced to do this. They did not need to write their names and other identifiable specifications.

The collected data were entered into the computer. To describe the collected data, descriptive statistics including frequency, mean, and standard deviation (SD) were used. Mann-Whitney and Kruskal-Wallis statistical tests were used to analyze the collected data, and the relationship between mental health and demographic characteristics. In all statistical tests, $P < 0.05$ was considered significant.

Results

1034 cases (94%) completed and returned the questionnaires. Their mean age was 22.27 ± 3.40 years with the minimum and maximum of 18 and 45 years, respectively. The mean score of mental health among the respondents was 32.10 ± 12.00. These scores were 32.45 ± 10.82, 27.22 ± 12.86, and 34.55 ± 11.66 in the students of Kurdistan University, Kurdistan University of Medical Sciences, and Islamic Azad University of Sanandaj, respectively. Of the total number of studied students, 261 (25.2%) had no mental disorders, and 773 (74.8%) had mental disorders. Among the students in Kurdistan University of Medical Sciences, 126 (51.2%) had psychiatric disorders, and 120 (48.8%) had suitable mental health, and had no mental disorders. In Kurdistan University, 278 students (79.9%) had mental disorders, and 70 (20.1%) of them had no mental disorders. 369 students (83.9%) in Islamic Azad University had psychiatric disorders, and 71 (16.1%) had no mental disorders.

Of the total students, 240 (23.2%) had no mental disorders, and 534 (51.6%), 248 (24%), and 12 (1.2%) of them had mild, moderate, and severe mental disorders. The amounts were 114 (46.3%), 92 (37.4%), 37 (15%), and 3 (1.2%) students in Kurdistan University of Medical Sciences, 64 (18.4%), 190 (54.6%), 92 (26.4%), and 2 (0.6%) students in Kurdistan University, and 62 (14.1%), 252 (57.3%), 119 (27%), and 7 (1.6%) students in Islamic Azad University, respectively.

Of the studied students, 32.1% were boys, and 83% were single (Table 1). Moreover, 80.4% were in bachelor, 17.2% in Masters and higher degrees, and the others were assistant.

There was a significant difference in mental health, based on the marital status; as it was better among single students (1.13 ± 0.43) compared to married students (2.21 ± 0.40) ($P = 0.01$).

Most of the studied subjects had a father with university education and a mother with high school education (Table 1).

Table 1. Frequency, percentage, and mean scores of mental health among the studied students and their relationship with different variables in year 2016

Variable		n (%)	Mean ± SD	T	P
Gender	Boy	332 (32.1)	1.11 ± 0.42	-1.87	0.060
	Girl	702 (67.9)	1.16 ± 0.43		
Marital status	Single	858 (83.0)	1.13 ± 0.43	-2.44	0.010
	Married	176 (17.0)	1.22 ± 0.40		
Variable		**n (%)**	**Mean ± SD**	**F**	**P**
Degree	Assistant	25 (2.4)	1.00 ± 0.45	7.44	0.001
	Bachelor	831 (80.4)	1.17 ± 0.41		
	Masters and higher	178 (17.2)	1.35 ± 0.47		
Father's education	Illiterate	79 (7.6)	1.10 ± 0.39	2.16	0.070
	Elementary	172 (16.7)	1.16 ± 0.48		
	Guidance	164 (15.9)	1.22 ± 0.39		
	High school	232 (22.4)	1.15 ± 0.40		
	Academic	387 (37.4)	1.12 ± 0.44		
Mother's education	Illiterate	168 (16.2)	1.10 ± 0.48	1.88	0.110
	Elementary	214 (20.7)	1.12 ± 0.45		
	Guidance	197 (19.1)	1.21 ± 0.35		
	High school	239 (23.1)	1.15 ± 0.43		
	Academic	216 (20.9)	1.14 ± 0.42		
Current home	With family	494 (47.8)	1.19 ± 0.42	5.09	0.006
	Single house	95 (9.2)	1.15 ± 0.38		
	student dormitory	445 (43.0)	1.10 ± 0.44		
University	Medical Sciences	246 (23.8)	0.97 ± 0.46	31.33	< 0.001
	Kurdistan	348 (33.6)	1.16 ± 0.39		
	Islamic Azad	440 (42.6)	1.23 ± 0.41		

SD: Standard deviation

There was a significant difference between students' educational level and their mental health (P = 0.001). Associate students had higher mental health than the others.

There was a significant difference between the current home and mental health status (P = 0.006). Students residing in the student dormitories had better mental health than the others.

There was a significant difference between the university and students' mental health (P < 0.001). The students from Kurdistan University of Medical Sciences had better mental health status than the others; and the students of Kurdistan University had better mental health status than the students from Islamic Azad University.

The results of the study revealed that, there was no significant differences in mental health based on parents' literacy (P > 0.050).

Based on degree of the students, social functional disorder had the highest and depression had the lowest score between the studied students, respectively (Table 2).

Except in the case of depression, there was a significant difference between the other dimensions of mental health and degree.

Table 2. Mean and standard deviation of the scores in different dimensions of mental health among the students according to their degree in year 2016

Examined dimensions	Assistant	Bachelor	Masters and higher	χ^2	P
Physical signs	0.91 ± 0.64	1.13 ± 0.56	1.02 ± 0.67	9.92	0.007
Anxiety and sleep disorders	0.91 ± 0.73	1.11 ± 0.64	0.95 ± 0.68	10.63	0.005
Social functional disorder	1.52 ± 0.47	1.63 ± 0.51	1.51 ± 0.54	8.55	0.010
Depression	0.64 ± 0.70	0.81 ± 0.76	0.72 ± 0.70	2.70	0.260

Table 3: Mean and standard deviation of the scores in different dimensions of mental health among the students according to their university in year 2016

Examined dimensions	Medical Sciences	Kurdistan	Islamic Azad	χ^2	P
Physical signs	0.91 ± 0.62	1.12 ± 0.52	1.22 ± 0.57	47.01	< 0.001
Anxiety and sleep disorders	0.88 ± 0.67	1.08 ± 0.62	1.19 ± 0.65	36.25	< 0.001
Social Functional Disorder	1.53 ± 0.49	1.64 ± 0.48	1.62 ± 0.56	6.24	0.040
Depression	0.57 ± 0.66	0.79 ± 0.71	0.91 ± 0.79	34.87	< 0.001

Bachelor students were more disturbed than other students in terms of anxiety and sleep disorders compared with other students and other aspects of mental health.

Based on the university, students from Islamic Azad University of Sanandaj had a worse mental health status than other universities; and students from Kurdistan University of Medical Sciences had a better mental health status than the others (Table 3).

There was a significant difference between all dimensions of mental health and university of education. The median score of the physical aspect among the students in Islamic Azad University was higher than other students, meaning that in this aspect of mental health, students of Islamic Azad University had a higher degree of disorder than other students and other aspects of mental health.

Discussion

This research, which studies mental health status and its related factors among the students of Kurdistan University of Medical Sciences, Kurdistan University, and Islamic Azad University of Sanandaj, indicates that the mental health status among the studied students was not very favorable, and about 75% of them had mental disorders. Although about 52% of the students in Kurdish University of Medical Sciences had some kinds of psychiatric disorders, compared to the students from Kurdistan and Islamic Azad universities, they were in a better position. Among three studied universities, Islamic Azad University of Sanandaj was ranked as the worst, and then was the Kurdistan University.

In a study by Dadkhah et al., the rate of mental disorders among the studied students was 28%,[14] that is not consistent with the findings of the present study. One of the reasons for the differences between these studies can be due to the studied population in two researches. Another difference may be to the interval between the two studies. For the time being, student problems, employment, marriage, etc. have increased, and studied students in this research have fewer mental health and more mental disorders than the students who have been studied in previous years. Another reason for this difference is the variety of disciplines studied in this research, which included various disciplines in the medical field, humanities, and engineering departments, while Dadkhah et al.[14] studied medical students only. In some researches from Iran, rate of mental disorders were various.[6,10,14,15,22-27]

For example, in a study by Namdar Areshtanab et al., the average of mental health score of the students was 25.71 ± 11.02. The highest and lowest mean score in their study were related to the dimensions of social function and depression, respectively.[24] The findings of our study showed that the average score of mental health of the studied students was 32.10 ± 12.00. In the present study, Kurdistan University of Medical Sciences students' had a mean score of 27.22 ± 12.87 that is consistent with the mean score of the findings in the study of Namdar Areshtanab et al.[24] The highest and lowest mean score of this study was related to the dimensions of social function and depression, which is consistent with Namdar Areshtanab et al.[24] findings.

A study in Sabzevar universities, Iran,

showed that 39.0% of the surveyed students were suspected to mental or physical disorders. Among them, 32.3% had physical impairment, 35.9% had anxiety disorder, 57.8% had social functional disorder, and 23.7% had depression.[23] The results of the present study conducted that social functional disorders had the highest score among 4 components of mental health, and depression had the lowest score. In our research, more than half of the samples had mental health disorders. This finding is similar to the results of Parvizrad et al.[3], Behrouzian and Neamatpour,[28] Ahmadi,[29] and Zeighami and Pour Bahaadini Zarandi.[30]

The results of this study showed that there was no statistically significant relationship between gender and mental health. This finding is similar to the results of Namdar Areshtanab et al. in Tabriz University of Medical Sciences,[24] Zare et al. in Shiraz University of Medical Sciences,[31] and also Parvizrad et al.,[3] Tavakolizadeh and Khodadadi,[22] and Adham et al.[32] in other cities of Iran; but this finding is not consistent with the results of the study by Mehri and Sedighy Some-Koochak;[23] because in their study, there was a significant difference between the level of anxiety and gender, and men were more anxious than women.

