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Vitamin D levels and menopause-related symptoms in postmenopausal women

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Abstract

Background: Menopause is an important period in women's life. It is characterized by many symptoms that affect women's quality of life. This study aimed to the evaluation of the relation between vitamin D levels and menopause-related symptoms.

Results: Vitamin D insufficiency was noted in 52.4% of the studied population. There was no statistically significant difference in any of the menopausal rating scale dimensions, psychological symptoms ($p=0.16$), somato-vegetative symptoms ($p=0.45$), or urogenital symptoms ($p=0.59$), between vitamin D sufficient and insufficient groups. The severity of the menopausal symptoms was affected by the presence of medical illness ($p<0.001$).

Conclusion: Vitamin D deficiency is an alarming issue among postmenopausal women. It was not associated with menopause-related symptoms.

Keywords: Vitamin D, Menopause, Postmenopause

Background

Menopause means the cessation of menstruation and typically occurs at the age of 45–55 years with a mean age of about 51 years. Women are said to be postmenopausal when menstruation has ceased for 6 to 12 months and blood serum levels of follicle-stimulating hormone (FSH) increase to at least 49 IU/L [1]. Many women experience menopause-related symptoms long after the final menstrual period. For example, women often experience hot flashes 4–10 years postmenopause [2–4]. Many also have mood disturbances, although the link with menopause is less clear [2, 5]. These symptoms can be severe enough to negatively impact the quality of life, work performance, and personal relationships [6, 7]. Recognizing the possible mechanisms underlying menopause-related symptoms help in the development of new therapeutic strategies.

Calcium balance studies have shown that calcium absorption declines with menopause. 25-Hydroxyvitamin D [25(OH) D] serves the purpose of calcium absorption and appears to be hormonally sensitive. Also, some of the symptoms associated with vitamin D deficiency, such as mood disturbance and musculoskeletal complaints [8], are similar to symptoms women may experience during the transition through menopause [9]. The primary aim of this study was to explore if there is any association between vitamin D status and the severity of menopause-related symptoms.

Methods

This cross-sectional study was conducted in the obstetrics and Gynecology Department of Suez Canal University Hospital. Postmenopausal women were divided into two groups regarding their levels of vitamin D: insufficient and normal (sufficient). The first group with insufficient serum 25(OH) D concentrations (i.e., ≥ 20 to <30 ng/mL) ($n=88$) and 2nd group with sufficient vitamin D levels ($n=80$) [10]. Women were recruited according to inclusion and exclusion criteria. **Inclusion criteria** were (a) women aged 50–70 years, (b) not taking

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hormonal therapy, and (c) reported menopausal symptoms. **Exclusion criteria** were (a) women already participating in a diet or exercise intervention, (b) history of bariatric surgery, (c) history of hysterectomy/oophorectomy, (d) women using medications known to impact hot flushes and/or weight (hormone therapy, oral contraceptives, gabapentin, selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors (SSRI/SNRIs), selective estrogen receptor modulators (SERMS), clonidine, antipsychotics, steroids, weight loss medications, chemotherapy), (e) women with possible medical conditions associated with vitamin D deficiency (following a malabsorption diet, colitis, pancreatic disease, current gall bladder problems, and liver disease), and (f) women with conditions that would influence vitamin D levels (high blood calcium or incident cancer).

Eligible women were evaluated thoroughly by proper history taking including any history of medical illness (diabetes, hypertension, and thyroid disease). Women were asked to complete the menopause rating scale. Women were interviewed in a private room. A researcher was available for help.

The severity of symptoms was classified as mild, moderate, and severe by the menopause rating scale (MRS). The scale consists of 11 symptoms in 3 domains:

- Somato-vegetative: including vasomotor symptoms (hot flushes, heart discomfort, sleep problems) and musculoskeletal symptoms (joint and muscular discomfort) (domain scores 0–16)
- Psychological symptoms (depressed mood, irritability, anxiety, physical, and mental exhaustion) (domain scores 0–16)
- Urogenital symptoms (sexual problems, bladder problems, and vaginal dryness) (domain scores 0–12). Each symptom is scored from none (scored as 0) to very severe (score as 4), giving a score range from 0 to 44. Summation scores for severity were classified as [11] Table 1:

All participants provided a 12-h fasting of a 5-mL sample of the blood, which was processed within 1 h of collection by centrifugation, and serum was collected and stored at -70°C . Participants were instructed to refrain from alcohol (48 h) and vigorous exercise (24 h) before

Table 1 Classification of the MRS severity

Severity	Score
None/little	0–4
Mild	5–8
Moderate	9–16
Severe/very severe	≥ 17

clinic appointments. The relation between vitamin D levels and menopausal symptoms was evaluated.

