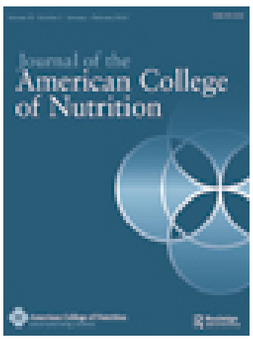

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The Association Between Vitamin D and Premenstrual Syndrome: A Systematic Review and Meta-Analysis of Current Literature

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ABSTRACT

A number of studies have assessed the association between vitamin D and premenstrual syndrome (PMS) in different populations, but the findings have been inconclusive. Herein, we systematically reviewed available observational and interventional evidence to elucidate the overall relationship between vitamin D and PMS. PubMed, Cochrane Library, ScienceDirect, Scopus, Google Scholar, and ISI Web of Science databases were searched for all available articles until September 2018. The Newcastle-Ottawa quality assessment scale and Jadad scale were used to assess the quality of the observational and interventional studies, respectively. A total of 16 studies out of 196 met our inclusion criteria and were included in the final analysis. Although no significant association between serum 25(OH)D and PMS (weighted mean difference (WMD) = 3.35; 95% confidence interval, −7.80 to 1.11; $p = 0.14$) was indicated in observational studies, vitamin D supplementation was effective in ameliorating PMS symptoms based upon findings from interventional studies. These results add to the existing literature supporting the fact that nutrition, especially vitamin D, plays an important role in women's health. Additional well-designed clinical trials should be considered in future research to develop firm conclusions on the efficacy of vitamin D on PMS.

KEY TEACHING POINTS

- 5–8% of women experience severe PMS.
- Nutrition especially vitamin D plays an important role in the women's health.
- Vitamin D could exert significant clinical effects on PMS symptoms.
- This is a systematic review and meta-analysis in this regard.

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Vitamin D; premenstrual syndrome; PMS; systematic review; meta-analysis

Introduction

Premenstrual syndrome (PMS) is characterized by cyclic occurrence of physical, affective, and behavioral symptoms in the luteal phase of the menstrual cycle (1). The main symptoms are dizziness, palpitations, headache, edema, mastalgia, abdominal pain, anxiety, depressive feelings, agitation, and aggression (2). Generally, symptoms are mild, but 5% to 8% of women experience severe PMS (3).

Hypotheses about the causes of PMS include endocrine factors such as hypoglycemia, hyperprolactinemia, fluctuations in the levels of circulating estradiol and progesterone, and excessive amounts of aldosterone or antidiuretic hormone or lower nocturnal melatonin concentrations, neurotransmitter involvement, including serotonin and gabaaminobutyric acid (GABA). None of these hypotheses has been scientifically proven (2). The manifestations of PMS may be serious enough to disturb women's regular functioning, quality of life, and social relationships and lead to increased rates of suicides, accidents, joblessness, work and school absenteeism, and poor scholastic execution. Moreover, reproductive health issues such as child abuse and domestic violence have also been documented in families with individuals experiencing PMS. This syndrome not only influences the individual herself but also has consequences for the family and even the society (4); therefore, sufficient attention is needed to decrease its undesirable effects.

Based on the literature, many different pharmacological treatments, including hormone therapy, have been recommended as possible options for women with PMS (5). These therapies may be effective at resolving PMS in many women, but they are also associated with significant side effects and can be expensive. Alternatives to hormone therapy, such as dietary supplementation, are being evaluated (6). Nonpharmacologic management with some evidence for efficacy includes cognitive-behavioral relaxation therapy, aerobic exercise, as well as calcium, magnesium, vitamin B6, or L-tryptophan supplementation or intake of complex carbohydrates (7).

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Vitamin D is a neurosteroid with the ability to cross the blood–brain barrier. Vitamin D receptors are distributed in areas of the brain associated with the development of depression and related mood disorders. Therefore, it has been speculated that vitamin D may exert significant clinical effects on symptoms such as anxiety, depression, or excessive emotional involvement (8). The initial suggestion that vitamin D may be linked to mood disorders was based on the relation between low vitamin D and high prevalence of seasonal affective disorder in winter at high latitudes (9). Since then, a number of studies had been published, but results have been often inconclusive as to whether low levels of vitamin D may be considered a cause or consequence of mood disorders (8). Based on these observations and the fact that these disorders share common features with PMS, the possibility that vitamin D itself can be useful in alleviating mood disorders associated with PMS has been evaluated in various studies. Several interventional studies found that vitamin D supplementation was associated with reductions in the incidence of several symptoms of PMS such as anxiety, irritability, crying easily, and disturbed relationships (8,10–12). Also, there is cross-sectional evidence indicating an evident association between PMS symptoms and vitamin D status (13,14). However, the results were inconsistent and several observational studies found no difference in vitamin D status in PMS and healthy subjects (15–18).

