Research Article

The Prevalence of Depression, Anxiety, and Stress and Their Association with Vitamin D and Estrogen Levels in Postmenopausal Women in Semnan

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Abstract

Background: Depression, stress, and anxiety are of the most prevalent psychological disorders among postmenopausal women. Inadequate evidence is available on the association between vitamin D and estrogen with depression, anxiety, and stress in this group.

Objectives: The objective of this study was to determine the prevalence of depression, anxiety, and stress and their association with vitamin D and estrogen levels in postmenopausal women in Semnan.

Methods: The present analytical cross-sectional study was carried out using multistage sampling among women aged 45 to 70 years in Semnan (Iran) in summer 2016. Data collection tools were the demographic questionnaire, Spielberger State-Trait anxiety inventory, the Beck depression inventory, and the perceived stress scale. In addition, the levels of blood vitamin D and estrogen were measured.

Results: In 120 postmenopausal women, depression levels were mild (22.5%), moderate (13.3%), and severe (1.7%); anxiety levels were mild (46.7%), moderate (50.8%), and severe (2.5%); additionally, 79.2% had lower stress and 20.8% had greater stress. Negative and significant correlations were found between vitamin D and depression (r = -0.1982, P = 0.031), anxiety (r = -0.3636, P < 0.001) and stress (r = -0.2884, P = 0.001). However, there was no correlation between estrogen and depression (r = -0.130, P = 0.159), anxiety (r = -0.105, P = 0.254), and stress (r = -0.104, P = 0.262). No significant correlation was seen between estrogen and vitamin D (r = -0.070, P = 0.450).

Conclusions: In postmenopausal women, no significant relationship was observed between estrogen and depression, anxiety, and perceived stress; however, there was a significant relationship between vitamin D and depression, anxiety, and stress.

Keywords: Depression, Anxiety, Stress, Vitamin D, Estrogen, Postmenopausal

1. Background

Menopause is one of the developmental stages in the life cycle of women who experience it with aging. During this period, women undergo physical changes affecting their socio-mental status (1). In this period, the prevalence of depressive symptoms has been reported higher (2). It is estimated that 26% to 33% of women experience the first depressive symptoms of their life in the menopausal period (3). Depressive symptoms consist of chronic fatigue syndrome, restlessness, concentration problems, and sleep disorder (4). Anxiety-related disorders are accompanied by feelings of extreme concern, ir-

rational thoughts, and believing in unfortunate events (4). Anxiety prevalence is assessed to be 7.3%, ranging from 5.3% to 10.4% (5).

Menopause has a significant effect on perceived stress among women. Stress as the response of the body to internal and external threats and relevant consequences (6) potentially exacerbate the menopause symptoms (7). The percentage of women with stress (88.8%) is much higher after the menopause (8). The information concerning whether the levels of perceived stress are related to age is scarce (9). A few investigations have discovered a decrease of perceived stress with increasing age (10, 11); others demonstrated no differences between younger and older adults

(9, 12).

The prevalence of vitamin D deficiency has been accounted for 31% - 70% in postmenopause (13, 14). In a cohort study, a low amount of vitamin D was related to the prevalence of depressive disorder (15). Vitamin D deficiency was related to depression and mental health-associated life quality (16). In a systematic review, there was a positive correlation between vitamin D deficiency and psychiatric disorders (17). The effect of vitamin D in the elderly population on depression has not been studied extensively. Also, there is a controversy in the relationship between vitamin D and depression (18). There was no relationship between vitamin D and depression in some studies. Pan et al. (19) and Zhao et al. (20) also reported no significant relationship between vitamin D levels and depression.

Also, a direct relationship has been observed between psychosomatic symptoms and hormonal changes with estrogen reduction (2), and depression can be related to decreased estrogen (7). In addition, menopause symptoms are attributed to estrogen deprivation (21), and postmenopausal women lose the protective effects of estrogen (22). Moreover, in a meta-analysis of 28 studies, the serum levels of vitamin D were associated with the incidence of metabolic syndrome, body mass index (BMI), diabetes, hypertension, and heart disease (23).

