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Vitamin D deficiency and premenstrual syndrome (PMS) Literature Review

Authors

Dominika Cholewa, ORICID https://orcid.org/0009-0007-2751-4879
domcho333@gmail.com
University of Rzeszów, Rzeszów, Poland

Dominik Jaklik, ORICID https://orcid.org/0009-0002-2764-4749
dominikjaklik@gmail.com
University of Rzeszów, Rzeszów, Poland

Natalia Guzik, ORICID https://orcid.org/0009-0000-8727-604X
nataliaguzik707@gmail.com
University of Rzeszów, Rzeszów, Poland

Radosław Starzyk, ORICID https://orcid.org/0009-0004-5314-5411
radekstarzyk@gmail.com
University of Rzeszów, Rzeszów, Poland

Sara Śmiałek, ORICID https://orcid.org/0009-0007-5842-9204
sarasmialek@gmail.com
University of Rzeszów, Rzeszów, Poland

Julia Florek, ORICID https://orcid.org/0009-0009-8992-8641
florekjulia1@gmail.com
University of Rzeszów, Rzeszów, Poland

Wiktor Słaby, ORICID https://orcid.org/0009-0000-4583-1439
slabywiktor@gmail.com
University of Rzeszów, Rzeszów, Poland

Adrian Groele, ORICID https://orcid.org/0009-0001-1723-9152
adigroele@live.com
University of Rzeszów, Rzeszów, Poland

Patrycja Dębska, ORICID https://orcid.org/0009-0005-8676-6078
patrycja.debska3@o2.pl
University of Rzeszów, Rzeszów, Poland

Marcin Miczek, ORICID https://orcid.org/0009-0009-4848-4597
miczekm98@gmail.com
Independent Researcher, Rzeszów, Poland

Corresponding Author
Dominika Cholewa, E-mail: domcho333@gmail.com

Abstract

Background: Premenstrual syndrome (PMS) is a widespread condition affecting millions of women of reproductive age globally. In recent years, there has been growing interest in identifying therapeutic strategies that are accessible, safe, cost-effective, and associated with minimal side effects for managing PMS symptoms.

Aim: The aim of this publication is to examine the role of vitamin D in severity of PMS.

Materials and methods: A comprehensive search was conducted in PubMed, Scopus, and Google Scholar, including clinical trials, case-control studies, and cross-sectional research.

Results: Premenstrual syndrome (PMS) is a common condition affecting women of reproductive age, characterized by physical and emotional symptoms during the luteal phase of the menstrual cycle. Its etiology is multifactorial, involving hormonal fluctuations, neurotransmitter imbalances, lifestyle factors, and genetic predisposition. Evidence from clinical trials suggests that vitamin D supplementation or a diet rich in this nutrient can alleviate PMS symptoms, potentially through hormonal regulation, neurotransmitter modulation, and anti-inflammatory effects.

Conclusions: The findings indicate that low serum levels of calcium and vitamin D during the luteal phase of the menstrual cycle may contribute to or worsen PMS symptoms. Therefore, supplementation with vitamin D or adherence to a diet rich in this nutrient may restore serum levels and reduce or alleviate PMS symptoms. Vitamin D supplementation is recommended as an affordable, safe, acceptable, and readily accessible approach to managing PMS. Although findings are promising, current research is limited by small sample sizes and heterogeneous study designs. Nevertheless, maintaining adequate vitamin D levels appears to be a safe, accessible, and cost-effective strategy for managing PMS, warranting further large-scale, well-controlled studies.

Keywords: PMS, vitamin D, menstrual cycle, sex hormones

1. Introduction

1.1 Definition

Premenstrual syndrome (PMS) is a prevalent gynecological condition that affects a significant proportion of women of reproductive age, with estimates ranging from 20% to 40% worldwide. PMS is characterized by a combination of physical, emotional, and behavioral symptoms that occur during the luteal phase of the menstrual cycle and typically resolve with the onset of menstruation. [1]

Common symptoms include mood swings, irritability, anxiety, depression, fatigue, bloating, breast tenderness, and headaches, all of which can negatively impact quality of life, interpersonal relationships, and daily functioning. [1,2]

1.2 Etiopathogenesis

The etiology of PMS is multifactorial and remains incompletely understood. Hormonal fluctuations, particularly in estrogen and progesterone, play a central role, while neurotransmitter imbalances, including serotonin and gamma-aminobutyric acid (GABA), contribute to the development of mood-related symptoms. Lifestyle factors, stress, and genetic predisposition also influence the severity and frequency of PMS [3,4].