Statistical analysis

The collected data was revised, coded, tabulated, and introduced to a PC using the Statistical Package for Social Science (SPSS 15.0.1 for windows; SPSS Inc, Chicago, IL, 2001). Data were presented as the mean and standard deviation (\pm SD) for quantitative parametric data, and median and interquartile range for quantitative nonparametric data. Frequency and percentage were used for presenting qualitative data. Suitable analysis was done according to the type of data obtained. Student *T* test or Mann–Whitney test was used to analyze quantitative data while chi-square test and Fisher's exact test were used to analyze qualitative data: *P* value: level of significance, $P > 0.05$: non-significant (NS), $P < 0.05$: significant (S), and $P < 0.01$: highly significant (HS).

Results

Vitamin D insufficiency was noted in 52.4% of the studied population. Table 2 showed that there was no statistically significant difference between vitamin D sufficient and insufficient groups in any of the patients' baseline characteristics ($P > 0.05$).

There was no statistically significant difference in the mean score of each item of the MRS between women with sufficient and insufficient vitamin D levels but for feeling anxious, where higher scores were reported among those with sufficient vitamin D levels (*P* value 0.039). Joint and muscular discomfort and feeling nervous and irritable had the highest scores among the symptoms forming the menopausal rating scale (MRS) in both groups (Table 3).

There was no statistically significant difference in any of the menopausal rating scale dimensions, psychological symptoms ($P = 0.12$), somato-vegetative symptoms ($P = 0.66$), or urogenital symptoms ($P = 0.63$), between vitamin D sufficient and insufficient groups (Table 4).

There was no statistically significant difference in the severity of menopausal symptoms among groups with normal and insufficient vitamin D levels. There were nine patients with mild menopausal symptoms with insufficient and sufficient vitamin D levels. There were 30 27 patients with moderate menopausal symptoms with insufficient and sufficient vitamin D levels, respectively. There were 49 and 44 patients with severe menopausal symptoms with insufficient and sufficient vitamin D levels, respectively (*P* value 0.97).

In Table 5, we used a multivariable linear regression analysis to assess the predictor of severity of menopausal symptoms. We found that the best-fitting predictor

Table 2 Relationship between vitamin D level categories and patients' baseline characteristics ($n = 168$)

Variables	Vitamin D level category		p value
	Sufficient ($n = 80, 47.6\%$)	Sufficient ($n = 80, 47.6\%$)	
Age (years), mean \pm SD	56.18 \pm 4	56.19 \pm 3.4	0.99 ^a
Age groups in years, n (%)			
• 50–55	32 (40)	28 (31.8)	0.28 ^b
• 55–60	33 (41.25)	47 (53.4)	
• ≥ 60	15 (18.75)	13 (14.7)	
Marital status, n (%)			
• Married	50 (62.5)	57 (64.8)	0.27 ^b
• Divorced	6 (7.5)	2 (2.2)	
• Widow	24 (30)	29 (33)	
Height (m), mean \pm SD	1.61 \pm 0.05	1.60 \pm 0.05	0.55 ^a
Weight (kg), mean \pm SD	82.7 \pm 13.3	82.4 \pm 13.9	0.86 ^a
BMI, mean \pm SD	31.7 \pm 4.6	31.9 \pm 5.3	0.85 ^a
BMI groups, n (%)			
• < 30	25 (31.25)	30 (34.1)	0.74 ^c
• ≥ 30	55 (68.75)	58 (65.9)	
Medical history (diabetes, hypertension, and thyroid disease), n (%)			
• Absent	58 (72.5)	62 (70.5)	0.76 ^b
• Present	22 (27.5)	26 (29.5)	
Parity, mean \pm SD	3.6 \pm 1.8	3.7 \pm 1.7	0.61 ^a
Duration of menopause (years)	6.35 \pm 5.1	5.51 \pm 3.6	0.21 ^a
Vitamin D concentration (mean \pm SD)	24.62 \pm 5.06	42.37 \pm 10.62	0.0001 ^a