In this study, it was found that single students had better mental health than married students, and there was a significant difference between them. This finding is consistent with Parvizrad et al.[3] and Farahbakhsh et al.;[33] but in a study by Mohammadzadeh et al.,[25] there was no significant difference between marital status and mental health.

There was a significant difference between students' educational level and mental health status. Associate students had better mental health than the others. This finding is not similar to the findings of the studies in Tabriz,[24] Ilam,[25] and and Mazendaran University of Medical Sciences[3] in Iran.

There was a significant difference between the current location and mental health status of the students. Students residing in student dormitories had better mental health than the others. In a study conducted in Ilam University, students who lived with their parents had a better mental health status compared to the students who lived in student dormitories and single residences.[25]

The results of statistical analysis showed that except for disorders in social function, there was a significant difference between all dimensions of mental health and field of study. There was a significant difference between students' age and all aspects of mental health. In a study by Yousefi et al.,[20] 41% of the surveyed students had mental disorders; but in a study by Anbari et al.,[10] the rate of mental disorders was mild.

Conclusion

The findings of the present study revealed that mental health status was bad among the respondents, and more than half of the respondents had mental health disorders. The findings of this study show the important role of parents, educational environment, household economics, and the current residence of the students, and students with educational and welfare facilities have higher levels of mental health. It is obvious that students surveyed in Kurdistan University of Medical Sciences, which has a better mental health status, and lack of proper educational facilities would cause more mental disorders. Providing more facilities for university students, and especially suitable accommodation facilities, can help them to improve their academic status.

Conflict of Interests

Authors have no conflict of interests.

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The relationship between cognitive fusion and cognitive distortion with death anxiety in patients with diabetes mellitus

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Original Article

Abstract

BACKGROUND: Nowadays, one of the most important methods for evaluation of treatment and care in diabetes mellitus, as a chronic disease, is to assess the death anxiety. The present study aimed to determine the relationship between cognitive fusion and cognitive distortion with death anxiety in patients with diabetes mellitus.

METHODS: In this descriptive correlational study, the statistical population consisted of all patients with type 2 diabetes mellitus in Ardabil City, Iran, in year 2016. 110 patients with diabetes mellitus were selected as the statistical sample using the convenience sampling method. For data collection, the cognitive fusion scale, cognitive distortion scale, and death anxiety scale were used. Data analysis was made using Pearson correlation coefficient and multiple regression analysis at the significant level of $P < 0.050$.

RESULTS: There was a significant relationship between the cognitive fusion (0.59) and cognitive distortion (0.62) with death anxiety in patients with diabetes mellitus. Moreover, multiple regression analysis showed that cognitive fusion and cognitive distortion could predict the death anxiety among the patients with diabetes mellitus (0.48).

CONCLUSION: It can be concluded that cognitive fusion and cognitive distortion are considered among the predicting variables related to death anxiety among the patients with diabetes mellitus.

KEYWORDS: Cognition, Anxiety, Diabetes Mellitus

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Introduction

Diabetes mellitus is considered as a chronic and complex disease that, if not addressed, will turn into a serious problem for countries. Death anxiety includes anticipating the death of oneself, and fear of death process of important people in life.[1]

One of the factors that can affect the death anxiety among the patients with diabetes mellitus is cognitive fusion.[2] Cognitive fusion is a cognitive and social concept which confuses the person, and after a while, he/she thinks that it is the correct interpretation of his personal experiences, and it cannot be distinguished from his real experiences.[3] Cognitive fusion occurs when a person is caught in his thoughts.[4] According to results of a research, cognitive fusion is one of the effective elements in quality of life of the patients with diabetes mellitus.[2] Cognitive fusions also has a role in beginning of people's death anxiety.[5]

Another factor that can affect the death anxiety among these patients is cognitive distortion.[6] Cognitive distortions are defined as wrong arguments which play important role in the development of many psychiatric disorders; so that, most of the times, we think that are the

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victims of our surrounding, and external events create distress, depression, and interpersonal problems for us, and the only way to get rid of these neuroses is fixing and changing these events. Cognitive therapists believe that wrong interpretation of external events cause negative emotions. These wrong interpretations, known as "cognitive distortions or errors", come to our minds automatically.[7] According to the results of the studies, cognitive distortion is one of the effective elements in quality of life[8] and general health.[9]

The number of patients suffer from diabetes mellitus is more than 250 million in the world, and it is estimated to rise up to 350 million in 2020, and up to 438 million in 2030.[10] In Iran, the Isfahan Endocrine Research Center has estimated the prevalence of diabetes about 2 to 3 percent in the general population, and in individuals over the age of 30 years old, it is up to the 7 percent.[11] Studies show that death anxiety and its results lead to the decrease of patient's general performance and his/her psychological well-being.[12]

Diabetes mellitus is one of the chronic illnesses, and nowadays one of the most important methods for evaluation of treatment and care is to assess the death anxiety. Since death anxiety is a multidimensional structure, it can be expected to affect many aspects of life of the patients with diabetes mellitus. Thus, recognition and identification of the components that may influence the death anxiety are important. Accordingly, the present study was performed with the purpose of investigating the relationship of the cognitive fusion and cognitive distortion with the death anxiety in patients with diabetes mellitus. The study hypotheses were as "the cognitive fusion is related to the death anxiety", and "the cognitive distortion is related to the death anxiety".

Materials and Methods

The statistical society of the study included all patients with diabetes mellitus who referred to Imam Khomeini Hospital in Ardebil City, Iran, in 2016. Based on the number of study variables via Gpower software,[13] with a mean of 0.10, the alpha coefficient of 0.05, and the test power of 0.90 in the software, 110 patients were selected through convenience sampling method. The inclusion criteria of the study were as diagnosis of diabetes by the specialist physicians, having at least reading and writing skills, so that the patient can answer the scales, lack of psychiatric disorder and severe physical problems (according to the patients, themselves), and signing informed consent by the patients. The study's exclusion criterion was getting involved in other chronic and risky diseases such as cancer, or heart and lung diseases. After selecting the sample, and ensuring that this test and its obtained results merely have a research aspect and emphasizing that no name and family name are required, the scales were applied on them.

Cognitive Fusion Scale: This scale is made for measuring people's cognitive fusion with seven questions in seven-point Likert scale (from 1, it is never correct to 7, it is always correct).[2] Scores are ranged between 7 and 49. In a study, the Cronbach's alpha coefficient of this scale was reported as 0.91, and its retest reliability was 0.86, within five weeks. Moreover, the correlation coefficient between this scale and Commitment and Acceptance Scale and Southampton Mindfulness Scale were 0.72 and 0.70, respectively.[9]

Cognitive Distortion Scale: This scale has 19 items, and is scored in 5-point Likert scale (from 1, strongly disagree to 5, strongly agree). This scale has three subscales of rejection in interpersonal relationships, unrealistic expectations in relationships, and misperception (misunderstanding) in interpersonal relationships.[14] Scores are ranged between 19 and 95. Psychometric studies have reported a high psychometric quality for this scale. The reliability coefficient was obtained

0.91 for the total scale through Cronbach's Alpha. In addition, the validity was simultaneously reported 0.43 through calculating the correlation with the Spielberger State-Trait Anxiety Inventory.[15]

Death Anxiety Scale: This tool was provided by Templer in 1970 to measure death anxiety, and it has 15 questions.[16] Testers show their responses with "Yes" or "No". The marks of this scale may be between 0 and 15, which high mark indicates high anxiety of people about death. In the main process, test-retest reliability coefficient scale and its validity at the same time according to correlation with the obvious anxiety and depression scales were 0.83, 0.27, and 0.40, respectively,[16] and in Iran, reliability coefficient is reported as 0.73.[17]

Data were analyzed using Pearson correlation coefficient and multiple regression analysis using SPSS software (version 23, IBM Corporation, Armonk, NY, USA) at the significance level of $P < 0.05$.

Results

Among the participants in the study, 58 patients were men (52.7%) and 52 patients were women (47.3%). The mean age ± standard deviation (SD) of the participants was 51.34 ± 4.42. Table 1 shows other demographic characteristics of the patients.

Pearson correlation coefficient test was showed the significant and positive relationship between the predictor variables (cognitive fusion and cognitive distortion) with the dependent variable of death anxiety (Pearson coefficient = 0.59, P = 0.001, and Pearson coefficient = 0.62, P = 0.001, respectively).

The results of table 2 show that by using multiple regression, 0.48 of death anxiety among the patients is explained by predictor variables (cognitive fusion and cognitive distortion). According to predicted beta coefficients, cognitive fusion (0.35) and cognitive distortion (0.43) had significant effect on the death anxiety.