To address the divergence mentioned above, we carried out this systematic review and meta-analysis on the observational and interventional studies to explore the association between vitamin D and PMS in general populations to reach a conclusion in this regard.

Methods and materials

This study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement and was registered on PROSPERO database (CRD42018109214) (19).

Data source and search strategy

We searched databases, including PubMed, Scopus, Cochrane Library, ScienceDirect, and ISI Web of Science, up to September 2018 to identify relevant studies. The reference lists of the included articles were also reviewed to identify additional eligible studies. In order to increase the power of our search strategy and minimize the chance of missing relevant articles, we also contacted the expert scientists in the field of vitamin D and PMS. The following search strategy was run in PubMed and tailored to each database when necessary: (((((((vitamin d[MeSH Terms]) OR 25 Hydroxyvitamin D[Title/Abstract]) OR cholecalciferol [Title/Abstract]) OR ergocalciferol[Title/Abstract]) OR calcitriol[Title/Abstract]) AND premenstrual syndrome[MeSH Terms]) OR premenstrual tension[Title/Abstract]) OR PMS[Title/Abstract].

Inclusion criteria

To be included in the study, publications investigating the association between vitamin D and PMS or its symptoms had to meet the following criteria: (1) original articles; (3) human studies with no restrictions on study parameters (study duration, design, or sample size); (5) adequate data to calculate a relevant measure of association (mean difference, odds ratio, Pearson's correlation coefficient [r], or Spearman's rho [ρ]); (4) articles published in English.

Data extraction

Pairs of independent reviewers screened the titles and abstracts of each study prior to full-text screening of candidate studies. Any discrepancies in terms of decision on a given study were dealt with via discussion and, if necessary, arbitration by a third reviewer. For all included studies, two reviewers independently extracted information, including first author's name, year of publication, country, sample size, participants' age, gender, study design, dietary and PMS assessment method, dosage of administered vitamin D, and statistical adjustment.

Study quality

The Newcastle-Ottawa Quality Assessment Scale was used to assess the quality of the observational studies (20). The scale consists of assessment of three domains: selection (5 points), comparability (2 points), and outcome (3 points), for a total score of 10 points. Studies scoring 7 to 10, 3 to 6, and 0 to 3 points were identified as high-, moderate-, and low-quality, respectively (21).

The Jadad scale for reporting randomized clinical trials was used to assess the quality of the interventional studies. In this scale, articles are evaluated based on randomization (mentioned as randomized gets 1 point and mentioned randomization methods gets another point), blinding (mentioned as double blind gets 1 point and mentioned blinding methods gets another point), and inclusion of participants (mentioned withdrawals and dropouts gets 1 point). Studies with 3 points or more are ranked as high-quality (22).

Statistical analysis

Meta-analysis was performed using weighted mean difference (WMD) with 95% confidence intervals (CIs) for assessing the association between serum vitamin D levels and PMS. If heterogeneity presented between studies, the random effects model was used; otherwise, the fixed effects model was used. Sensitivity analyses were also performed to assess the influence of each individual study on the stability of the meta-analysis results. Each time, one study was excluded to show the impact of that study on the combined effect estimate. We also conducted subgroup analyses based on different factors including quality, location, and design of the studies.

Assessment of heterogeneity

Heterogeneity of the study results was estimated by the chi-squared (χ^2) test and quantified using the I^2 statistic, which

