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Original Research Article

THE LINK BETWEEN CHOLECALCIFEROL INTAKE AND MANIFESTATIONS OF DEPRESSION AND MENSTRUAL ANOMALIES IN PREMENSTRUAL SYNDROME

NAEEM A[1], SHAIKH K[1], BATOOL S[1], ANESS A[1], MUMTAZ S[2], SIDDIQUI K[*3]

[1]*Department of Physiology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan*
[2]*Department of Physiology Indus Medical College, TMK, Pakistan*
[3]*Institute of Biotechnology and Genetic Engineering University of Sindh, Jamshoro, Pakistan*
**Correspondence author email address: Siddiqui.koml@usindh.edu.pk*

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Abstract: *Diminished vitamin D levels have been linked to manifestations of premenstrual discomfort and mood disturbances. Our study delved into the connection between reduced cholecalciferol concentrations and depressive tendencies alongside diverse menstrual inconsistencies observed in individuals with PMS. A cross-sectional study was conducted involving 250 female participants sourced from the Gynecology Outpatient Department at Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro Hyderabad, Pakistan. This study encompassed women aged 15 to 45, especially those in good health but with a documented history of depression and PMS. The Beck Depression Inventory was employed to clinically assess the incidence of depression, while the premenstrual syndrome scale was utilized to gauge PMS. The Chi-square test was applied for statistical analysis to juxtapose two quantitative parameters: vitamin D levels and Beck's scores, dysmenorrhea, menstrual flow, and age at menarche. Our analysis showed that 37.2% of the participants grappled with heavy menstrual flow, whereas 45.6% suffered from dysmenorrhea. Alarmingly, vitamin D was deficient in 61.2%, while an additional 34% displayed suboptimal levels. Regarding mental health indicators, 35.2% exhibited signs of mild depressive episodes during their premenstrual cycle, with a further 36.4% experiencing more acute depressive states. Among the vitamin D-deficient group, 18.8% were borderline for clinical depression, with 28.8% categorized under the severe depression bracket. Our statistical findings highlighted a pronounced linkage between Beck's depression indices and vitamin D concentrations, yielding a P-value of 0.001. In dysmenorrhea, 39.6% of the afflicted females had compromised vitamin D levels. Additionally, vitamin D deficiency was present in 36.8% of participants reporting intense menstrual flow. Notably, 9.6% of females who reached menarche at 12 exhibited reduced vitamin D levels, compared to a mere 0.8% with early menarche and satisfactory vitamin D metrics. There appears to be an inverse relationship between vitamin D concentrations and depressive symptoms, suggesting that optimal vitamin D levels could potentially ameliorate depressive manifestations.*

Keywords: Vitamin D (VD), Premenstrual Syndrome, Dysmenorrhea, Menarche, Depression, Beck's Scores

Introduction

PMS is a common and intricate health concern, manifesting in mental and physical difficulties. Continuous therapies might not guarantee complete alleviation of all symptoms. PMS and its acute variant, PMDD, are frequently associated with mood conditions, notably acute depression, leading to significant life disruptions from emotional variability, distress, and unease. In young individuals, personality characteristics are integral to their perceived health status and how they handle various health issues. Research into PMS and depression suggests differing underlying causes (Haoran et al., 2018). A detailed study involving twins highlighted that the genetic and environmental contributors to premenstrual issues and profound depression are distinct. It seems that family and surroundings play a minor role in influencing premenstrual symptoms. Dysmenorrhea, which affects women during their reproductive years, is widespread and can adversely affect life satisfaction. Certain studies point towards a potential link between vitamin D and calcium shortages and early manifestations of dysmenorrhea (Gollenberg et al., 2010).

Serotonin, a key neurotransmitter, undergoes variations during the menstrual cycle, influenced by hormones such as estrogens and progesterone. These alterations can lead to changed eating habits, fluid buildup, and a sense of melancholy. The brain houses receptors for vitamin D, promoting the creation of the TPH2 enzyme that transforms tryptophan into serotonin. Vitamin D, being soluble in fats, binds to its specific receptor, orchestrating several critical biological processes, with its primary role being the oversight of calcium and phosphate balance. Evidence suggests insufficient vitamin D can increase the susceptibility to certain non-bone-related health issues (Abdi et al., 2021). A significant portion of women, around 80%, experience at least a single emotional or physical change during their menstrual phases. Estrogen affects neurotransmitters like serotonin, acetylcholine, dopamine, and noradrenaline, which are crucial in directing thought