Table 1. Demographic characteristics of the participants in the study

Variable	Index	n (%)
Age (year)	30-40	16 (14.5)
	41-51	37 (33.7)
	52-62	39 (35.4)
	63 and higher	18 (16.4)
Education	Elementary school	27 (24.5)
	Guidance school	29 (26.4)
	High school	35 (31.8)
	Academic degree	19 (17.3)
Economic status	Good	29 (26.4)
	Average	57 (51.8)
	Weak	24 (21.8)

The mean ± SD of cognitive fusion, cognitive distortion, and death anxiety variables were as 25.31 ± 5.74, 46.39 ± 7.65, and 8.88 ± 3.24, respectively.
SD: Standard deviation

Discussion

The results of this study showed that there were significant correlations between variables of cognitive fusion and cognitive distortion with death anxiety among the patients with diabetes mellitus. One of the objectives of this study was to present a regression model based on the predictor variables to predict the death anxiety, and results showed that these variables can predict the death anxiety. The first part of the study showed that there was a significant relationship between cognitive fusion and death anxiety of patients. The obtained result were consistent with the results of the studies of Aqajani and Samadifard,[2] Gillanders et al,[3] Trindade and Ferreira,[4] and Samadifard and Mikaeili.[5]

Table 2. Results of Multiple regression to predict death anxiety

Variable	β	T	P	R	R^2
Cognitive fusion	0.35	4.4	0.001	0.68	0.48
Cognitive distortion	0.43	5.4	0.001		

In explaining the result, we can say that cognitive fusion is the most powerful predictor of anxiety syndrome. People with higher levels of cognitive fusion are more likely to develop anxiety.[6] In cognitive fusion, person is so impressed by his thoughts that they seem completely real; so, experience and behavior will be dominant sources of behavior regulation, and he will be less sensitive to direct results.[7]

The results also showed that there was a significant relationship between cognitive distortion and death anxiety of patients with diabetes mellitus. This result was also consistent with the results of the studies of Ellis and MacLaren[7] and Belir et al.[8] In explaining the result, cognitive distortion can have a key role in psychological parameters such as aggression, agitation, depression, and disturbed interpersonal relationships. Based on its theories and models, the structure of cognitive distortion is composed of various factors and components. These components may be related to internal and personality factors, or to social conditions and cultural grounds.[7,8]

It seems that the patients with high cognitive fusion and distortion cannot make appropriate decisions when facing with problems, and this causes the emergence of the death anxiety among them.

The present study confronted with some restrictions. This study was performed on the patients with diabetes mellitus in Ardebil City that makes it difficult to expand the results to other patients. Therefore, it is recommended to perform a similar study on these patients in other cities, and to compare the results with those of the present study. Moreover, due to some restrictions, some variables such as education, economic status, etc. were not investigated in this study; surely, examining them can help clarifying the death anxiety in patients as much as possible. From the other limitations of this study, we can refer to the use of convenience sampling method. It is suggested to use random sampling method in other researches in order to more confident expansion of the results.

Conclusion

It can be concluded that cognitive fusion and cognitive distortion are among the variables that are related to the death anxiety among the patients with diabetes mellitus, and have the ability to predict it.

It is recommended to help the patients to decrease their death anxiety through trainings for overcoming the cognitive fusion and distortion.

Conflict of Interests

Authors have no conflict of interests.

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Investigating the relationship between the level of serum albumin and body mass index, as nutritional indicators, with dialysis adequacy in patients under hemodialysis

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Original Article

Abstract

BACKGROUND: Patients with end-stage renal disease (ESRD) who undergo hemodialysis have many complications; one of the most important of which is malnutrition, which affects these patients' quality of life. The aim of this study was to evaluate serum albumin and body mass index (BMI) as nutritional indicators, and their relationship with dialysis adequacy in patients under hemodialysis.

METHODS: In this study, 100 patients who underwent hemodialysis in Razi Hospital, Qaemshahr City, Iran, in 2016 were selected via convenience sampling method. The data were collected using demographic questionnaire, albumin test, and measuring height and weight of patients. Data were analyzed using linear regression and correlation coefficient tests.

RESULTS: The correlation between the hemodialysis adequacy with albumin was 0.634, which was significant ($P < 0.050$). For the second hypothesis, the quality of dialysis with BMI was not positively correlated. The correlation between the hemodialysis adequacy with BMI was -0.007, which was not significant ($P > 0.050$). Although, in the third hypothesis, the regression between the adequacy of hemodialysis, as a dependent variable, and serum albumin and BMI, as independent variables, indicated significant relationship between serum albumin and hemodialysis adequacy; but there was no significant relationship between BMI and adequacy of hemodialysis.

CONCLUSION: Adequacy of hemodialysis is in relationship with malnutrition and improving the KT/V dialysis adequacy may have a significant effect on the malnutrition control in these patients.

KEYWORDS: Hemodialysis, Serum Albumin, Body Mass Index

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Introduction

Chronic kidney disease (CKD) is a public health problem.[1] CKD is defined as progressive and irreversible loss of renal function.[2] Reduced renal function and progression of end-stage renal disease (ESRD) depend on underlying disorder, urinary protein excretion, and high blood pressure. Disease in people with high levels of protein excretion or high blood pressure progresses faster than other patients.[3] Two major treatments for ESRD include hemodialysis and transplantation.[2] Hemodialysis aims to remove nitrogen, toxic substances, and excess water from the blood.[3]

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Prolonged prognosis of patients under chronic hemodialysis is affected by the adequacy of hemodialysis treatment, and its evaluation is very important in the management of these patients.[4-6]

Variables that allow us to correctly evaluate the adequacy of dialysis are measurable, mostly affected by dialysis and a reflection of metabolic disorders of urea. Since 1993, the guideline of Nephrologists Association has determined the adequacy of dialysis as the minimum reduction ratio of urea reduction ratio (URR) 65%, and Kt/V > 1.2.[7]

In dialysis, urea clearance is calculated using the Kt/V formula. K as dialyzer clearance of urea, which depends on the coefficient of removal of the substance in the filter (KOA); which is constant for each filter, and the blood flow; t demonstrates time, and V as the volume of urea distribution in body fluids, which depends on height, weights, and gender. Kt/V is calculated at a normal level of 1.2. According to valid sources, a level below 0.8 is considered as inadequate.[7,8] Protein-energy malnutrition, as one of the most important risk factors for cardiovascular diseases, is common among patients under hemodialysis.[9]

If urea clearance is inadequate, hemodialysis will be inadequate regardless of plasma urea. On the other hand, only low plasma urea level does not necessarily indicate adequate dialysis. Urea plasma depends not only on the amount of urea, but also its production. The amount of urea produced is related to the protein received. The low level of plasma urea before dialysis may be due to low protein intake. Therefore, in evaluating the adequacy of dialysis, what is important is urea clearance in a 4-hour phase of dialysis, and does not depend on the plasma level of urea alone.[8]

Patient with CKD should initially receive low-protein diets, which will slow down the progression of kidney failure, and delay the need for dialysis and kidney transplant as replacement therapies. However, after patient's progression to advanced kidney failure and treatment with dialysis, the need to use protein is essentially increasing. Some of the patients continue to follow the same diet pattern due to the habit of consuming low-protein diets, anorexia, lack of awareness, and even the false education given to them.[10] Malnutrition in patients under hemodialysis leads to decreased quality of life, and increased incidence of diseases and mortality.[11] To evaluate the nutritional status of the these patient, there are several ways, including patient interview, comparing actual and required weight, measuring the thickness of the skin of the arm and arm circumflex, bioempedance or estimating muscle mass by measuring resistance and body reactions to an alternating electric current, measuring serum albumin, urea, and nitrogen, and calculating the rate of urea production.[10] Low serum albumin is one of the most important causes of mortality in patients under hemodialysis.[9]

Shasti and Baba Haji reported that only half of the patients (50.5%) had adequate dialysis with Kt/V of more than 1.2, and only 46% with URR of more than 65%.[8] Saad et al., in studying the quality of life predictors in patients with CKD that underwent hemodialysis, showed that serum phosphate levels, weight between two dialysis sessions, and dialysis adequacy are associated with higher levels of quality of life.[12] Machingura et al. reported that 76.7% of patients that underwent hemodialysis in Parirenyatwa group of hospitals and Chitungwiza central hospital in Zimbabwe had hypoalbuminemia, and monitoring serum albumin was necessary to reduce mortality in these patients.[13] In another study, the prevalence of malnutrition was high with an outbreak of 29 at younger age and in people with low income families. Moreover, there was a longer hemodialysis duration, higher KT/V, and inadequate calories and protein intake. Reversing this situation needed more nutritional care.[14]

The aim of this study was to evaluate serum albumin and body mass index (BMI) as nutritional indicators, and their relationship with dialysis adequacy in Razi hospital in Qaemshahr City, Iran. The results of this study were presented to the relevant authorities to increase the life span, and improve the quality of life among the patients under hemodialysis.