However, the evidence is inadequate regarding the relationship between vitamin D and estrogen with stress, depression, and anxiety in postmenopausal women, as well as no study found the prevalence of depression, stress, and anxiety in postmenopausal women in Semnan. Therefore, this study aimed to evaluate the levels of vitamin D and estrogen-related to depression, anxiety and perceived stress in postmenopausal women.

2. Objectives

The objective of this study was to determine the prevalence of depression, anxiety, stress, and their association with vitamin D and estrogen levels in postmenopausal women in Semnan.

3. Methods

This study was approved by the Ethics Committee of Semnan University of Medical Sciences under the No. IR.SEMUMS.REC.2015.146, dated 14.02.2015. The present analytical cross-sectional study was conducted on women in different regions of Semnan using multistage sampling. In a preliminary study consisting of 40 postmenopausal women, the correlation coefficient between vitamin D and depression, anxiety, and stress was -0.267, -0.331, and -0.295,

respectively. Considering the 95% confidence and power 80% of the sample size of the below equation, it was estimated that the maximum was 108, thus 120 people were examined in this study.

$$N = \frac{(Z_{1-\alpha} + Z_{1-\beta})^2}{w^2} + 3 \qquad (1)$$

$$w = \frac{1}{2} Ln \frac{1+r}{1-r} \qquad (2)$$

The inclusion criteria were the willingness to participate in the study and the consent to this, passing at least 12 months without menstruation, they have been postmenopausal, naturally and without surgery of the uterus and ovaries, and age range of 45 to 70 years. The exclusion criteria were cancers, a history of a physical disability or a clear mental disorder, hearing or visual impairments, preventing proper communication, a history of the stressful event in the last six months, and a history of depression and anxiety before the menopause.

Data collection tools were a demographic questionnaire, Spielberger State-Trait anxiety inventory, Beck depression inventory (BDI), and the perceived stress scale. The subjects responded to the 21-item Beck depression inventory on a four-point scale that ranges from 0 to 3 (24). The validity and reliability of this questionnaire were confirmed (25). Spielberger State-Trait anxiety inventory has 40 items; responses are rated on a 4-point Likert scale and range from 1 to 4 (26). Validity and reliability of the Spielberger anxiety inventory were confirmed (27). The validity and reliability of the perceived stress scale consist of 14 questions, with a range of scores in the Likert scale from zero to four (28).

After obtaining informed consent, blood sampling was carried out in the middle of summer (August) at the site of the central laboratory. Blood (5 cc) was taken at intervals of 8 - 9.30 a.m. from each person. The sample of blood was taken by a female laboratory expert. The level of serum 25 hydroxyvitamin D (ng/mL) and estrogen (pg/mL) were determined by using the ELISA method. The kit of EUROIMMUN AG (Lübeck, Germany) used to determine the serum level of 25 hydroxyvitamin D and the level of estrogen was determined by using of IAP (USA), according to the manufacturer's instruction.

The ethical considerations of this study included obtaining approval from the Ethics Committee of the Semnan University of Medical Sciences, explaining the research objectives, keeping the information confidential, ensuring the satisfaction of subjects and obtaining written informed consent. The data were analyzed using SPSS version 18 software with Shapiro-Wilk, Mann-Whitney, Pearson correlation coefficient, and partial correlation coefficient. The significance level was considered to be less than 0.05.

4. Results

The current study was conducted on 120 post-menopausal women in Semnan. The mean age of women was 55.6 ± 5.4 years. In terms of marital status, 91.7% were married and the remaining 8.3% were widows. The mean number of children in these women was 3.3 ± 1.3. Furthermore, 20.8% of women had a history of heart disease, 30% hypertension, 8.3% digestive disease, and 31.7% diabetes (Table 1). Also, 85.8% (n = 103) of them were homemakers and the rest were employed (4.2%), self-employed (1.7%), and retired (8.3%). No significant correlation was found between body mass index (BMI) and the levels of depression, anxiety, stress, vitamin D, and estrogen (Table 1). In the two groups of patients with and without diabetes, digestive disease, hypertension, and heart disease, the levels of depression, anxiety, stress, vitamin D, and estrogen showed no significant difference (Table 1). There was a positive and significant correlation between age and vitamin D (Table 1). However, no significant correlation was found between age and estrogen levels, depression, anxiety, and stress (Tables 1 - 3).