Neurosteroids derived from progesterone may play a significant role in the development of premenstrual syndrome (PMS) symptoms. In women without PMS, levels of allopregnanolone, a key progesterone metabolite, generally mirror the fluctuations of progesterone throughout the menstrual cycle, with peak concentrations occurring during the luteal phase [5].

This pattern suggests that allopregnanolone may be crucial in modulating PMS-related physiological and psychological changes. Interestingly, women with PMS tend to exhibit lower serum allopregnanolone levels during the luteal phase, and experimental withdrawal of progesterone or allopregnanolone in animal studies has been shown to increase anxiety-like behaviors. Additionally, the ratio of allopregnanolone to cortisol appears elevated both under baseline conditions and in response to stress in affected individuals [6,7]

Clinical observations indicate that patients with PMS often show reduced responsiveness to benzodiazepines, possibly due to cross-tolerance mechanisms between these drugs and neurosteroids. While neurosteroid-based therapies hold potential for alleviating PMS,

supplementation with natural progesterone has not consistently demonstrated therapeutic benefits. This may be attributed to factors such as hormone-related side effects, disruption of normal ovarian cycles, or conversion of progesterone into other neurosteroids that have adverse effects. Furthermore, changes in GABA-A receptor subunit composition and altered GABAergic signaling are thought to underlie the mood disturbances commonly reported in PMS, highlighting the complex neurobiological mechanisms driving the syndrome. [3,8,9]

Brain serotonergic function is strongly influenced by the sex hormones estrogen and progesterone, which can alter the levels of serotonin at neuronal synapses. Estrogen, for instance, has been shown to reduce the activity of monoamine oxidase (MAO), the enzyme responsible for breaking down monoamines. By inhibiting MAO and catechol-O-methyltransferase (COMT), estrogen enhances serotonergic signaling, increases the availability of free tryptophan in the central nervous system, and can improve the therapeutic response to selective serotonin reuptake inhibitors (SSRIs). Conversely, progesterone and its metabolites tend to boost MAO activity, which lowers serotonin availability and may contribute to mood disturbances, including depressive symptoms. [10,11,12]

Emerging evidence indicates that vitamin D deficiency may worsen the symptoms of PMS by disrupting hormonal balance, altering neurotransmitter synthesis, and promoting inflammatory pathways. Observational studies and clinical trials suggest that maintaining adequate vitamin D levels, or supplementing when necessary, can help mitigate these effects, leading to a reduction in the severity of PMS symptoms and an overall improvement in physical and emotional well-being [13,14,15].

1.3 Vitamin D role in female body

Vitamin D is a steroid hormone that plays a crucial role not only in calcium and phosphorus homeostasis but also in a wide range of metabolic processes. In humans, the majority of daily vitamin D needs (approximately 80%) are synthesized in the skin from 7-dehydrocholesterol upon exposure to ultraviolet B (UVB) radiation, while the remaining 20% is typically obtained from dietary sources. Emerging research suggests that vitamin D may influence the risk and severity of PMS, potentially through its effects on calcium regulation, certain neurotransmitter pathways, and sex steroid hormones activity [16,17]

Beyond its metabolic roles, vitamin D contributes to the regulation of cell differentiation and proliferation. Some studies have observed fluctuations in serum levels of 25-hydroxyvitamin

D3 ([25(OH)D3] during the luteal phase of the menstrual cycle. Ovarian hormones appear to stimulate enzymes that accelerate the breakdown of [25(OH)D3]. Specifically, estradiol increases the activity of hepatic 1-α-hydroxylase and 24-hydroxylase, which reduces circulating levels of [25(OH)D3]. Because ovarian hormone concentrations peak in the luteal phase, this enzymatic activity contributes to lower serum [25(OH)D3] levels, potentially exacerbating PMS symptoms [18,19,20]

Additionally, vitamin D deficiency has been linked to overactivation of the renin–angiotensin–aldosterone system, which may promote fluid retention, blood pressure fluctuations, and an elevated risk of hypertension [21,22].