^a P values are based on independent ttest. Statistical significance at $P < 0.05$

^b P values are based on chi-square test. Statistical significance at $P < 0.05$

^c P values are based on Fisher's exact test. Statistical significance at $P < 0.05$

Table 3 Descriptive statistics of menopausal rating scale (MRS) among studied sample ($n = 168$)

Symptom	Sufficient vit. D	Insufficient vit. D	P value
Hot flushes and sweating	1.49 \pm 1.23	1.58 \pm 1.21	0.626
Palpitations/chest tightness	1.59 \pm 1.40	1.58 \pm 1.17	0.968
Sleep disorders	1.78 \pm 1.35	1.94 \pm 1.13	0.383
Feeling depressed or down	2.06 \pm 0.99	2.05 \pm 1.02	0.912
Feeling nervous or irritable	2.17 \pm 1.14	2.01 \pm 1.12	0.379
Feeling anxious	1.8 \pm 1.36	1.39 \pm 1.22	0.039
Physical and mental exhaustion	1.86 \pm 1.2	1.74 \pm 1.19	0.503
Change in sexual desire	0.98 \pm 1.15	1.2 \pm 1.34	0.237
Dysuria/polyuria/incontinence	1.31 \pm 1.05	1.11 \pm 1.23	0.263
Dryness of vagina	0.8 \pm 0.92	0.97 \pm 1.19	0.317
Joint and muscular discomfort	2.16 \pm 1.01	2.1 \pm 1.1	0.712

for the severity of menopausal symptoms score was the presence of medical illness ($P < 0.001$). To illustrate, there is an increase in the odds of having severe menopausal symptoms in females who suffer medical illness by 41% more than those who do not have any medical illness, OR = 1.41 (3.039–7.461) ($P < 0.001$).

Discussion

About 52.4% of the study subjects suffered from vitamin D insufficiency. A study conducted in India showed that vitamin D deficiency and insufficiency were prevalent among 70% and 23% of postmenopausal women, respectively [12]. Another study reported that 52.37% of

Table 4 Relationship between vitamin D level categories and menopausal rating scale (MRS) dimensions (n = 168)

Symptoms	Vitamin D level category mean ± SD		P value
	Sufficient (n = 80)	Insufficient (n = 88)	
Psychological symptoms	7.9 ± 3.5	7.1 ± 2.6	0.12 ^a
Somato-vegetative symptoms	7.02 ± 3.8	7.25 ± 3.04	0.66 ^a
Urogenital symptoms	3.08 ± 2.3	3.3 ± 2.9	0.63 ^a
Total score	17.97 ± 7.81	17.64 ± 6.25	0.76 ^a

^a P values are based on Mann–Whitney U test. Statistical significance at P < 0.05

Table 5 Multivariate linear regression about severity of menopausal symptoms

Predictors	Unstandardized coefficients		Standardized coefficients Beta	Odds ratio (95% CI)	P value
	B	Std. error			
Constant	32.242	11.612			0.006
Age	−0.358	0.204	−0.172	0.84 (−0.762–0.046)	0.08
Wight	0.051	0.032	0.119	1.13 (−0.011–0.114)	0.108
Duration of menopause	−0.148	0.135	−0.106	0.90 (−0.415–0.119)	0.275
Medical illness					
Present vs absent	5.250	1.120	0.342	1.41 (3.039–7.461)	< 0.001*
Vit. D level	0.003	0.037	0.006	1.01 (−0.07–0.077)	0.93

ANOVA < 0.001, R² = 0.224

* Statistical significance at P < 0.05

postmenopausal women had vitamin D deficiency. This would be rendered to the reduced capacity of the aging skin to effectively synthesize vitamin D [13]. Also, a paradox exists in countries with a low-sun incidence, when compared to countries with a higher solar incidence, such as those of Mediterranean Europe. In the Middle East (lower latitudes), there is a high prevalence of vitamin D deficiency, which can be explained by the habitual use of clothing covering almost the entire body [14].