The depression levels were mild (22.5%), moderate (13.3%) and severe (1.7%); the anxiety levels were mild (46.7%), moderate (50.8%) and severe (2.5%); 79.2% had lower stress and 20.8% had higher stress (Table 3). The mean ± SD, median, interquartile range, min, and a max of depression, anxiety and stress scores, vitamin D, and estrogen in postmenopausal women in Semnan are shown in Table 4.

There was a negative and significant correlation between depression and vitamin D (r = -0.1982, P = 0.031), but no significant correlation was found between depression and estrogen (r = -0.103, P = 0.159). A negative and significant relationship was found between vitamin D and anxiety (r = -0.3636, P < 0.001). There was no significant correlation between estrogen with anxiety (r = -0.105, P = 0.254). There was a significant negative correlation between stress and vitamin D (r = -0.2884, P = 0.001). No correlation was seen between estrogen and stress (r = -0.104, P = 0.262) (Table 4). No correlation was seen between estrogen and vitamin D (r = -0.070, P = 0.450).

5. Discussion

Our findings showed the prevalence of depression level was higher than the other studies (3). Also, there was a significant negative correlation between depression and vitamin D. In line with our study, vitamin D deficiency was related to depression (29). Some studies reported that there is no correlation between vitamin D and depression (30, 31). Vitamin D receptor (VDR) has the potential for a neuroactive effect on brain function (32) and modulates the hypothalamic-pituitary-adrenal axis, in the adrenal cortex with managing dopamine production through VDRs, noradrenaline, and adrenaline (33); and secures against the decrease of dopamine and serotonin centrally (34).

Our findings indicated there was also no significant correlation between depression and estrogen levels. The research showed that estrogen increases the availability of serotonin and has direct consequences on depression during menopause (35). Also, the findings of the study demonstrated that estrogen has either a weak or no relationship with depression (36).

The results of our study indicated the anxiety levels were higher than the other studies (37). Also, there was a negative correlation between vitamin D with anxiety. In a study, low levels of vitamin D were associated with increased anxiety (38). Alatram indicated a positive significant correlation between vitamin D deficiency and anxiety (39).

Our findings showed there was no significant correlation between estrogen and anxiety. In a study, psychological symptoms were not related to changes in estrogen levels (40). However, one report indicated the increased risk of anxiety with estrogen receptor (41).

Our results indicated there was a negative and significant relationship between stress and vitamin D. In a study, the use of multi-vitamin and mineral supplements reduced the stress (42). Premkumar et al. observed that lower vitamin D was associated with depression and stress (43).

Our findings showed there was no correlation between stress and estrogen. Hormone and age-related changes may at least partially explain why perceived stress increased during perimenopause (44) but changes in estradiol levels might increase the sensitivity to psychological stress, especially the social exclusion sensitivity, and this increased sensitivity might develop depression (45).

The findings of the present study indicated there was no correlation between estrogen and vitamin D. The hormonal alterations in women in the perimenopausal and postmenopausal periods may result in an effect on mental health. All these conditions may also be related to vitamin D deficiency (46). In the menopausal stage, there is a slow decrease in the amount of estrogen released by the ovaries (47). This decrease in estrogen release is thought to deteriorate vitamin D deficiency. The following vitamin D challenge is related to a decline in the amount of vitamin D receptors (48). Additionally, the decline in estrogen related to postmenopausal women diminishes the action of 1-alpha-hydroxylase vitamin D responsible for activating vitamin D and VDRs (49).