Materials and Methods

In this descriptive correlational study, which was done in Razi hospital in year 2016, the study population consisted of people who had a medical record in hospital, and according to their scheduled appointments referred to hospital for hemodialysis. We included patient who aged 18 years and more, hemodialyzed at least 1 and at most 3 times in a week, and had no kidney transplant and mental disorders (major depressive disorder or bipolar mood disorder).

To collect the data, the researcher enquired permission from the related authorities of Mazandaran University of Medical Sciences, and Razi Hospital in Qaemshahr, and completed the research data using patient records and laboratory tests.

In order to collect the data in this study, researchers were present in the environment and collected the required information by using a demographic questionnaire and patient records. The adequacy of dialysis was calculated using the Kt/V formula as: $Kt/V = -\ln(R - 0.008 \times t) + [(4 - 3.5\ R) + UF/W]$

The range for reporting Kt/V score was considered from 0.7 to 1.3.

BMI was obtained from the squared height on the patient's weight.

Serum albumin was obtained from a patient's blood sample.

After collecting information regarding variables of the research, Kolmogorov-Smirnov test was performed to determine the normality of the data. In the case of normal data, we used parametric tests to examine the hypotheses; otherwise we used a nonparametric coefficient.

The study hypothesis were as the adequacy of hemodialysis has a significant positive relationship with serum albumin; the adequacy of hemodialysis has a significant positive relationship with BMI; and the adequacy of dialysis has a significant positive correlation with serum albumin and BMI. To examine this hypothesis, we have used dual linear regression test.

Results

In our study, among 100 patients, 52 cases (52%) were men and 48 (48%) were women, 13 (13%) were single and 87 (87%) were married. 5 persons aged 18-30 years (5%), 3 persons (3%) 30-40 years, 12 persons (12%) 40-50 years, 24 persons (24%) 50-60 years, and 56 persons (56%) over 60 years. The number of dialysis sessions was reported to be twice a week in 12 cases (12%), and three times a week in 88 cases (88%). Based on occupational status, 3 cases (3%) were government employees, 35 cases (35%) were retired, 50 cases (50%) were housekeeper, and 12 cases (12%) had other occupations.

In our study, 54 cases (54%) were hemodialyzed with A-V fistulas, 38 cases (38 %) had A-V grafts, 5 cases (5%) had temporary dialysis catheters, and 3 cases (3%) had permanent catheter catheters.

Finally, the descriptive data analyses showed that 43 cases (43%) have progressed to ESRD due to diabetes mellitus, 46 cases (46%) due to hypertension, and 11 cases (11%) due to other medical causes.

Table 1 shows the results of testing the normal variables in each group. The method of conclusion in this test was that if the level of significance (P) was less than 0.05, the data were abnormal and, if more than 0.05, the data were normal.

According to table 1, the KT/V was not a normal variable, but the serum albumin and BMI were normal.

Table 1. Kolmogorov-Smirnov statistics to determine normal or non-normal variables

Variables	Kolmogorov-Smirnov statistics	P	Test result
KT/V	2.44	< 0.0001	Non-normal
Serum albumin	1.22	0.0997	normal
BMI	0.96	0.3203	normal

BMI: Body mass index

Before examining the research hypotheses, we examined descriptive variables. Table 2 shows descriptive indicators such as average, median, mode, standard deviation, minimum and maximum. The KT/V as the variable had an average of 1.18, median of 1.20, a mode of 1.20, a standard deviation of 0.50, a minimum of 0.80, and a maximum of 1.30. In the case of serum albumin, the average was 3.36, median 3.70, mode 4.00, standard deviation 0.50, minimum 2.50 and maximum 5.00. For BMI, the average was 24.30, median 24.43, mode 30.19, standard deviation 4.9, minimum 16.00, and maximum 20.36.

To test the research hypotheses, correlation coefficient and linear regression were used. The correlation between the adequacies of hemodialysis with albumin was 0.634, which was statistically significant (P < 0.0001). The correlation between the hemodialysis adequacy and BMI was -0.007, which was not significant (P = 0.9440).

Table 3 shows the correlation between adequacy of hemodialysis, as a dependent variable, and serum albumin and BMI as independent variables.

According to table 3, the relationship between serum albumin and hemodialysis adequacy with regression coefficient of 0.129 and t of 7.81 was statistically significant; but BMI with regression coefficient of -0.001 and t of -0.72 had not statistically significant relationship with hemodialysis adequacy; it should be noted that the coefficient of determination of the R^2 model iwass 0.386. The result confirms that there was a significant relationship between serum albumin and hemodialysis adequacy, but there was no significant relationship between BMI and hemodialysis adequacy.

Discussion

The result of our study in the first hypothesis showed that the adequacy of hemodialysis with had a significant positive correlation serum albumin. In explaining the reason, it should be said that CKD varies from proteinuria to increasing serum creatinine, which is indicative of decreased glomerular filtration, and ultimately complete loss of renal function and ESRD.[2] Prolonged prognosis of patients under chronic hemodialysis is affected by the adequacy of dialysis treatment, and its evaluation is very important in the management of these patients.[7] Protein-energy malnutrition, as one of the most important risk factors for cardiovascular diseases, is common among patients under hemodialysis.[9,15-17] Therefore, assessment of nutrition status in patients is necessary for both malnutrition prevention, and intervention in malnutrition cases.[1]

Hashemi and Garshad, in their study on the evaluation of the adequacy of hemodialysis and other biochemical factors related to it in patient under hemodialysis in Bojnourd City, Iran, did not find any correlation between the adequacy of hemodialysis and serum albumin.[16]

Table 2. Descriptive indexes of research variables

Variables	Number	Average	Median	Mode	Standard deviation	Minimum	Maximum
KT/V	100	1.18	1.20	1.20	0.10	0.80	1.30
Serum albumin	100	3.63	3.70	4.00	0.50	2.50	5.00
BMI	100	24.30	23.44	19.30	4.19	16.00	36.20

BMI: Body mass index

Table 3. Regression coefficients between the hemodialysis adequacy with serum albumin and body mass index

Dependent variable	Independent variables	R^2 determination Coefficient	B (beta)	t statistics	P
Dialysis adequacy (KT/V)	Constant	0.386	0.751	10.10	< 0.0001
	Serum albumin		0.129	7.81	< 0.0001
	BMI		-0.001	-0.72	0.4737

BMI: Body mass index

Contrary to our results, another study by Rashidfarokhi et al., with the aim of evaluating dietary protein intake by calculation of urea generation rate in patients under chronic hemodialysis in Kerman, Iran, did not show a significant relationship between serum albumin and hemodialysis adequacy.[17] It seems the probable reason for this inconsistency is that serum albumin is also altered by other factors such as liver problems, plasma volume changes, and inflammatory conditions.

In a study by Garagarza et al. in Portugal, to investigate the relationship between hypophosphatemia, nutritional status, and body composition with mortality in patients under hemodialysis, patients with lower plasma albumin levels had lower survival rates.[18] Azar et al. conducted a study to investigate the association between hemodialysis dose improvement and nutritional status among the patients under hemodialysis. The results showed a significant positive correlation between the adequacy of hemodialysis and serum albumin.[19] Teixeira Nunes et al. found a significant positive correlation between the adequacy of hemodialysis and BMI;[20] that was not consistent with the results of our study.

Moreover, Teixeira Nunes et al.,[20] and Stolic et al.,[21] in separate studies aimed to evaluate hemodialysis adequacy and nutritional status in patients under hemodialysis, and found a significant positive relationship between albumin and hemodialysis adequacy markers. Another study by Song et al. in China, aimed to analyze factors associated with death in patients on maintenance hemodialysis, and found a significant positive association between albumin and dialysis adequacy with death.[22] The results of the studies mentioned above are consistent with the present study. Therefore, it seems that improving hemodialysis adequacy, and increasing the frequency of dialysis per week can lead to a better excretion of uremic toxins, and thus improve appetite and protein intake in patients. Consequently, malnutrition in patients under hemodialysis can be controlled by improving the adequacy of hemodialysis.

Unlike the results of a study in Birjand on patients under chronic hemodialysis,[23] there was not a significant positive correlation between BMI and dialysis adequacy in our study.

Zafar Mohtashami et al., in a study on determining the adequacy of hemodialysis in patients under chronic hemodialysis in Khorramabad, Iran, showed a significant positive correlation between BMI and dialysis adequacy.[24] Likely, the probable causes of these inconsistent findings are the patients' different races, underlying diseases such as diabetes mellitus, and patients' lack of protein intake.

Conclusion

The results of our study indicated that a significant relationship existed between adequacy of dialysis and malnutrition; and promoting Kt/V dialysis adequacy may have a great impact on malnutrition control in these patients.

Conflict of Interests

Authors have no conflict of interests.

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The prevalence and the risk factors associated with tranquilizer abuse in the population with the age of over 18 years in Iran

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Original Article

Abstract

BACKGROUND: Non-medical use of prescription drugs is a growing global health concern. The real scale of the problem is unknown. Statistics indicate that taking painkillers and sedatives leads to dependency and addiction to the drugs administered. Therefore, this study aimed to determine the prevalence and risk factors of drug abuse for causing lethargy and sedation in the population with the age of over 18 years in Sanandaj City, Iran.