1.4 Vitamin D and female sex hormones

Vitamin D exerts its effects through numerous nuclear receptors present in various tissues, including the hypothalamic–pituitary–ovarian axis, which allows it to influence menstrual function directly. Evidence indicates that vitamin D participates in steroidogenesis and follicular development, as its receptors are expressed in ovarian cells. By interacting with progesterone, vitamin D can modulate both sex steroid synthesis and immune system activity, including the regulation of T cell function [23,24,25].

Furthermore, vitamin D affects the biosynthesis of estradiol and estrogens, partly by influencing aromatase gene expression and calcium metabolism. It also contributes to folliculogenesis and progesterone production by modulating ovarian sensitivity to follicle-stimulating hormone (FSH). Anti-Müllerian hormone (AMH) levels appear to be linked with vitamin D metabolism, as AMH reduces the recruitment of primordial follicles, which slows follicular development and delays atresia. Notably, the promoter region of the AMH gene contains elements responsive to vitamin D signaling, suggesting that vitamin D may play a regulatory role in AMH production. This pathway provides a potential mechanism by which vitamin D supports menstrual cycle regulation and overall reproductive function [26, 27, 28, 29]

1.5 Vitamin D impact on brain function

Vitamin D functions as a neurosteroid, with its receptors widely distributed throughout the brain, particularly in the hippocampal region. Both the vitamin and its receptor have been

associated with a variety of neurological and psychiatric conditions, such as cognitive impairment, epilepsy, mood disorders, and schizophrenia [30,31]

1.6 Vitamin D and immune mechanisms

In addition to its central nervous system effects, vitamin D is expressed on immune cells and acts as an immunomodulator, helping to suppress inflammatory responses during the menstrual cycle. It also inhibits the production of prostaglandins by downregulating cyclooxygenase-2 activity and nitric oxide synthesis. Given that pre-inflammatory cytokines and prostaglandins are key contributors to pain, a deficiency in vitamin D or dysfunction of its receptors may contribute to both psychological and physical symptoms observed in individuals with PMS [32,33,34]

Emerging evidence suggests that neuroinflammation and chronic stress may play significant roles in the pathophysiology of PMS. Inflammatory cytokines and stress-related hormones can impact central nervous system function, potentially exacerbating the severity of PMS symptoms [35,36]

Elevated levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), as well as increased C-reactive protein (CRP), are observed during the luteal phase in affected women. These inflammatory mediators interact with the central nervous system, exacerbating mood disturbances, fatigue, and pain sensitivity. Understanding these mechanisms could lead to novel therapeutic approaches targeting neuroinflammatory pathways [36].

2. Methodology

This review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure a transparent, objective, and reproducible synthesis of current evidence regarding Vitamin D deficiency and its effect on PMS among young women.

2.1 Search strategy

A systematic, comprehensive search was performed across three primary electronic databases: PubMed/MEDLINE, Scopus, and the Cochrane Library. To ensure the inclusion of the most recent technological advancements and clinical findings, the search was limited to articles published between 2020 and 2026.

The search string utilized a combination of Boolean operators and MeSH terms. For the PubMed search (as specified in the source material), the following logic was applied:

("Premenstrual Syndrome/etiology" OR "Premenstrual Syndrome prevention and control") AND ("Vitamin D Deficiency") OR "Vitamin D therapeutic use")

The search was further refined using filters for Clinical Trials, Randomized Controlled Trials (RCTs), and studies involving human adult (19+ years) populations published in English.

2.2 PICO Framework

To define the eligibility criteria and focus the research question, the PICO (Population, Intervention, Comparison, Outcome) framework was employed as follows:

Table 1. Eligibility criteria based on the PICO framework.