Feeling anxious was significantly elevated among women with sufficient vitamin D levels. Another study reported a significant association between anxiety and vitamin D levels; however, their studied population had insufficient vitamin D [15]. An earlier one declined an association between vitamin D levels and anxiety [16]. Conflicting results were reported regarding the association between vitamin D and anxiety. Some studies confirmed a positive association [17, 18] while others declined this point [19, 20]. However, these studies targeted different populations (patients with rheumatoid arthritis and children and adolescents on dialysis, and pregnant women). Vitamin D has a neuroprotective effect through inhibition of oxidative damage of the brain tissue [21]. Additionally, decreased estrogen level affects CNS function through impaired synaptic processing and electrical excitability leading to anxiety [22].

Joint and muscular discomfort and irritability had the highest score among menopausal women. This agreed with previous results reporting joint pain and irritability among 90.3% and 84.9% of postmenopausal women [22]. Another one reported joint and muscle pain as the most prevalent symptom among menopausal women (87%) [23]. This was rendered to estrogen deficiency which might be related to the musculoskeletal system symptoms [24]. Variable results would be rendered to different social, cultural, and environmental characters of the studied populations [25].

There was no statistically significant difference in the severity of menopausal symptoms between vitamin D sufficient and insufficient groups (P = 0.97). This agreed with the results reported by a previous study [26], although they recruited women with an increased average of age (66 years), increased duration of menopausal years (16 years postmenopause), and discouraged women with severe symptoms from participating in the study. However, another study reported lower vitamin D levels among women with greater menopausal symptoms especially vasomotor symptoms [27]. This was rendered to their recruitment of breast cancer survivors on aromatase inhibitors. Another contradictory finding was reported [10]. This contradiction would be explained by their inclusion of women with vitamin D deficiency while

the current study did not. Additionally, they used different reference ranges than those reported in this study.

Vitamin D levels had no role in the prediction of the severity of menopausal symptoms together with other patient-related factors, but for medical illness ($P < 0.001$). This was in accordance with a previously published study [26], while contradictory results were reported where vitamin D levels were significantly associated with anxiety levels irrespective of age and depression levels [28]. Compelling evidence supports the role of vitamin D in the developing brain as well as in the adult brain function. The vitamin D receptors and the biosynthetic machinery for the hydroxylation of vitamin D have been found, in neurons, glial cells, and the pituitary gland. Thus, neurological and psychological actions of vitamin D have been claimed [29]. Additionally, another study reported that chronic diseases were related to the increased severity of menopausal symptoms [10, 30]. This would be rendered to the addition of symptoms related to these illnesses.

Strength and limitations

We recruited women with a relatively short duration of menopause. Also, women with severe symptoms were recruited. This study has some limitations. We recruited a small number of participants. This was a hospital-based study limiting the generalizability of the results. Patients with vitamin D deficiency were not included.

Conclusion

Vitamin D deficiency is an alarming issue among postmenopausal women; however, it was not associated with the severity of menopausal symptoms. Egypt being a Middle East country receives plenty of sunshine but at the same time exhibits rising vitamin D deficiency as Egypt embraces diversity in cultural practices and regional differences along with a distinct dietary pattern.

Abbreviations

25(OH) D: 25-Hydroxyvitamin D; FSH: Follicle-stimulating hormone; SSRIs: Selective serotonin reuptake inhibitors; SNRIs: Selective norepinephrine reuptake inhibitors; SERM: Selective estrogen receptor modulators; MRS: Menopause rating scale; CRP: C-reactive protein; CNS: Central nervous system.

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Authors' contributions

M Lotfy: protocol/project development, data collection and management, and manuscript writing/editing. NH Hakim: data collection and analysis. A Hassan: data collection and management, and manuscript writing/editing. OT Taha: data collection and management, data analysis, and manuscript writing/editing. MM Elbeily: protocol/project development, data collection and management, and manuscript writing/editing. The authors read and approved the final manuscript.

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was conducted after the approval of our research ethics committee. Informed consent was obtained from all participants before recruitment.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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