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processes, emotions, and behavioral adaptations. Thus, reduced estrogen concentration in the luteal phase might be instrumental in precipitating PMS indicators. Age progression (surpassing 30) and inherited traits are highlighted as potential predispositions for PMS. Some research insights tie lowered 25(OH) D concentrations with an increased propensity for emotional conditions, including PMS, seasonal affective syndrome, generalized mood disorders, and major depression episodes. Growing evidence posits a biochemical connection between vitamin D levels and female mood-related challenges, necessitating thorough scientific scrutiny (Jangpangi et al., 2016). The recent inquiry endeavored to pinpoint diminished vitamin D concentrations in females presenting depressive tendencies tied to PMS, focusing on the interplay between low cholecalciferol presence, depression, and menstrual irregularities in PMS-affected women.

Methodology

AThe study was designed as a cross-sectional investigation spanning six months. The research took place at the Open-Patient Department (OPD) of Gynecology, within the premises of Liaquat University of Medical & Health Sciences (LUMHS), situated in Jamshoro Hyderabad, Pakistan.

The research utilized a non-probability purposive sampling method. The sample size was determined to be n= 250, deduced through the calculator tool provided by the World Health Organization (WHO).

The study focused on female patients aged 15 to 45, particularly those presenting a historical trace of depression coupled with PMS. The exclusion criteria filtered outpatients diagnosed with Hypertension, Diabetes Mellitus, Chronic Kidney Disease, and Autoimmune diseases. Additionally, patients with underlying Cardiac and Endocrine Disorders or those undergoing treatment regimes involving corticosteroids or anti-psychotic medications were also omitted from the study.

The study's initiation was contingent on the Ethical Review Committee (ERC) greenlighting. All potential candidates matching the inclusion criteria were approached. Their participation was voluntary, with informed consent obtained before any data collection. A structured proforma was employed to gather necessary patient information. From every participant, a 5cc blood sample was extracted for laboratory analysis. The Vitamin D3 concentration was assessed utilizing a specialized Vitamin D3 kit compatible with the Cobas E411 Analyzer (part of the Roche Cobas system). This assay procedure was executed with the diagnostic and research lab in Jamshoro/Hyderabad. For gauging the prevalence of depression, Beck's Depression Inventory was adopted. Concurrently, the premenstrual syndrome scale facilitated the evaluation of PMS symptoms among the subjects.

The SPSS software suite (version 26.0) was the tool of choice for the analytical phase. The Chi-square test became instrumental in drawing comparative insights between two quantifiable variables: vitamin D levels versus Beck's scores, dysmenorrhea, menstrual flow volume, and the age of first menstruation (menarche). A P-value threshold of 0.05 was set as the benchmark for discerning statistical significance. Additionally, Pearson correlation methods were employed to discern and quantify any relationships between the abovementioned variables.

Results

Within our comprehensive assessment of the participants' menstrual characteristics and associated health parameters, we identified notable patterns in menstruation duration: 33.6% of participants exhibited a 5-day cycle, whereas 29.2% had a 6-day cycle. This concentration within the 5 to 6-day window indicates the prevalent menstruation duration within this cohort. A further granular breakdown may be necessary to explore potential external influencing factors such as age or Body Mass Index (BMI). Regarding menstrual flow intensity, 37.2% of the respondents documented an intensified flow. Such patterns can potentially correlate with conditions including, but not limited to, fibroids, polyps, or hormonal discrepancies. Alarmingly, 45.6% reported experiencing dysmenorrhea, highlighting an immediate necessity to delve into possible correlations, for instance, vitamin D levels or the manifestation of depressive symptoms. In the context of vitamin D levels, our data revealed that an overwhelming 61.2% were deficient, and an additional 34% were approaching the deficiency threshold. Such pronounced discrepancies in vitamin D levels warrant a deeper examination of possible contributing factors, encompassing lifestyle choices, dietary habits, sun exposure, or latent health conditions. Transitioning to mental health, we observed that 35.2% faced mild depressive episodes, whereas a close 36.4% grappled with severe depressive manifestations during their premenstrual period. These findings accentuate the importance of embedding mental health assessments within standard care protocols for individuals with PMS. They also underscore the need to investigate potential physiological associations between mood variations and vitamin D concentrations. Such revelations accentuate the imperative for augmented research endeavors to decode the intricate nexus binding menstrual health, psychological states, and nutritional parameters in women.