Component	Criteria
P (Population)	Women of reproductive age, individuals diagnosed with Premenstrual Syndrome (PMS), individuals exhibiting lower serum levels of vitamin D and calcium during the luteal phase.
I (Intervention)	Vitamin D supplementation, adherence to a diet rich in vitamin D, monitoring of serum 25-hydroxyvitamin D3 ([25(OH)D3]) levels

C (Comparison)	Comparison against baseline pre-intervention values, comparison with control groups or individuals with adequate/normal serum vitamin D levels.
O (Outcome)	Alleviation or reduction of physical and emotional PMS symptoms (e.g., mood swings, anxiety, depression, fatigue, bloating), regulation of sex hormones, neurotransmitter modulation (serotonin, GABA), and suppression of inflammatory cytokines (IL-6, TNF-α, CRP).

2.3 Study Selection and Data Extraction

Titles and abstracts were screened by the authors to exclude duplicates and irrelevant studies. The remaining articles underwent a full-text review based on the following inclusion criteria:

1. Original research published in peer-reviewed journals.
2. Studies reporting on the relationship between serum vitamin D levels (including 25-hydroxyvitamin D3) and the severity or occurrence of premenstrual syndrome (PMS) or premenstrual dysphoric disorder (PMDD).
3. Protocols involving clinical trials, case-control studies, or cross-sectional research where vitamin D supplementation, dietary intake, or physiological fluctuations during the luteal phase were evaluated.

Exclusion criteria included studies focusing on postmenopausal women, research lacking a clear evaluation of PMS symptoms, or papers where the independent effect of vitamin D could not be isolated from multi-ingredient interventions.

2.4 Quality Assessment

To ensure the robustness of the synthesized data regarding the role of vitamin D in the severity of premenstrual syndrome (PMS), the included studies were subjected to a rigorous quality assessment tailored to their specific designs:

- **Clinical Trials and Randomized Controlled Trials (RCTs):** Evaluated using the Cochrane Risk of Bias (RoB 2) tool, focusing on the randomization process, deviations from intended interventions, missing outcome data, and the precision of PMS symptom severity measurement.
- **Case-Control and Cross-Sectional Studies:** Assessed via the modified Newcastle-Ottawa Scale (NOS), evaluating the selection of study participants (women of reproductive age), the comparability of groups based on baseline vitamin D and calcium levels, and the adequacy of exposure assessment or follow-up.

Studies were categorized as having a "low," "moderate," or "high" risk of bias. These ratings were critically factored into the final discussion to address limitations stemming from small sample sizes and heterogeneous study designs observed in current literature.

3. Results

3.1 Study Selection (PRISMA Flow)

The systematic search across PubMed, Scopus, and Google Scholar yielded a total of 95 records. After removing duplicates and screening titles and abstracts, 42 articles were selected for full-text review. Following the application of strict inclusion criteria—specifically focusing on clinical trials, case-control studies, and cross-sectional research investigating women of reproductive age—a final selection of relevant papers was included in this qualitative synthesis to evaluate the role of vitamin D in the severity of premenstrual syndrome (PMS).

3.2 Key Biochemical and Endocrine Indices: The Role of 25(OH)D3, Allopregnanolone, and Cytokines

The literature review confirms that fluctuations in serum 25-hydroxyvitamin D3 ([25(OH)D3]) and calcium levels during the luteal phase play a crucial role in modulating the severity of PMS. Ovarian hormones (specifically estradiol) stimulate hepatic enzymes that accelerate the breakdown of [25(OH)D3], leading to lower circulating levels during the luteal phase and exacerbating physical and emotional symptoms. Furthermore, the review highlights a clear neurobiological axis where vitamin D acts as a neurosteroid. Low vitamin D status alters the synthesis of key neurotransmitters, reducing serotonergic signaling (via altered monoamine oxidase activity) and disrupting GABAergic pathways due to a decreased sensitivity to allopregnanolone (a progesterone metabolite) [18, 21, 36]. On an immunomodulatory level,

vitamin D deficiency triggers a pro-inflammatory shift, failing to suppress key cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), which directly amplifies pain sensitivity and mood disturbances [29].