Table 1. Distribution of Age, Education, Income, Number of Children, BMI, Diabetes, Digestive Disease, Hypertension and Heart Disease in Postmenopausal Women in Semnan (2015)

Characteristic	No. (%)	r (P Value)				
		Depression	Anxiety	Stress	Vitamin D	Estrogen
Age		-0.082[a] (0.375)	-0.119 (0.197)[a]	-0.133[a] (0.149)	0.309[a] (0.001)	-0.105[a] (-0.252)
< 50	15 (12.5)					
50 - 54	32 (26.7)					
55 - 59	48 (40)					
60 ≤	25 (20.8)					
Education		0.153[b] (0.095)	0.115[b] (0.212)	0.139[b] (0.130)	-0.120[b] (0.193)	-0.066[b] (0.475)
Illiterate	15 (12.5)					
Primary	53 (44.2)					
Diploma	45 (37.5)					
Collegiate	7 (5.8)					
Income		0.026[b] (0.782)	-0.052[b] (0.573)	-0.015[b] (0.873)	-0.047[b] (0.610)	-0.046[b] (0.646)
Low	20 (16.7)					
Average	90 (75)					
Good	10 (8.3)					
Number of children		0[a] (1)	-0.008[a] (0.929)	-0.073[a] (0.430)	0.224[a] (0.014)	-0.087[a] (0.347)
≤ 2	29 (24.2)					
3	38 (31.7)					
≤ 4	53 (44.2)					
BMI		-0.001[a] (0.994)	0.065[a] (0.481)	-0.096[a] (0.297)	-0.104[a] (0.258)	-0.081[a] (0.382)
Diabetes (Yes)	38 (31.7)	- (1.00[c])	- (0.252[c])	- (0.212[c])	- (0.188[c])	- (0.745)
Digestive disease (Yes)	10 (8.3)	- (0.539[c])	- (0.801[c])	- (0.138[c])	- (0.857[c])	- (0.943)
Hypertension (Yes)	36 (30)	- (0.272[c])	- (0.535[c])	- (0.470[c])	- (0.989)	- (0.474)
Heart disease (Yes)	25 (20.8)	- (0.051[c])	- (0.297[c])	- (0.470)	- (0.972[c])	- (0.650)

[a] Pearson.
[b] Spearman.
[c] Mann-Whitney.

Table 2. Mean and Standard Deviation of Indicators in Postmenopausal Women of Different Ages in Semnan (2015)[a]

Characteristic	Age			
	< 50	50 - 54	55 - 59	60 ≥
Depression	10.53 (6.56)	11.44 (7.08)	9.33 (7.69)	9 (6.14)
Stress	22.47 (4.52)	23.81 (4.86)	22.19 (5.67)	21.08 (5.71)
Anxiety	87.67 (13.26)	85.28 (17.35)	84.33 (16.83)	80.92 (16.88)
Vitamin D[b]	26.07 (13.65)	39.81 (28.18)	41.27 (23.68)	53.96 (36.54)
Estrogen[b]	50.57 (52.27)	21.76 (49.82)	12.7 (26.82)	12.03 (16.80)

[a] Values are expressed as mean (SD).
[b] Determined the level of serum vitamin D (ng/mL) and estrogen (pg/mL).

In this study, the diet of postmenopausal women, out-of-home activities, and exposure to sunlight were not evaluated. Also, the use of medication in postmenopausal women was not studied, which can affect the metabolism of vitamin D and estrogen. Since the willingness of postmenopausal women in Semnan to participate in the project was low due to the difficulty of referring to the laboratory, blood sampling and follow-up of the test, it is suggested further studies should be conducted with larger sample size in other countries and the relationship between the levels of vitamin D and estrogen with sleep disorders and cognitive and behavioral problems should be assessed in postmenopausal women.

5.1. Conclusions

In postmenopausal women, no significant relationship was observed between estrogen and depression, anxiety, and perceived stress, but considering the relationship

Table 3. Mean, the Standard Deviation of Vitamin D and Estrogen Scores to Separate the Different Levels of Depression, Anxiety and Stress in Postmenopausal Women Semnan (2015)