Table 1 Clinical Information of the patients (n=250)

Category	Subcategory	Data
Marriage Status	Wedded	162 (Count: 64.8%)
Marriage Status	Single	88 (Count: 35.2%)
Duration of Menstruation	4 days span	45 (Approximately 18.0%)
Duration of Menstruation	5 days span	84 (Approximately 33.6%)
Duration of Menstruation	6 days span	73 (Approximately 29.2%)

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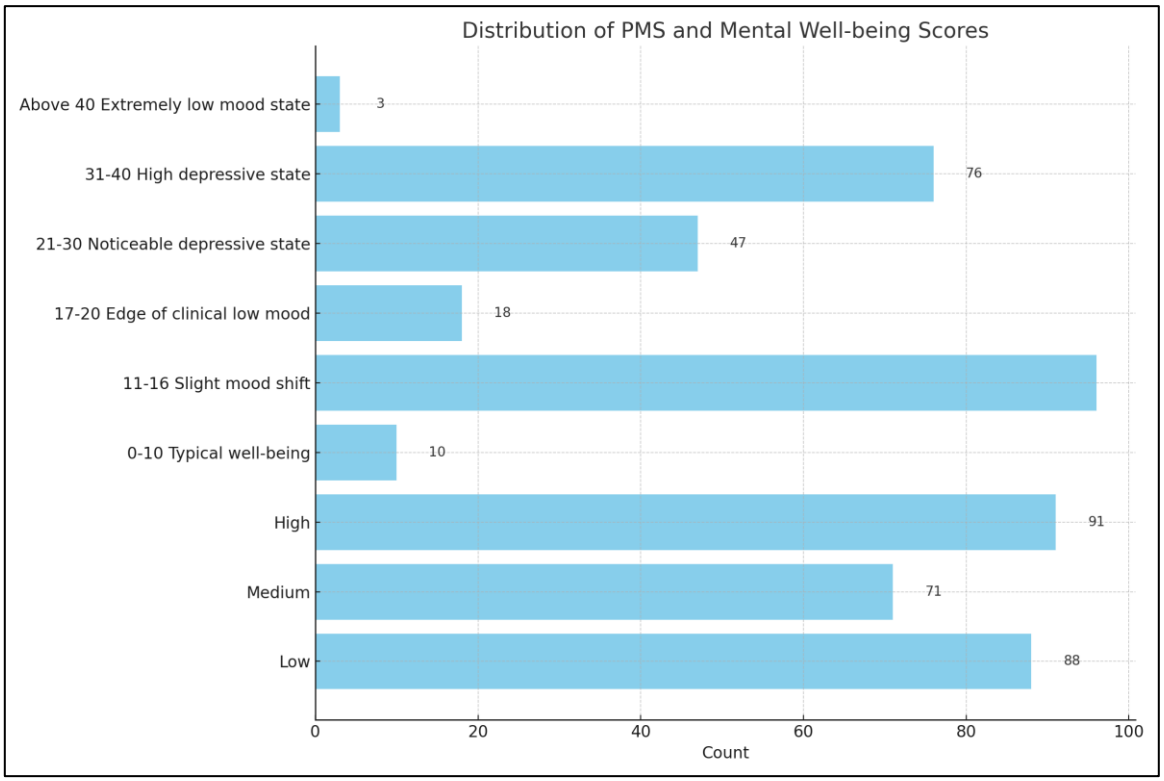
Duration of Menstruation	7 days span	44 (Approximately 17.6%)
Duration of Menstruation	8 days span	4 (Approximately 1.6%)
Flow Intensity During Menstruation	Light	83 (~33.2%)
Flow Intensity During Menstruation	Average	74 (~29.6%)
Flow Intensity During Menstruation	Intense	93 (~37.2%)
Presence of Menstrual Pain	Affirmative	114 (About 45.6%)
Presence of Menstrual Pain	Negative	136 (About 54.4%)
Level of Vitamin D	Lacking	153 (Roughly 61.2%)
Level of Vitamin D	Below Average	85 (Roughly 34.0%)
Level of Vitamin D	Adequate	12 (Roughly 4.8%)

Table 2 Distribution of PMS and Beck's Scores in Cases

Score/Intensity Level	Count	Percentage
Low	88	35.2%
Medium	71	28.4%
High	91	36.4%
0-10 Typical well-being	10	4.0%
11-16 Slight mood shift	96	38.4%
17-20 Edge of clinical low mood	18	7.2%
21-30 Noticeable depressive state	47	18.8%
31-40 High depressive state	76	30.4%
Above 40 Extremely low mood state	03	1.2%



The above chart represents the distributions of PMS and Beck's scores. Each bar indicates the frequency of individuals in each category, with percentages annotated on the bars.