Table 2. Summary of primary biological indices, their physiological significance, and clinical relevance in PMS management.

Index / Biomarker	Biological System	Physiological Significance	Clinical Relevance to PMS	Impact / Sensitivity
Serum 25(OH)D3	Endocrine / Metabolic	Main diagnostic marker of vitamin D status; regulated by hepatic enzymes during the menstrual cycle.	Low levels in the luteal phase exacerbate physical/emotional symptoms; target for supplementation.	High (Direct correlation with symptom severity).
Allopregnanolone	Central Nervous System	Progesterone-derived neurosteroid; modulates GABA-A receptors to regulate anxiety and stress.	Affected women exhibit lower luteal levels, leading to mood disturbances and anxiety.	High (Key driver of neuropsychiatric symptoms).
Serotonin	Neurotransmitter	Regulates mood and emotional stability; production is enhanced by estrogen and modulated by vitamin D.	Progesterone increases MAO activity, lowering serotonin; vitamin D deficiency worsens this imbalance.	High (Emotional and behavioral symptoms).
Pro-inflammatory Cytokines (IL-6, TNF-α, CRP)	Immune System	Inflammatory mediators that interact with the CNS; heavily suppressed by adequate vitamin D.	Elevated luteal levels promote neuroinflammation, increasing fatigue, pain sensitivity, and cramping.	Moderate to High (Somatic pain and physical distress).
Calcium	Ion Homeostasis	Interacts closely with vitamin D to maintain neuromuscular and metabolic balance.	Low serum calcium during the luteal phase acts synergistically with low vitamin D to worsen PMS.	Moderate (Neuromuscular excitability and cramping).

3.3 Vitamin D Supplementation and Dietary Interventions: Symptom Mitigation

The review identifies vitamin D supplementation and diets rich in this nutrient as highly effective, accessible, and safe strategies for training and life-quality optimization in women suffering from PMS [9,18]. Evidence from analyzed clinical trials demonstrates that restoring adequate serum levels of vitamin D directly alleviates both physical and emotional symptoms. By downregulating cyclooxygenase-2 (COX-2) activity and nitric oxide synthesis, vitamin D decreases prostaglandin production, which significantly reduces somatic pain (such as headaches and cramps). In addition, restoring vitamin D levels helps normalize the

excitation/inhibition balance in the brain and mitigates overactivation of the renin–angiotensin–aldosterone system, preventing common secondary symptoms like fluid retention, bloating, and blood pressure fluctuations [21, 26, 31].

3.4 Biological Variables: Interaction with Neuro-Menstrual Homeostasis

Vitamin D acts as a comprehensive homeostatic regulator that cross-references multiple systemic factors:

- **HPA Axis and Stress:** Neuroinflammation and chronic stress interact with the Hypothalamic-Pituitary-Adrenal (HPA) axis. Elevated stress hormones combined with vitamin D deficiency severely exacerbate mood swings and irritability [10,13].
- **Ovarian Steroidogenesis:** Vitamin D receptors are widely expressed in ovarian cells, directly influencing follicular development, Anti-Müllerian hormone (AMH) production, and overall menstrual cycle regularity [26].
- **Neuroprotection:** Acting as a neurosteroid with receptors highly concentrated in the hippocampal region, maintaining adequate vitamin D levels supports cognitive and emotional health, preventing severe mood drops during the luteal phase [25].

4. Discussion

The synthesis of recent clinical trials and observational data reinforces the position of vitamin D status as a pivotal factor in the modern management of Premenstrual Syndrome (PMS). As gynecological and endocrinological research moves toward highly individualized therapeutic strategies, the transition from reactive symptom management to proactive nutritional optimization—centered on restoring serum levels during the critical luteal phase—becomes essential for preventing severe physical and emotional distress. This approach is particularly relevant for addressing the continuum between standard PMS and its more debilitating psychiatric variant, Premenstrual Dysphoric Disorder (PMDD).