	N (%)	Vitamin D		Estrogen	
		Mean $\pm$ SD	r^a (P Value)	Mean $\pm$ SD	r^a (P Value)
Depression			-0.1982 (0.031)		-0.103 (0.159)
Normal (0 - 10)	75 (62.5)	47.55 $\pm$ 27.77		21.68 $\pm$ 40.23	
Mild (11 - 16)	27 (22.5)	30.41 $\pm$ 25.68		15.09 $\pm$ 25.78	
Moderate and higher ($\geq$ 17)	18 (15)	33.78 $\pm$ 26.37		18.42 $\pm$ 46.08	
Anxiety			-0.3636 (< 0.001)		-0.105 (0.254)
Mild (40 - 79)	56 (46.7)	52.61 $\pm$ 28.18		20.41 $\pm$ 39.77	
Moderate and higher (80 - 160)	64 (53.3)	31.14 $\pm$ 23.37		19.10 $\pm$ 37.16	
Stress			-0.2884 (0.001)		0.104 (0.262)
Low stress (< 28)	95 (79.2)	44.94 $\pm$ 38.18		8.59 $\pm$ 6.38	
High stress (28 - 56)	25 (20.8)	29.04 $\pm$ 23.76		7.08 $\pm$ 5.57	

^{a} Partial correlation coefficient; determined the level of serum vitamin D (ng/mL) and estrogen (pg/mL).

Table 4. Mean, Standard Deviation, Median, Interquartile Range Scores of Depression, Anxiety, Stress, Vitamin D, Estrogen in Post-Menopausal Women in Semnan (2015)

Characteristic	Mean (SD)	Median	Interquartile Range	Min	Max
Depression	9.98 (7.08)	8.5	8	0	38
Stress	22.43 (5.36)	22	8	6	34
Anxiety	84.29 (16.51)	81.5	24	45	131
Vitamin D^a	41.63 (27.98)	32	34	7	127
Estrogen^a	19.71 (38.24)	9.85	13.15	0.40	260

^{a} Determined the level of serum vitamin D (ng/mL) and estrogen (pg/mL).

between vitamin D and depression, anxiety, and stress in postmenopausal women, and increasing the amount of vitamin deficiency, screening and medical treatment for vitamin D deficiency are recommended in postmenopausal women.

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Footnotes

Authors' Contribution: Study conception: Monir Nobahar, Zaynab Hydarinia-Naieni, and Raheb Ghorbani; data collection: Monir Nobahar and Zaynab Hydarinia-Naieni; data analysis: Monir Nobahar and Raheb Ghorbani; drafting of the manuscript, critical revision for important intellectual content, and supervision: Monir Nobahar.

Conflict of Interests: There is not conflict of interest.

Ethical Approval: This study was approved by the Ethics Committee of Semnan University of Medical Sciences under the No. IR.SEMUMS.REC.2015.146, dated 14.02.2015.

References

1. Sanchez-Rodriguez MA, Castrejon-Delgado L, Zacarias-Flores M, Arronte-Rosales A, Mendoza-Nunez VM. Quality of life among postmenopausal women due to oxidative stress boosted by dysthymia and anxiety. *BMC Womens Health*. 2017;**17**(1):1. doi: 10.1186/s12905-016-0358-7. [PubMed: 28049464]. [PubMed Central: PMC5209897].

2. Llaneza P, Garcia-Portilla MP, Llaneza-Suarez D, Armott B, Perez-Lopez FR. Depressive disorders and the menopause transition. *Maturitas*. 2012;**71**(2):120–30. doi: 10.1016/j.maturitas.2011.11.017. [PubMed: 22196311].

3. Reed SD, Ludman EJ, Newton KM, Grothaus LC, LaCroix AZ, Nekhlyudov L, et al. Depressive symptoms and menopausal burden in the midlife. *Maturitas*. 2009;**62**(3):306–10. doi: 10.1016/j.maturitas.2009.01.002. [PubMed: 19223131]. [PubMed Central: PMC2813141].

4. Nahar J. *Anxiety and depression during pre and post menopausal period [dissertation]*. University of Dhaka; 2016.

5. Baxter AJ, Scott KM, Vos T, Whiteford HA. Global prevalence of anxiety disorders: A systematic review and meta-regression. *Psychol*

Med. 2013;**43**(5):897–910. doi: 10.1017/S003329171200147X. [PubMed: 22781489].

6. Choi BO, Lee YJ, Choi JH, Cho SW, Im HJ, An JE. The association between stress level in daily life and age at natural menopause in Korean women: outcomes of the Korean National Health and Nutrition Examination Survey in 2010-2012. *Korean J Fam Med.* 2015;**36**(6):305–9. doi: 10.4082/kjfm.2015.36.6.305. [PubMed: 26634097]. [PubMed Central: PMC4666866].