METHODS: This descriptive-analytic study was conducted in year 2015. The sample size was 1750 people, and cluster sampling method was performed from all health care centers in Sanandaj City. Data were collected using a researcher-made questionnaire to assess intractable consumption and tranquilizer drug abuse, and addiction to these medications. Data were analyzed using chi-square test and logistic regression analysis to identify socio-demographic and risk behavior correlated with abuse tranquilizer or sedative drugs.

RESULTS: 80% of the participants had intractable consumption, and 18% of those with intractable consumption had dependency to these drugs (having two symptoms of withdrawal and denial of medications according to DSM-IV). The factors affecting consumption and drug abuse can be arbitrary, job, availability of pharmaceuticals, insurance, family history of addiction, marital status, physical or mental illness, and conflict in the family.

CONCLUSION: Dependency to lethargy-inducing drugs and tranquilizers was high in the study population. So, planning to make people aware of the consequences of taking drugs, especially tranquilizers and lethargy-inducing drugs, is very important.

KEYWORDS: Substance Abuse, Pain, Chronic Pain, Drugs

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Introduction

The growing non-medical use of prescription drugs is a global health concern. Non-medical use of prescription drugs such as sedatives, tranquilizers, stimulants, and pain relievers, is defined as taking medications without a doctor's prescription, for periods longer than prescribed, or for reasons other than the medication's intended purpose for example 'to get high'.[1] Drugs include tranquilizers, and in the second rank, pain killers, which are among sensitive substances which may create dependence and consequent damage.[2] If these drugs be used under medical supervision with an appropriate dose, there are no special consequences; but, if taken without

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prescription and medical supervision, and with inappropriate continuous doses, they could endanger physical and mental health. They could also create dependence, addiction, and even death.[3,4] Evidence also shows that dependence on these drugs can underlie addiction and consumption of other illicit drugs.[5]

The magnitude of this problem is unknown, it is mostly due to the lack of information about non-medical use of prescription drugs, which are related to gaps in the monitoring of the legal use of drugs for medical purposes that is prescribed by the healthcare professionals.[6] Lethargy and sleep-inducing drugs which are widely used in Iran, should not be underestimated. Their withdrawal symptoms may be associated with seizures; they are hazardous and more challenging to quit compared with other addictive substances.[7] After cannabis, non-medical use of opioid analgesics in the United States has the second rank concerning drug abuse.[8,9] In Switzerland, after alcohol, cigarettes, and cannabis consumption in men, taking drugs without prescription is worrying.[9] In 2005, 6.6% of the American teens reported the abuse of tranquilizers and pain killers.[10]

A study by Guo et al. in 2012, to determine the prevalence of non-medical use (without prescription) of pain killers among 11,906 high school students in south China showed that, 11.3% of the students used tranquilizers without prescription.[11] Another study in Rafsanjan, Iran, showed that 7.4% of the students reported abuse of benzodiazepines.[12] The variables associated with intractable consumption include age, sex, race, celibacy, unemployment, low education levels, poor health, insurance coverage, history of smoking, alcohol, and other drugs,[13,14] low income families, lack of family support,[15] conflict in the family,[10] addiction of relatives or peers, and increase in drugs availability.[1,16] Most of the studies and monitoring tools are related to drug abuse and illegal use of drugs or consumption of alcohol and tobacco;[17-20] however, non-medical use of prescription drugs is a unique category of substance abuse, and need to be addressed at different levels.[6]

Considering the prevalence of intractable consumption and its consequences, in order to design interventions, understanding the underlying factors associated with this behavior is important. Due to the lack of information regarding intractable consumption, and dependence on tranquilizers and lethargy-inducing drugs in Sanandaj, Iran, this study aimed to determine the prevalence and factors associated with the abuse of tranquilizer and lethargy-inducing drugs in the population over 18 years of age. In understanding the current situation, findings of this study may develop appropriate intervention programs to increase public awareness, and make a change in the behavior of the future population.

Materials and Methods

This descriptive-analytic study was conducted in 2015. As the amount of the prevalence of drug abuse was considered 10 percent, with 95% of confidence interval, the required sample size was calculated as 864; in compliance with Scheme 2, the total volume of sample was calculated as 1728 participants. For this purpose, 70 clusters of 25 patients were selected and cluster sampling was performed from different areas of the city of Sanandaj. The number of clusters in each region were determined according to the number of households and population covered by health centers in the region (70 clusters of 25 people). After determining household cluster heads by referring to the beneficiary houses, the questionnaire was completed for all persons over 18 years old. Questionnaires completing method was interview, especially for the illiterates.

Data were collected using a researcher-made questionnaire to assess intractable

consumption and tranquilizer drug abuse, and addiction to these medications. The questionnaire was consisted of three sections. The first section included demographic variables (age, sex, occupation, education, marital status, income, and insurance coverage), variables associated with the family (family history of addiction and satisfaction rate), and a question on the history of medical or psychiatric conditions; the second section was consisted of data related to intractable consumption (how to obtain the drug, type of drug, and duration of usage); and the third section was consisted of data related to addiction and drug dependency (signs and symptoms of withdrawal and suspension of drugs). Finally, an optional question was asked to determine the dependency to cigarette, hookah, and other narcotics. Content and face validity method was used to determine the validity of the questionnaire.

First, using literature review, searching the data bases and experts` opinion, three sections of the questionnaire were adjusted. Then, the questionnaire was presented to three faculty members at Kurdistan University of Medical Sciences, Sanandaj, Iran, and some physicians working in the clinic for addiction treatment and counseling centers for behavioral disorders. Their opinions were applied, and final version of questionnaire was prepared. To determine the reliability of questionnaire, a pilot study on a pilot sample was conducted, and the necessary changes were made. Eventually, questionnaire reliability was confirmed (Cronbach's alpha = 0.92). Informed consent was obtained and the purpose of the study was explained to study population.

Data were analyzed using chi-square test and Multivariate logistic regression via SPSS software (version 16, SPSS Inc., Chicago, IL, USA).

Results

The age range of study participants was 18 years (Table 1).

Table 1. Demographic variables of participants

Variable		n (%)
Age (year)	Under 30	918 (35.5)
	30 to 39	506 (28.9)
	40 to 49	327 (18.7)
	50 to 59	178 (10.2)
	60 and above	124 (7.1)
Occupational status	Full time	604 (34.5)
	Part-time (with irregular income)	147 (8.4)
	Unemployed	213 (12.2)
	Housekeeper	323 (18.4)
	Student	466 (26.6)
Educational status	Illiterate	200 (11.4)
	Elementary	231 (13.2)
	Secondary	320 (18.5)
	High school	554 (31.6)
	Higher education	449 (25.6)

A total of 883 participants (50.4%) were women and 870 (49.6%) were men. In terms of marital status, 469 (26.8%) were single, 1151 (65.7%) were married, 71 (4.1%) were divorced, and 62 (3.5%) were widowed. Total of 208 (11.9%) participants have reported a history of physical or mental illness and 16% had addiction family history. Regarding health insurance services, 585 (33.4%) participants were not covered by any health insurance services.

Considering family relationships satisfaction, participants were divided into two groups, singles in their relationship with their parents, and married people in their relationship with their spouses (Table 2).

Table 2. The status of satisfaction level in the family

Marital status	Satisfaction level				
	Highly satisfied	Satisfied	Moderate	Unsatisfied	Highly Unsatisfied
Single	15.5	9.4	2.2	1.4	1.4
Married	39.2	20.1	3.2	3.2	1.4

Table 3. The relationship between socio-demographic factors and drug dependency

Variable		Dependence [n (%)]		P*
		Yes	No	
Age	Under 30 years	116 (23.0)	388 (77.0)	0.013
	30 to 39 years	114 (26.6)	315 (73.4)	
	40 to 49 years	45 (17.5)	212 (82.5)	
	50 to 59 years	23 (15.8)	123 (84.2)	
	60 and above	20 (27.4)	53 (72.6)	
Occupational status	Full-time	81 (16.5)	410 (83.5)	< 0.001
	Part-time (with irregular income)	51 (41.5)	72 (58.5)	
	Unemployed	35 (22.2)	123 (77.8)	
	Housekeeper	69 (26.4)	192 (73.6)	
	Student	82 (21.8)	294 (78.2)	
Owner and tenant	Owner	143 (17.6)	669 (83.0)	< 0.001
	Tenant	175 (29.3)	422 (70.6)	
Marital status	Married	78 (20.7)	298 (79.3)	< 0.001
	Single	196 (21.1)	731 (78.9)	
	Separated from their spouse	39 (59.1)	27 (40.9)	
	Widow	5 (12.8)	34 (87.2)	
Physical or mental illness	Sick	61 (36.7)	105 (63.3)	< 0.001
	Healthy	257 (20.7)	986 (79.3)	
Insurance coverage	Insured	178 (19.4)	740 (80.6)	< 0.001
	Uninsured	140 (28.5)	351 (71.5)	
Family history of addiction	Positive	86 (34.8)	161 (65.2)	< 0.001
	Negative	232 (20.0)	930 (80.0)	
Substance abuse	People who smoke and used hookah	162 (31.1)	358 (68.8)	< 0.001
	Not smoke	156 (17.6)	733 (8.2)	
	People who used narcotics reported tranquilizers abuse	116(40.5)	171 (59.5)	
	Not abuse	199 (17.8)	917 (82.1)	

* Chi-square test

80% of the participants had intractable consumption; and 18% of the participants with intractable consumption had dependency to these drugs. The results showed a significant relationship between age and dependency on drugs. Greatest amount of substance abuse (27.4%) were found in the participants over 60 years (Table 3).