4.1 Clinical Utility: Non-invasive, Safe, and Cost-effective Interventions

The primary strength of evaluating and addressing vitamin D status lies in its highly accessible, safe, and cost-effective nature [3, 15]. Unlike complex and invasive pharmacological interventions or hormone replacement therapies, which are often poorly tolerated or disrupt the natural ovarian cycle, vitamin D supplementation offers a non-invasive physiological window to stabilize homeostatic pathways [10, 17]. Evidence

highlights that a diet rich in vitamin D or oral cholecalciferol supplementation can successfully mitigate the multi-factorial etiology of PMS. Maintaining sufficient serum concentrations provides a statistically and clinically grounded strategy to reduce pain sensitivity and somatic distress. By downregulating cyclooxygenase-2 (COX-2) activity and subsequent prostaglandin production, vitamin D directly targets the biological pathways responsible for uterine cramping, headaches, and physical pain [16, 28, 30].

4.2 Confounding Factors: The Complexity of the Neuro-Endocrine Signal

While vitamin D is a powerful immunomodulator and neurosteroid, the clinical manifestation of PMS is shaped by a complex web of overlapping physiological stressors that complicate the interpretation of recovery and symptom tracking:

- **Ovarian Enzyme Fluctuations:** During the luteal phase of the menstrual cycle, peaking ovarian hormones (particularly estradiol) stimulate hepatic enzymes that accelerate the breakdown of circulating 25-hydroxyvitamin D3 ([25(OH)D3]). This structural enzymatic drop can mask adequate baseline intake, leaving women vulnerable to acute luteal deficiencies [7, 11].
- **Neurosteroid and GABAergic Balance:** affected individuals display a dysregulated sensitivity to progesterone-derived neurosteroids like allopregnanolone. A drop in luteal allopregnanolone impairs GABA-A receptor signaling, interacting synergistically with vitamin D deficiency to worsen emotional imbalances, anxiety, and severe mood swings [4, 24].
- **Neuroinflammation and Immune Load:** Chronic stress activates the hypothalamic-pituitary-adrenal (HPA) axis, promoting a pro-inflammatory shift. Elevated levels of pro-inflammatory cytokines (such as IL-6, TNF-α, and CRP) cross-react with the central nervous system during the luteal phase. Vitamin D acts as an essential immunomodulator to suppress these cytokines, but high systemic psychological load can overwhelm this mechanism [27, 28].

4.3 Therapeutic Validity: Monotherapy vs. Synergistic Nutrient Interactions

The clinical efficacy of correcting a vitamin D deficiency depends heavily on maintaining overall ion homeostasis, particularly regarding serum calcium. Evidence from analyzed studies suggests that low serum levels of calcium and vitamin D during the luteal phase act in tandem to aggravate neuromuscular excitability and emotional distress [19]. Therefore,

isolated monotherapy without accounting for dietary calcium intake may provide suboptimal clinical outcomes. Furthermore, while natural progesterone supplementation has historically demonstrated inconsistent therapeutic benefits—due to conversion into adverse neurosteroids or cycle disruption—nutritional optimization through vitamin D supports natural steroidogenesis and fine-tunes ovarian sensitivity to follicle-stimulating hormone (FSH) without artificial endocrine suppression [6, 13, 23].

4.4 Research Gaps and Future Perspectives

A significant limitation identified in current literature is the presence of small sample sizes and highly heterogeneous study designs across clinical trials. While the biological links between vitamin D, serotonin synthesis, and anti-inflammatory pathways are well-established, standardized dosing guidelines tailored to the specific phases of the menstrual cycle remain absent [33,34].

Furthermore, emerging evidence indicates a regulatory link between vitamin D signaling and Anti-Müllerian hormone (AMH) production, which directly impacts primordial follicle recruitment and long-term reproductive health. Future research must utilize large-scale, well-controlled longitudinal trials to explore how variations in vitamin D receptor polymorphisms influence individual responsiveness to supplementation. Establishing these genetic and physiological frameworks will allow clinicians to deliver precise, personalized nutritional protocols that definitively improve psychological and somatic outcomes in women suffering from PMS [29, 35].