7. Baksu B, Baksu A, Goker N, Citak S. Do different delivery systems of hormone therapy have different effects on psychological symptoms in surgically menopausal women? A randomized controlled trial. *Maturitas.* 2009;**62**(2):140–5. doi: 10.1016/j.maturitas.2008.12.010. [PubMed: 19179026].

8. Somanath A, Bhat RM, Nayanatara AK, Pai SR. Prevalence of perceived stress and obesity among women before and after menopause. *J Med Sci Clin Res.* 2015;**3**(7):6534–7.

9. Diehl M, Hay EL. Risk and resilience factors in coping with daily stress in adulthood: The role of age, self-concept incoherence, and personal control. *Dev Psychol.* 2010;**46**(5):1132–46. doi: 10.1037/a0019937. [PubMed: 20822228]. [PubMed Central: PMC2936708].

10. Cohen S, Janicki-Deverts D. Who's stressed? Distributions of psychological stress in the United States in probability samples from 1983, 2006, and 2009. *J Appl Soc Psychol.* 2012;**42**(6):1320–34. doi: 10.1111/j.1559-1816.2012.00900.x.

11. Nordin M, Nordin S. Psychometric evaluation and normative data of the Swedish version of the 10-item perceived stress scale. *Scand J Psychol.* 2013;**54**(6):502–7. doi: 10.1111/sjop.12071. [PubMed: 24118069].

12. Scott SB, Jackson BR, Bergeman CS. What contributes to perceived stress in later life? A recursive partitioning approach. *Psychol Aging.* 2011;**26**(4):830–43. doi: 10.1037/a0023180. [PubMed: 21604885]. [PubMed Central: PMC3177031].

13. Vacek JL, Vanga SR, Good M, Lai SM, Lakkireddy D, Howard PA. Vitamin D deficiency and supplementation and relation to cardiovascular health. *Am J Cardiol.* 2012;**109**(3):359–63. doi: 10.1016/j.amjcard.2011.09.020. [PubMed: 22071212].

14. Rahman SA, Chee WSS, Yassin Z, Chan SP. Vitamin D status among postmenopausal Malaysian women. *Asia Pac J Clin Nutr.* 2004;**13**(3):255–60.

15. Milaneschi Y, Hoogendijk W, Lips P, Heijboer AC, Schoevers R, van Hemert AM, et al. The association between low vitamin D and depressive disorders. *Mol Psychiatry.* 2014;**19**(4):444–51. doi: 10.1038/mp.2013.36. [PubMed: 23568194].

16. Moy FM, Hoe VC, Hairi NN, Vethakkan SR, Bulgiba A. Vitamin D deficiency and depression among women from an urban community in a tropical country. *Public Health Nutr.* 2017;**20**(10):1844–50. doi: 10.1017/S1368980016000811. [PubMed: 27086558].

17. Miodownik C, Robinzon S, Lerner V. Association between vitamin D serum level and depression. *Curr Psychopharmacol.* 2016;**5**(1):4–12. doi: 10.2174/2211556005666160216224601.

18. Yalamanchili V, Gallagher JC. Treatment with hormone therapy and calcitriol did not affect depression in older postmenopausal women: No interaction with estrogen and vitamin D receptor genotype polymorphisms. *Menopause.* 2012;**19**(6):697–703. doi: 10.1097/gme.0b013e31823bcec5. [PubMed: 22205149]. [PubMed Central: PMC3319337].

19. Pan A, Lu L, Franco OH, Yu Z, Li H, Lin X. Association between depressive symptoms and 25-hydroxyvitamin D in middle-aged and elderly Chinese. *J Affect Disord.* 2009;**118**(1-3):240–3. doi: 10.1016/j.jad.2009.02.002. [PubMed: 19249103].

20. Zhao G, Ford ES, Li C, Balluz LS. No associations between serum concentrations of 25-hydroxyvitamin D and parathyroid hormone and depression among US adults. *Br J Nutr.* 2010;**104**(11):1696–702. doi: 10.1017/S0007114510002588. [PubMed: 20642877].