Presented in Table 3 is the intricate association between vitamin D concentrations and the prevalence of depression. A deep dive into the data reveals that among those grappling with a vitamin D deficiency, 18.8% were teetering on the threshold of clinical depression. This becomes particularly concerning when acknowledging that the incidence of severe depression soared to 28.8% for this group. Contrarily, participants maintaining optimum vitamin D levels exhibited a notably diminished susceptibility to depressive episodes. While individual variances exist, the overarching data suggests a compelling correlation between the intensity of depressive markers and vitamin D

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concentrations, as indexed by Beck's scores, underpinned by a significant P-value of 0.001.

Table 4 shows us the potential linkage between dysmenorrhea prevalence and vitamin D status. A significant 39.6% of respondents reported dysmenorrhea were concurrently vitamin D deficient. This is juxtaposed with a mere 0.8% prevalence of dysmenorrhea among those whose vitamin D levels were within the acceptable range. Such a stark differential highlights the imperative for rigorous research into vitamin D's role in menstrual health and accentuates the potential therapeutic avenues this could open, should this correlation be causative.

Table 3 Association between Beck's score and vitamin D level (n=250)

Mood Evaluation	Vitamin D Level: Normal	Vitamin D Level: Low	Vitamin D Level: Very Low	Total
0-10 Average mood	4 (1.6%)	6 (2.4%)	0 (0.0%)	10 (4.0%)
11-16 Slight mood shift	6 (2.4%)	12 (4.8%)	0 (0.0%)	18 (7.2%)
17-20 Edge of clinical low mood	47 (18.8%)	43 (17.2%)	6 (2.4%)	96 (38.4%)
21-30 Noticeable depressive state	21 (8.4%)	22 (8.8%)	4 (1.6%)	47 (18.8%)
31-40 High depressive state	72 (28.8%)	2 (0.8%)	2 (0.8%)	76 (30.4%)
Above 40 Critically low mood	3 (1.2%)	0 (0.0%)	0 (0.0%)	3 (1.2%)
Total	153 (61.2%)	85 (34.0%)	12 (4.8%)	250 (100.0%)