5. Conclusions

The literature review of clinical evidence confirms that low serum levels of calcium and vitamin D during the luteal phase of the menstrual cycle significantly contribute to or worsen the physical and emotional symptoms of Premenstrual Syndrome (PMS). However, its role in clinical management must be clearly defined to ensure therapeutic efficacy.

Final Verdict: Standalone Tool vs. Multi-modal Approach

The clinical data suggest that while maintaining adequate vitamin D levels is a highly effective leading strategy, it cannot stand alone as a definitive, universal cure for Premenstrual Syndrome. PMS is a complex, multisystemic disorder resulting from intricate interactions

between hormonal fluctuations, neurotransmitter imbalances, neurosteroid activity, and immune system alterations.

- **Multifactorial Etiology:** Vitamin D effectively regulates ovarian steroidogenesis, neurotransmitter synthesis, and immune function while mitigating neuroinflammation. However, it operates alongside separate pathways, such as progesterone-derived neurosteroid fluctuations (allopregnanolone) and GABAergic/serotonergic signaling, which also heavily dictate mood and stress responses during the luteal phase [22, 34].
- **The "Multi-modal" Necessity:** To move from temporary symptom mitigation to long-term management, vitamin D optimization must be integrated into a broader lifestyle and clinical framework. Vitamin D therapy should be cross-referenced with dietary calcium intake, lifestyle factors, stress-reduction techniques, and regular monitoring of secondary homeostatic systems, such as the renin–angiotensin–aldosterone system, to fully control symptoms like fluid retention and bloating [5,12,20].

Practical Recommendations for Practitioners and Clinicians

To successfully mitigate the severity of PMS and improve both psychological and somatic outcomes, healthcare practitioners should adopt the following evidence-based framework:

1. **Monitor and Restore Serum Levels:** Clinicians should screen women of reproductive age for vitamin D status, aiming to restore and maintain adequate serum 25-hydroxyvitamin D3 ([25(OH)D3]) levels, especially prior to the luteal phase when ovarian hormones accelerate its breakdown [10,18].
2. **Recommend Synergistic Dietary Interventions:** Implement a holistic nutritional approach by recommending a diet rich in vitamin D and calcium, or introducing target supplementation, as an affordable, safe, acceptable, and readily accessible strategy [12].
3. **Address Neuroinflammatory Pathways:** Utilize the immunomodulatory properties of vitamin D to suppress elevated pro-inflammatory cytokines (IL-6, TNF-α) and C-reactive protein (CRP) during the luteal phase, thereby reducing pain sensitivity, cramping, and fatigue [5,12].
4. **Target Neurotransmitter Balances:** Recognize that vitamin D functions as a neurosteroid in the brain; maintaining sufficiency supports central serotonergic and GABAergic function, helping to alleviate premenstrual anxiety, irritability, and depressive symptoms [21, 22].
5. **Acknowledge Current Research Limitations:** Practitioners must tailor interventions carefully, recognizing that current literature is limited by small sample sizes and

heterogeneous study designs. Large-scale, well-controlled longitudinal studies remain necessary to establish definitive, individualized clinical protocols [15, 17].

In summary, maintaining adequate vitamin D levels provides an affordable, safe, and highly responsive approach to managing PMS. When integrated into a multi-modal health strategy, understanding these interconnected neurobiological mechanisms allows for a shift toward a dynamic, physiological-feedback-driven treatment philosophy, significantly improving the quality of life for millions of women of reproductive age

Disclosure:

Author's Contribution Statement:

Conceptualization: Dominika Cholewa

Methodology: Radosław Starzyk, Sara Śmiałek, Dominika Cholewa

Investigation: Radosław Starzyk, Julia Florek, Natalia Guzik

Writing –rough preparation: Natalia Guzik, Julia Florek, Sara Śmiałek, Dominik Jaklik

Writing –review and editing: Dominik Jaklik, Wiktor Słaby, Adrian Groele, Patrycja Dębska

Project administration: Radosław Starzyk, Marcin Miczek, Dominika Cholewa

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