There was also a significant relation between occupation and tranquilizer dependency (P < 0.001); so that 41.5% of the part-time people (with irregular income) were dependent to tranquilizers. There was a significant association between the owner and tenant dependency on drugs (P < 0.001). 29.3% of the people who reported drug dependency were tenants. People separated from their spouse with 59.1%, had the highest drug abuse. There was a significant relationship between marital status and dependency on tranquilizers (P < 0.001). There was positive correlation between the availability of drugs and drug dependency (P < 0.001). 43.4% of participants mentioned drug availability as the reason for intractable consumption, and 27.7% have reported drug abuse. There was a significant correlation between physical or mental illness, insurance coverage, and family history of addiction with drugs dependency (P < 0.001). 36.7% of people who had history of disease, reported drug abuse. 28.5% of people who were not covered by any health insurance had drug abuse, and 34.8% of those who had family history of addiction had drug dependency (Table 3).

Conflict in the family were among the factors that played a role in drug dependency to tranquilizers (P = 0.014).

Table 4. Logistic regressions for tranquilizers/sedatives abuse and self-medication, odds ratios and 95% confidence intervals for explanatory variables

Explanatory variables*	P	Explanatory variables (b)	
		Odds ratio	95%CI
Age (under 30 years/other)	0.357	1.018	0.981-1.056
Sex (female/male)	0.321	1.305	0.771-2.209
Occupational status (full time/other)	0.011	0.968	0.758-1.235
Owner (owner/tenant)	0.372	1.310	0.725-2.367
The number of family members (4 member/other)	0.894	1.013	0.842-1.219
Marital status (married/other)	0.289	1.649	0.655-4.692
Positive income	0.031	1.000	1.000-1.000
physical or mental illness (Sick/Healthy)	< 0.001	1.626	0.607-4.357
Family history of addiction (not history/ family history)	< 0.001	1.645	0.762-3.550
Insurance coverage (uninsured/ insurance coverage)	< 0.001	1.040	0.569-1.899
Educational status (illiterate/other)	0.633	1.079	0.790-1.474
Positive substance abuse	0.019	1.023	0.563-1.592

* Variable(s) entered on step 1: age, sex, job, owner, number of family members, marital status, income, physical or mental illness, substance abuse, family history of addiction, education, insurance coverage.
CI: Confidence interval

Most of the substance abuse in singles (31.5%), was in those who were unsatisfied in their family relations with their parents. 37.5% of married people, who were very dissatisfied in their relations with their spouse, had the greatest dependency on drugs (P = 0.020). Substance abuse was one of the factors affecting drug dependency (P < 0.001). 31.1% of people who smoke and used hookah, and 34.7% of people who used narcotics, reported tranquilizers abuse (Table 3).

It should be noted that in univariate analysis between sex, education, number of family members, and income, with drug abuse, no significant correlation was seen. The multivariate analyses of tranquilizers/sedatives abuse showed a strong association with job, income, other illicit substance use, family history of addiction, insurance coverage, physical or mental illness; these were strongly associated with tranquilizers/sedatives abuse (Table 4).

Discussion

The present study showed that 80% of the study population had intractable consumption. Of this number, 18% reported tranquilizers abuse. The results showed a high percentage of addiction and tranquilizer abuse. Although the results of our study included general population, and showed a greater percentage of dependency on tranquilizers, it was similar to most of the studies on this subject.

In a study by Bali et al., the prevalence of intractable consumption was 10%, and 13% of those who used tranquilizers without physician prescription, were dependent to drugs.[21] Moreover, in a study by Becker et al., 2.3% of participants used tranquilizers for non-medical purpose, and 8.9% of the people had dependency to these drugs.[13]

On the one hand, available data indicates increased substance abuse, and prescribing medicines are rapidly becoming the drug of choice by various sectors of society; on the other hand, the states simply cannot declare these substances illegal, as these medications are essential for many people around the world to achieve and maintain good quality of everyday life. So, a part of addiction in the community will be ignored; which has serious consequences, including accidents caused by drug overdose, poisoning, and death due to substance abuse.[22]

The results of this study showed the individual and social factors influencing drug abuse, including age, occupation, being renter, the history of disease, tobacco and other illegal substances use, family history of addiction, lack of insurance coverage, drug availability, and the

family's conflict. In this regard, our study was similar to the study by Becker et al.,[13] which have evaluated the same factors. In a study by Kokkevi and Stefanis,[23] non-medical use of drugs was related to using other substance, and family satisfaction. In Guo et al. study,[11] the non-medical use of drugs in students was associated with the satisfaction from relationships with parents, teachers, and friends.

Family tensions and discontent of people from their relationship with other family members are among the problems facing our community. It can be said that a family history of addiction somehow, caused the dissatisfaction of people from their family relationship. Informing families and also teaching life skills to them, and establishing a warm, friendly, and free of tension environment could be effective to reduce family harms, including addiction.[24]

In the present study, no significant difference was found between sex and non-medical use of drugs which was consistent with the study by Guo et al.;[11] but was not consistent with Kokkevi and Stefanis study[23] which showed that women were tranquilizer consumers more.

In our study, the motivation of 73.6% of participants to intractable consumption was pain relief; which was similar to the findings of Boyd[25] who showed that 75% of students used tranquilizers for insomnia, and 79% used analgesics for pain relief. In our study, 1.5% of participants reported euphoria as their motivation to intractable consumption. It had a significant association with drug dependency. In the study by Boyd,[25] 11% have reported drug abuse for the sake of euphoric experience.

In Iran, the drug use culture is incorrect; unfortunately, access to tranquilizers is very easy anytime and anywhere; and a large number of participants mentioned high costs of health services and health insurance as the reason for intractable consumption. In this regard, interventional planning to reform drug distribution system, and reducing health care costs is necessary. Moreover, training programs for all age and sex groups regarding the ration for prescribing drugs use, and the consequences of intractable consumption can be effective to disseminate correct culture of drug use.

This was the first study to examine addiction to tranquilizers in Iran. The strength of this study was high volume of samples that were included in the general population in Sanandaj City, from different regions and sectors.

The study also has several limitations:

1. In this study, young people under 18 years were not included.
2. Awareness on the effects of self-medication was not assessed.
3. Since it was a self-reported study, so data accuracy deliberate depended on the individuals.
4. As this study was conducted in Sanandaj City, the results could not be generalized to other cities.
5. Rural community has not been evaluated.

Prevention programs of substance abuse toward general people should be expanded and take care to educate people on the risks of abuse of the drugs.

Conclusion

The findings show a high level of self-medication in the studied community. Moreover, self-medication is directly related to the consumption of tranquilizers and painkillers. Thus, controlling the sale of medicines in pharmacies as well as the appropriate prescription by the physicians is necessary; besides, extensive and continuous information to the public about the evils of self-medication is necessary.

Conflict of Interests

Authors have no conflict of interests.

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The prevalence of infertility and related factors in patients referred to infertility center in Besat hospital, Sanandaj, Iran

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Original Article

Abstract

BACKGROUND: Infertility is considered as a prominent health care issue. The present study aimed to determine the prevalence rate of infertility and certain factors relevant to it.

METHODS: The current study was performed on every couple who visited the infertility center of Besat hospital located in Sanandaj City, Iran, in a period between 2014 and 2015. The study population was comprised of 579 patients. A certain questionnaire was used for data collection. Data was analyzed using STATA Ver.11 software. Descriptive statistics as well as chi-square, t, and Fisher's exact tests were used.

RESULTS: Out of 579 cases, 372 ones (64.3%) showed primary infertility, and 207 cases (35.7%) had secondary infertility. The most prevalent cause of infertility in women was found to be in relationship with ovarian factors (33.5%), and in men, male factors were the first cause (30.2%). Other observed causes of infertility were uterine factors (5.5%), tubular factors (12.8%), and unknown factors (18%). No significant relationship could be found between women's age groups and the male factors of infertility (P = 0.813); while there was in fact a meaningful statistical relationship between women's age groups and ovarian factors (P = 0.001).

CONCLUSION: The current study shows that prevalence rates of primary and secondary infertilities were 64.3% and 35.7%, respectively. Most commonly found causes of infertility in men were male factors, and in women, tubal, ovarian, and unknown factors.