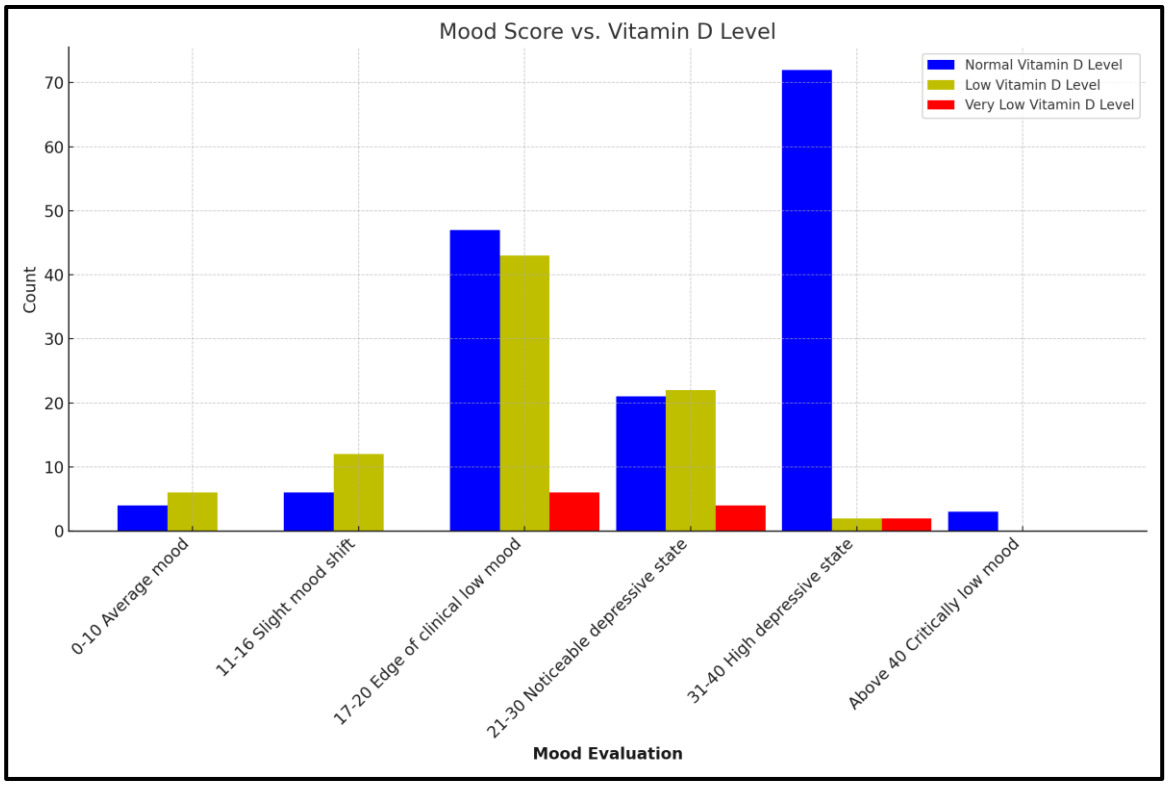

Table 4 Association between dysmenorrhea and vitamin D level (n=250)

Menstrual Discomfort	Vitamin D Level: Sufficient	Vitamin D Level: Low	Vitamin D Level: Deficient	Total
Absent	54 (21.6%)	72 (28.8%)	10 (4.0%)	136 (54.4%)
Present	99 (39.6%)	13 (5.2%)	2 (0.8%)	114 (45.6%)
Total	153 (61.2%)	85 (34.0%)	12 (4.8%)	250 (100.0%)
Key: D= deficiency, S= Sufficiency, Ins=Insufficiency				

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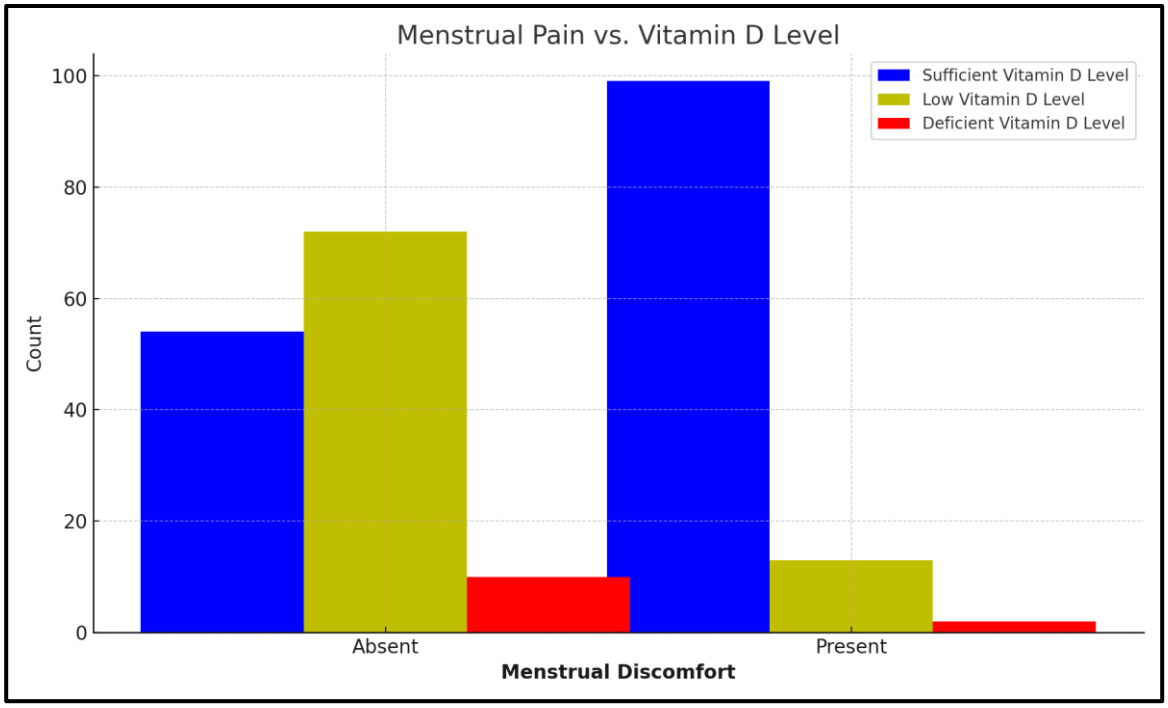