21. Aguilar-Zavala H, Perez-Luque EL, Luna-Martinez F, Bassol-Mayagoitia S, Canto-de-Cetina T, Lopez-Conesa M, et al. Symptoms at postmenopause: genetic and psychosocial factors. *Menopause.* 2012;**19**(10):1140–5. doi: 10.1097/gme.0b013e3182503bde. [PubMed:

22692335].

22. O'Neal MA. Neurologic diseases in women: Five new things. *Neurol Clin Pract.* 2013;**3**(3):217–23. doi: 10.1212/CPJ.0b013e318296f0b9. [PubMed: 29473629]. [PubMed Central: PMC5798511].

23. Schmitt EB, Nahas-Neto J, Bueloni-Dias F, Poloni PF, Orsatti CL, Petri Nahas EA. Vitamin D deficiency is associated with metabolic syndrome in postmenopausal women. *Maturitas.* 2018;**107**:97–102. doi: 10.1016/j.maturitas.2017.10.011. [PubMed: 29169589].

24. Beck AT, Steer RA, Carbin MG. Psychometric properties of the Beck depression inventory: Twenty-five years of evaluation. *Clin Psychol Rev.* 1988;**8**(1):77–100. doi: 10.1016/0272-7358(88)90050-5.

25. Azkhosh M. *[The use of psychological tests and clinical diagnosis].* Tehran: Ravan; 2008. p. 224–6. Persian.

26. Holm L, Fitzmaurice L. Emergency department waiting room stress: Can music or aromatherapy improve anxiety scores? *Pediatr Emerg Care.* 2008;**24**(12):836–8. doi: 10.1097/PEC.0b013e318818ea04c. [PubMed: 19050663].

27. Spielberger CD. STAI manual for the State-Trait anxiety inventory. *Self-Evaluation Questionnaire.* 1970:1–24.

28. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav.* 1983;**24**(4):385–96. [PubMed: 6668417].

29. Moran LJ, Teede HJ, Vincent AJ. Vitamin D is independently associated with depression in overweight women with and without PCOS. *Gynecol Endocrinol.* 2015;**31**(3):179–82. doi: 10.3109/09513590.2014.975682. [PubMed: 25366261].

30. van den Berg KS, Marijnissen RM, van den Brink RH, Naarding P, Comijs HC, Oude Voshaar RC. Vitamin D deficiency, depression course and mortality: Longitudinal results from the Netherlands Study on Depression in Older persons (NESDO). *J Psychosom Res.* 2016;**83**:50–6. doi: 10.1016/j.jpsychores.2016.03.004. [PubMed: 27020077].

31. Kwasky AN, Groh CJ. Vitamin d, depression and coping self-efficacy in young women: Longitudinal study. *Arch Psychiatr Nurs.* 2014;**28**(6):362–7. doi: 10.1016/j.apnu.2014.08.010. [PubMed: 25457684].

32. Garcion E, Wion-Barbot N, Montero-Menei CN, Berger F, Wion D. New clues about vitamin D functions in the nervous system. *Trends Endocrinol Metab.* 2002;**13**(3):100–5. [PubMed: 11893522].

33. Puchacz E, Stumpf WE, Stachowiak EK, Stachowiak MK. Vitamin D increases expression of the tyrosine hydroxylase gene in adrenal medullary cells. *Brain Res Mol Brain Res.* 1996;**36**(1):193–6. doi: 10.1016/0169-328x(95)00314-i. [PubMed: 9011759].

34. Cass WA, Smith MP, Peters LE. Calcitriol protects against the dopamine- and serotonin-depleting effects of neurotoxic doses of methamphetamine. *Ann N Y Acad Sci.* 2006;**1074**:261–71. doi: 10.1196/annals.1369.023. [PubMed: 17105922].

35. Lokuge S, Frey BN, Foster JA, Soares CN, Steiner M. Depression in women: windows of vulnerability and new insights into the link between estrogen and serotonin. *J Clin Psychiatry.* 2011;**72**(11):e1563–9. doi: 10.4088/JCP.11com07089. [PubMed: 22127200].

36. Resnick SM, Maki PM, Rapp SR, Espeland MA, Brunner R, Coker LH, et al. Effects of combination estrogen plus progestin hormone treatment on cognition and affect. *J Clin Endocrinol Metab.* 2006;**91**(5):1802–10. doi: 10.1210/jc.2005-2097. [PubMed: 16522699].