KEYWORDS: Male Infertility, Female Infertility, Causality

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Introduction

Infertility is considered a major health care problem, which can be defined as the lack of occurrence of pregnancy after having one year of regular intercourse without using any contraception methods.[1] The prevalence rate of infertility has been estimated as 3.5-16.7 percent in developed countries, and 6.9-9.3 percent in developing countries;[2] while the average infertility rate reported for Iran is 13.2%.[3] It has been reported that from the total infertilities, 40% are detected in men, 40% in women, and 20% are recognized in both sexes.[4]

Infertile couples are at the risk of

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psychological disorders. As one of the major psychological disorders that accompany infertility, depression critically affects the life of both infertile men and women, as well as their treatment, and the matter of following-up their treatment.[5] Infertility is not simply a health problem; it is also associated with social injustice and inequality,[6] and leads to distress and depression, and potentially ostracism and discrimination.[7,8]

Infertility can be divided into two types of primary and secondary. The secondary infertility is defined as the inability to give birth despite of being exposed to pregnancy for a period of one year.[9] Different studies have shown that infertility, whether primary or secondary, takes place in almost 15% of all the women worldwide,[10] and the incidence rate of female infertility is rising every year.[6]

Numerous reasons are considered as the causes for infertility, and often several reasons in combination are the cause of infertility.[11] The causes of infertility vary, including varicocele, azoospermia of vas deferens obstruction, sperm problems (dysmorphology, low number, and low mobility), and sensitivity to sperm that are male problems; plus female problems that include body weight, nutrition disorders, ovulation problems, smoking, age, cervix disorders, luteal phase defects, endometriosis, poor quality of ovulation, obstruction of the fallopian tubes, and polycystic ovarian syndrome.[12-15]

The most commonly observed reasons of female infertility are ovulation defect, and low ovarian reserve in the ovaries as a result of aging; in addition, being overweight in women affects androgen and estrogen production, and this cause is responsible for 12% of all infertility cases in women.[14] The most prevalently seen cause of male infertility is varicocele;[15,16] which is defined as dilated and twisted veins of the pampiniform plexus in the spermatic cord.[17] The age of onset of infertility is usually during puberty or immediately after it.[18]

Considering the importance of infertility issue as a health consideration, which tremendously affects the lives of couples, and given the lack of information about the prevalence of infertility in Kurdistan Province, Iran, the aim of the current study was to determine the prevalence of infertility and its related factors in patients referred to the infertility center of Besat hospital in Sanandaj City, in a period between 2014 and 2015.

Materials and Methods

The current descriptive analytical cross-sectional study was conducted on every couple who had referred to the infertility center of Besat hospital, in a period between 2014 and 2015. The study population included 579 patients enrolled using census sampling method.

A questionnaire was utilized in order to collect the data. Certain data including demographics, the final diagnosis of the cause of infertility, infertility duration, marriage age, and marriage duration were obtained from the patients' medical records.

Data was analyzed using Stata software (version 11, StataCorp LLC., College Station, TX, USA). Descriptive statistics, mean, and standard deviation, as well as t (for quantitative variables), chi-square, and Fisher's exact (for qualitative variables) tests were utilized to analyze the data.

Results

The results of the current study revealed that the mean age of men, the mean age of women, the mean marriage duration, and the mean infertility duration were 35.6 ± 7.6, 31.2 ± 6.6, 8.7 ± 5.9, and 4.8 years, respectively. Education level of most of the participants was below high school diploma. The majority of men were self-employed (75.0%), and most of women were housewives (89.0%), whereas the rest were employees (10.6%). Most of the participants had a history of consanguineous marriage, and a history of infertility in their family.

Among 579 cases, 372 cases (64.3%) had primary infertility, and 207 (35.7%) had secondary infertility.

Table 1. The frequency of different infertility causes in terms of women's age

Women age groups	The causes of infertility [n (%)]					
	Male factors	Ovarian factors	Uterine factors	Tubal factors	Unknown factors	Total
Less than 25 (years)	35 (28.0)	59 (47.2)	7 (5.6)	7 (5.6)	17 (13.6)	125 (100)
25-35 (years)	88 (30.7)	98 (34.1)	12 (4.2)	37 (12.9)	52 (18.1)	287 (100)
Over 35 (years)	52 (31.3)	37 (22.3)	13 (7.8)	30 (18.1)	34 (20.5)	166 (100)
Total	175 (30.3)	194 (33.7)	32 (5.5)	74 (12.8)	104 (17.8)	579 (100)

The most observed infertility cause among women was connected to ovarian factors (33.5%) and in men, the common causes were male factors (30.2%). Uterine factors (5.5%), tubular factors (12.8%), and unknown factors (18%) were the other causes of infertility.

In women of less than 25 years of age, the most prevalent causes of infertility were ovarian factors (47.2%); in women of 25-35 years of age, ovarian factors (34.15%) were also the major cause of infertility; and finally, the most commonly observed infertility cause in women of over 35 years of age, was the male factor (31.33%).

In women of less than 25 years of age, 28% of infertility causes of couples were related to the male factor, and 72% were related to other factors; while in women of 25-35 years of age, 30.66% of infertility causes were related to the male factors, and 69.34% were related to other factors (Table 1).

There was not a meaningful relationship between women's age groups and male factors of infertility (P = 0.813); while there was a significant relationship between women's age groups and ovarian factors (P = 0.001). This implied that in women of less than 25 years of age, 47.2% of infertility were related to ovarian factors, and in women of 25-35 years of age, and those over 35 years of age, the percentages were 34.1 and 24.3, respectively. In women who were under 25 years of age, 5.6% of infertilities were related to tubal factors, while in women of 25-35 years of age and those over 35 years, the percentages were 12.9 and 18.1 respectively

The results obtained here showed that there were no meaningful relationship between women's age groups and uterine factors of infertility (P = 0.262) (Table 2).

There was in fact a meaningful relationship between women's age group and tubal factors of infertility (P = 0.007) (Table 3).

There was also a statistically meaningful relationship between women's age groups and unknown factors of infertility (P = 0.310) (Table 4).

Even though no statistically significant relationship was found between the marriage duration with the male, uterine, unknown, and tubal factors, there was in fact a statistically significant relationship between marriage duration and ovarian factors of infertility (P = 0.002) in couples who were into their marriage for less than 10 years (38.2%); and in couples who had been married for more than 10 years, an infertility rate of 25.8% was observed.

Table 2. The relationship between the age group of women with uterine factors of infertility among the subjects

Women age groups	Cause of infertility [n (%)]			Chi-square	P
	Uterine factors	Other factors	Total		
Less than 25 (years)	7 (5.6)	119 (94.4)	126 (100)	2.86	0.262
25-35 (years)	12 (4.2)	275 (95.8)	287 (100)		
Over 35 (years)	13 (7.8)	153 (92.2)	166 (100)		
Total	32 (5.5)	546 (94.5)	579 (100)		

Table 3. The relationship between the age group of women with tubal factors of infertility among the subjects

Women age groups	Cause of infertility [n (%)]			Chi-square	P
	Tubal factors	Other factors	Total		
Less than 25 (years)	7(5.6)	119 (94.4)	126 (100)	9.94	0.007
25-35 (years)	37 (12.9)	250 (87.1)	287 (100)		
Over 35 (years)	30 (18.1)	136 (81.9)	166 (100)		
Total	74 (12.8)	504 (87.2)	579 (100)		

Table 4. The relationship between the age group of women and unknown factors of infertility among the subjects

Age groups (years)	Cause of infertility [n (%)]			Chi-square	P
	Tubal factors	Other factors	Total		
Less than 25	17(13.6)	109 (86.4)	126 (100)	2.34	0.310
25-35	52(15.1)	235 (81.9)	287 (100)		
Over 35	35 (20.4)	131 (79.6)	166 (100)		
Total	104 (17.8)	475 (82.2)	579 (100)		

Discussion

In the current study, the mean age of women and men were 31.2 ± 6.6 and 35.6 ± 7.6 years, respectively. The average length of marriage was 8.7 ± 5.9 years, and the average length of infertility was 4.8 ± 4.7 years. The most prevalent infertility type was detected as primary, which male factors were the causes in men, and ovarian factors were the causes for it in women. In the present work, out of 579 cases, 372 cases (64.3%) had primary infertility, and 207 (35.7%) had secondary infertility. The results also revealed that there was no statistically meaningful relationship between the age group of women with male and uterine factors of infertility; however, there in fact was a significant relationship between the age group of women with tubular and unknown factors.

In a study performed by Masoumi et al. in Hamadan, Iran, from 1200 cases, 834 cases (69.5%) suffered from primary infertility, and 366 (30.5%) had secondary infertility. Moreover, the average length of marriage of infertile couples was 7.6 ± 5.3 years, and their duration of infertility was 4.6 ± 5.1 years;[19] which is almost identical to the current study.

In the present work, 10.6% of women were employees, and 89.4% were housewives. In a study conducted by Pal et al., almost less than one tenth (9.3%) of infertile women were involved in income-generating activities, while the majority of them [264 (90.7%)] were housewives;[20] which is consistent with the present study findings.

In the current study, almost 51.2% of infertility causes were related to female factors, while in a study performed by Masoumi et al. amongst the various reasons of infertility, 88.6% were related to female factors.[19]

Studies have shown that various factors including social, individual, economic, and irrational thoughts about having children might negatively impact the life quality of infertile women. In addition, the life quality of infertile couples is directly related to their sexual satisfaction, self-esteem, social support, as well as marital satisfaction.[21] Infertility imposes certain potentially undesirable effects on the life quality of infertile couples,[22] and it variously impacts multiple dimensions of functioning and health in these couples, including sexual functioning and martial adjustments.[23]

Conclusion

The results of this work show that infertility is one of the major problems of couples that are a several years into their marriage. The most observed cause of infertility in men was found to be male factors and for women, the major causes were tubal, ovarian, and unknown factors. Further studies with a bigger population are required to achieve more

accurate results, and to be able to make more serious decisions.