Statistical analysis: p-value = 0.001 (Significant observation)

Discussion

Evidence suggests a tangible link between hypovitaminosis D and heightened susceptibility to depressive states, particularly among females contending with premenstrual syndrome (PMS). The lacunae in extant epidemiological datasets spurred this rigorous inquiry. Notably, the emotional vicissitudes characteristic of PMS often exacerbate melancholic sentiments in women during their pre-menstrual phase. Such emotional perturbations can be theoretically ascribed to serotonin flux, underpinning mood variances, sleep irregularities, and atypical hunger patterns - quintessential PMS symptoms (Borrione et al., 2018).

Modern-day lifestyle nuances, typified by constrained outdoor activities and suboptimal dietary vitamin D assimilation, might be pivotal in the observed pervasiveness of vitamin D deficits. Our empirical data elucidate that 33.6% of our cohort experienced menstrual cycles spanning 5 to 6 days, with an intensified menstrual flow and dysmenorrhea documented by 37.2% and 45.6% of participants, respectively. Moreover, a disconcerting 61.2% manifested vitamin D inadequacies, with another 34% teetering on the brink of insufficiency. Sequelae of such deficiencies were discernible: 35.2% exhibited mild depression, and 36.4% grappled with severe depression during PMS. In-depth analysis revealed that 18.8% had borderline clinical depression, escalating to 28.8% amidst those manifestly deficient in vitamin D. Conversely, optimal vitamin D indices were inversely correlated with depressive inclinations (Kim et al., 2018).

Historical research trajectories, exemplified by Wittchen et al. (2002), corroborate the comorbidity interlinking mood disorders and PMDD, while another seminal work by Yonkers et al. (2003) accentuates the concomitance between major depressive states and PMS. The symptomatic nexus, especially mood modulation, engenders a hypothesis suggesting a potential intersection between PMS and conditions like hypovitaminosis D, hyperparathyroidism, and calcium homeostasis aberrations. However, recent empirical findings juxtapose similar Calcitriol and Calcifediol blood concentrations between PMDD-afflicted females and their healthy cohorts (Dhar and Barton, 2016).

The contemporary medical literature, vis-à-vis vitamin D prophylaxis for PMS attenuation, remains embryonic. Notwithstanding, there's an unequivocal association between dietary vitamin D paucity and PMS onset. A salient revelation underscores a 41% diminution in PMS susceptibility over a biennial period amongst females with apex dietary vitamin D intake, approximating 400 IU daily. This juxtaposes starkly against their counterparts with diminutive intake. The intricate relationship delineating primary dysmenorrhea severity and the paucity of vitamin D and calcium necessitates rigorous scrutiny. Supplementation might offer therapeutic alleviation of these symptoms (Bikle, 2016).

It's imperative to underscore that vitamin D's role in female reproductive health transcends rudimentary nutrient dynamics. It potentially influences calcium homeostasis, endocrine rhythms, and neurotransmitter functionality. An avant-garde study encompassing 897 teenage females from Iran delineates the transformative efficacy of robust vitamin D supplementation regimens on PMS and dysmenorrhea manifestations (Wittchen et al., 2002). A decline in PMS

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prevalence from 14.9% to 4.8% and dysmenorrhea from 35.9% to 32.4% post-supplementation is a testament to its potential. Hence, vitamin D supplementation emerges as a beacon of hope in ameliorating life quality among females with pronounced hypovitaminosis D, concomitant with mood aberrations allied to PMS. Prospective research endeavors should rigorously probe this nexus to corroborate these findings and hone therapeutic paradigms (Potter et al., 2009).

Conclusion

Vitamin D insufficiency has emerged as a potential contributor to the onset and severity of premenstrual syndrome (PMS) symptoms. Notably, an evident inverse correlation has been established between vitamin D concentrations and the extent of depressive manifestations. This relationship extends to determinants like Beck's score, PMS intensity, dysmenorrhea, and intensified menstrual flow. Given these associations, it's prudent to recommend systematic vitamin D screenings from the initiation of menarche. Such proactive measures could significantly curtail the onset of menstrual anomalies and depressive episodes. Employing serum vitamin D levels during the PMS phase as a diagnostic tool for depression can pave the way for more tailored interventions.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Not applicable
Consent for publication
Not applicable
Funding
Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

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