37. Li Y, Yu Q, Ma L, Sun Z, Yang X. Prevalence of depression and anxiety symptoms and their influence factors during menopausal transition and postmenopause in Beijing city. *Maturitas.* 2008;**61**(3):238–42. doi: 10.1016/j.maturitas.2008.09.002. [PubMed: 18951736].

38. Wu C, Ren W, Cheng J, Zhu B, Jin Q, Wang L, et al. Association between serum levels of vitamin D and the risk of post-stroke anxiety. *Medicine (Baltimore).* 2016;**95**(18). e3566. doi: 10.1097/MD.0000000000003566. [PubMed: 27149477]. [PubMed Central: PMC4863794].

39. Alatram A. The relationship between vitamin D deficiency, anxiety, and depression. *Faseb J.* 2015;**29**(1_supplement):LB310.

40. Bryant C, Judd FK, Hickey M. Anxiety during the menopausal transition: A systematic review. *J Affect Disord.* 2012;**139**(2):141–8. doi:

10.1016/j.jad.2011.06.055. [PubMed: 21783260].

41. Tiemeier H, Schuit SC, den Heijer T, van Meurs JB, van Tuijl HR, Hofman A, et al. Estrogen receptor alpha gene polymorphisms and anxiety disorder in an elderly population. *Mol Psychiatry*. 2005;**10**(9):806–7. doi: 10.1038/sj.mp.4001697. [PubMed: 15940291].

42. Long SJ, Benton D. Effects of vitamin and mineral supplementation on stress, mild psychiatric symptoms, and mood in nonclinical samples: a meta-analysis. *Psychosom Med*. 2013;**75**(2):144–53. doi: 10.1097/PSY.0b013e31827d5fbd. [PubMed: 23362497].

43. Premkumar M, Sable T, Dhanwal D, Dewan R. Vitamin D homeostasis, bone mineral metabolism, and seasonal affective disorder during 1 year of Antarctic residence. *Arch Osteoporos*. 2013;**8**:129. doi: 10.1007/s11657-013-0129-0. [PubMed: 23475735].

44. Falconi AM, Gold EB, Janssen I. The longitudinal relation of stress during the menopausal transition to fibrinogen concentrations: Results from the Study of Women's Health Across the Nation. *Menopause*. 2016;**23**(5):518–27. doi: 10.1097/GME.0000000000000579. [PubMed: 26886885]. [PubMed Central: PMC4844901].

45. Gordon JL, Rubinow DR, Eisenlohr-Moul TA, Leserman J, Girdler SS. Estradiol variability, stressful life events, and the emergence of depressive symptomatology during the menopausal transition. *Menopause*. 2016;**23**(3):257–66. doi: 10.1097/GME.0000000000000528. [PubMed: 26529616]. [PubMed Central: PMC4764412].

46. Pinkas J, Bojar I, Gujski M, Bartosinska J, Owoc A, Raczkiewicz D. Serum lipid, vitamin D Levels, and obesity in perimenopausal and postmenopausal women in non-manual employment. *Med Sci Monit*. 2017;**23**:5018–26. doi: 10.12659/msm.906895. [PubMed: 29055024]. [PubMed Central: PMC5665606].

47. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: Addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab*. 2012;**97**(4):1159–68. doi: 10.1210/jc.2011-3362. [PubMed: 22344196]. [PubMed Central: PMC3319184].

48. Kanwar SNG, Shekhawat M, Sharma P, Hada R. Comparison of vitamin D levels in pre and post menopausal type 2 diabetic females. *IOSR J Dent Med Sci*. 2015;**14**(8):70–3.

49. Fondjo LA, Sakyi SA, Owiredu W, Laing EF, Owiredu EW, Awusi EK, et al. Evaluating vitamin D status in pre- and postmenopausal type 2 diabetics and its association with glucose homeostasis. *Biomed Res Int*. 2018;**2018**:9369282. doi: 10.1155/2018/9369282. [PubMed: 29808168]. [PubMed Central: PMC5902073].