Conflict of Interests

Authors have no conflict of interests.

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The frequency of skin cancers in Kermanshah City, Iran, during the years 2003-2012

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Short Communication

Abstract

BACKGROUND: Skin cancer is the most common malignancy in the world, and besides the malignant type that has a high mortality rate, other cancers causes many complications and deaths as well. The incidence of skin cancer has increased over the recent decades. The present study aimed to assess the incidence of skin cancers in the city of Kermanshah, Iran, in a period between 2003 and 2012.

METHODS: This was a retrospective cohort study, for which all the data was collected from the Cancer Registry Health Center in Kermanshah Province. The study population consisted of 2,660 individuals that had been diagnosed with skin cancer between the years 2003 and 2012. Analysis of obtained data was performed using SPSS statistical software.

RESULTS: The prevalence of skin cancer in Kermanshah was 2,660 people over the last ten years. Skin cancer had a uniform trend, but it had increased from 212 individuals to 282 over the past decade. Although this cancer could be found in all ages, but in 2004, it was mostly diagnosed in the seventh decade of life.

CONCLUSION: The results showed that the prevalence of skin cancer is in fact high. Given that skin cancer is one of the most common cancers, it is necessary to take steps toward reducing the risk factors of this cancer by management and proper planning.

KEYWORDS: Skin Cancer, Age, Prevalence

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Introduction

Cancer is a generic name for a large number of diseases associated with abnormal growth of cells.[1] Skin cancer is a major public health problem. Recent studies in most countries indicate a high prevalence of skin cancer, and an increasing incidence rate of this disease. Despite the decrease in the overall amount of cancer in recent years, skin cancer has had a 3-5 percent increase each year with the potential for prevention and treatment.[2]

Skin cancer alone, accounts for 32.7% of all the cancer cases in Iran, being the most common type of cancer in men, and the second most common cancer in women after breast cancer.[3] The incidence of this cancer is 16.15% in Iran,[4] while in 2004, it was 10.13 per 100,000 people.[5] Exposure to chronic light of the sun leads to creation of certain chemical agents that cause skin tumors.[6]

A study by Yazdanfar and Ghasemi in Hamadan, Iran, showed that most of the patient with skin cancer during the years 1991-2007 were men (67.2%).[7] In another study

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by Noorbala in Yazd, Iran, skin cancer was reported as 646 (27.3%) among 2360 cases of cancer during the years 1988-1996, with the highest incidence of skin cancer.[8]

Considering the prevalence of skin cancer and the lack of comprehensive information on this type of cancer, this study was conducted to determine the prevalence of skin cancer in Kermanshah City, Iran, in a period between the years 2003 and 2012.

Materials and Methods

In this historical cohort study, the data on skin cancer were collected from Kermanshah Health Center for a period between 2003 and 2012. It should be noted that the aim of this study was to obtain the frequency of skin cancer in all age groups. The statistical population of the study was comprised of all the people who were diagnosed with skin cancer during ten years. Information obtained from archival records (including hospitals, and all specialized diagnostic centers for skin cancer in Kermanshah) in health care centers.

The data was analyzed using SPSS software (version 18, SPSS Inc., Chicago, IL, USA), and descriptive statistics tables and charts.

Results

According to the results, 2,660 persons were diagnosed with skin cancer over this 10-year period, which included 1578 men and 1082 women.

The frequency of skin cancer in terms of age is demonstrated in table 1. It shows that the ages of 0-9 years, and the ages of 70-79 years have the lowest and the highest rates of prevalence, respectively. Observing the frequency of skin cancer over studied 10 years showed that the rate of this cancer considerably varied at different points in time, with the highest rates in years 2005 and 2011, with 309 and 307 cases, respectively. The number of people suffering from this cancer was 212 in 2003, and 282 in 2012.

The frequency of skin cancer in Kermanshah City during a period between the years 2003 and 2012 is shown in figure 1.

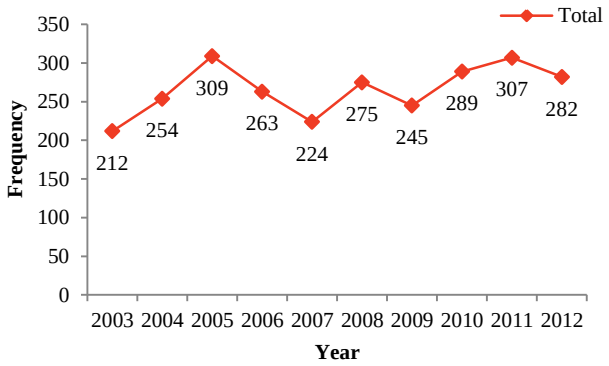

Figure 1. The frequency of skin cancer in Kermanshah City, Iran, during a period between the years 2003 and 2012

Table 1. The frequency of patients with different age group with skin cancer in Kermanshah City, Iran, during a period between the years 2003 and 2012

Year	Age groups (years)										Men	Women	Total
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	+90			
2003	0	2	3	11	19	26	50	68	20	13	117	95	212
2004	0	1	5	17	41	47	56	60	20	7	147	107	254
2005	1	2	5	10	34	61	58	89	39	10	182	127	309
2006	0	1	6	16	28	47	46	73	40	6	143	120	263
2007	4	1	3	14	25	45	41	62	29	0	134	90	224
2008	0	1	4	20	34	57	71	50	37	1	167	108	275
2009	2	1	3	18	25	60	58	54	23	1	145	100	245
2010	3	0	2	15	30	54	65	81	37	2	172	117	289
2011	0	2	3	20	40	53	68	71	49	1	187	120	307
2012	1	2	4	13	32	55	70	63	37	5	184	98	282
Total	11	13	38	154	308	505	583	671	331	46	1578	1082	2660

The frequency of skin cancer among the men was higher than that of the women. The frequency of skin cancer in terms of gender in Kermanshah during studied 10 years is demonstrated in figure 2.

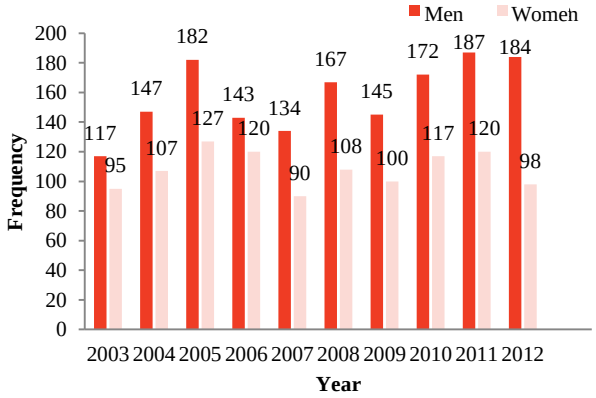

Figure 2. The frequency of skin cancer in terms of gender in Kermanshah City, Iran, during a period between the years 2003 and 2012

Discussion

The results of this study showed that within studied 10 year period, 2,660 persons were diagnosed with skin cancer. Afzali et al. study, which assessed the data collected during the years of 1999 to 2012, showed that the provinces of Khuzestan and Fars have the highest incidence of skin cancer in the South of Iran. It appears that the incidence of skin cancer, that is high in southern provinces of the country, is due to more exposure to sunlight, increased life expectancy, and exposure to various risk factors.[9]

Our results showed that the rate of skin cancer rises from the age of 50 years. A study by Yazdanfar and Ghasemi suggests that skin cancer is more common in older ages,[7] which is consistent with the present study. Noorbal et al. study showed that frequency of skin cancer increased in Yazd City, during 9 years;[8] the findings were similar with the results of this study.

The present study was conducted in order to determine the prevalence of skin cancer at different ages, in a period of ten years, and as it was revealed that 1,578 men (59.32%) and 1,082 women (40.68%) had skin cancers. Yazdanfar and Ghasemi study showed that most people with skin cancer in Hamadan were men (67.2%) in a 17-years period;[7] which is in conformity with the results of the present study. Moreover, A study conducted by Amouzgar et al. at Qaem hospital in Mashhad, Iran, showed that men are more affected by skin cancer.[10] Afzali et al. study also showed that skin cancer was found in 15.84% of men and in 13.69% of women in Kermanshah.[9] It seems that the more prevalence rate among the men is due to having routine activities in open and sunny environments, or more exposure to carcinogens.[11,12]

Conclusion

Given the high rates of skin cancer, if the disease is detected and diagnosed at an early stage, it can be cured and better predicted. Given that one of the risk factors for skin cancer is exposure to sunlight, there are ways to prevent it, such as limiting out-of-home activities or stopping these activities altogether, avoiding exposure to sunlight between 10 am and 4 pm, and wearing protective clothing such as wide hats and long-sleeved shirts, as well as using protective sunscreen with the sun protection factor (SPF) of 15 and higher. Overall, paying attention to prevention and early detection of skin cancer is of immense importance.

Conflict of Interests

Authors have no conflict of interests.

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