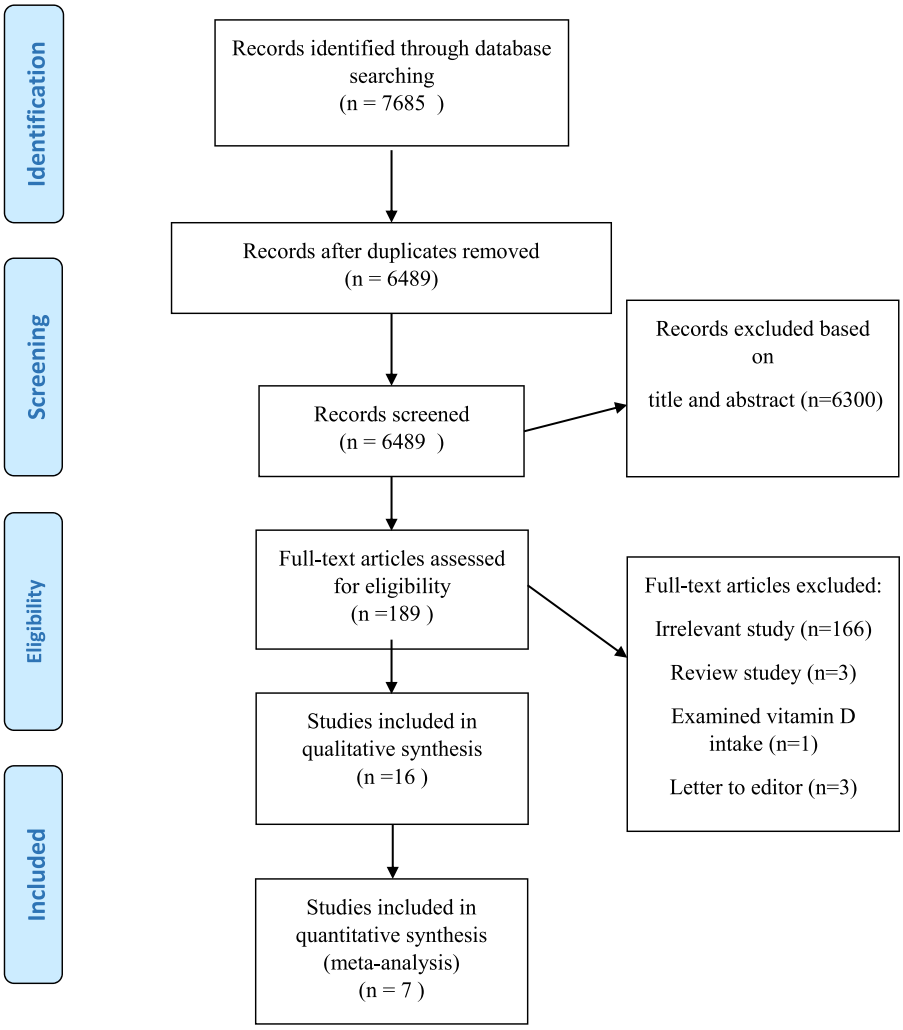

Figure 1. The flow diagram of study selection.

represents the percentage of total variation across studies attributable to heterogeneity rather than to chance. I^2 was calculated using the formula: $I^2 = 100\% \times (Q - df)/Q$ (where Q is the chi squared statistic, and df is the degree of freedom), and an I^2 value of 75% or greater was deemed to indicate a high level of inconsistency. Significant heterogeneity was defined as a p value of <0.05 (21).

Assessment of publication bias

Publication bias was assessed by visual inspection of the funnel plots, and Egger's and Begg's tests were conducted to determine the degree of funnel plot asymmetry, with $p < 0.05$ representing significant publication bias (21).

Results

Search results

Our initial search through databases identified a total of 7685 articles. Removing duplicates yielded 6489 articles, which were reviewed based on the title and abstract by two independent reviewers and 6300 irrelevant studies excluded at this stage. One hundred eighty-nine articles were retrieved and reviewed based on full text, and 16 articles met the inclusion criteria and were included in our systematic review and meta-analysis. The PRISMA flow diagram summarizes the results of the study selection process for this systematic review and meta-analysis (Figure 1).

Overview of included studies

A total of 16 articles including 5 interventional (8,10–12,23) and 11 observational studies (13–18,24–28) with a total of 4946 participants were included in our systematic review. Of these studies, 7 were eligible to be included in the meta-analysis (14–18,24,28). The included studies were conducted between 1995 and 2018. Among the included studies, 8 were from Iran (10–12,17,23,24,26,28), 4 were from the United States (14–16,18), and the others were published from Canada (13), Italy (8), Kuwait (25), and Jordan (27). Among the included observational studies, 7 and 4 studies had cross-sectional (13–15,18,25–27) and case control designs (16,17,24,28), respectively. Among interventional studies, 3 were randomized clinical trials (RCTs) (8,12,23) and 2 were of quasi-experimental design (10,11). Only 5 studies (13,15–18) examined the dietary intakes of participants and

Table 1. Characteristics of interventional studies.

Author, Year	Location	Sample size	Age range	Duration	Study design	DAM	PMSAM	Vitamin D dosage	Adjustment	Result	Quality score
Tartagni et al. 2016	Italy	158	15–21	4 months	RCT	–	PDSR	25,000 IU every 2 weeks	–	Vitamin D significantly decrease PMS symptoms	3/5
Khajehei et al. 2009	Iran	180	18–26	2 months	RCT	–	GHQ-28	200 mg D plus 500 mg Calcium twice daily	–	Vitamin D plus calcium significantly decrease PMS score	5/5
Dadkhah et al. 2016	Iran	86	15–45	2 months	RCT	–	PDSR	200 mg daily	–	NS	3/5
Bahrami et al. 2018	Iran	897	12–18	9 weeks	Quasi-experimental	–	COPE	50,000 IU/week	age, education level, and stress	Vitamin D significantly decreases PMS prevalence and its symptoms like backache and tendency to cry easily	1/5
Karimi et al. 2018	Iran	40	22–48	2 months	Quasi-experimental	–	PSST	200 IU D plus 500 mg calcium twice daily	–	Vitamin D plus calcium significantly decrease PMS score	1/5

Note. DAM = Dietary Assessment Method; MSAM = Premenstrual Syndrome Assessment Method; PMS = premenstrual syndrome; RCT = randomized clinical trial; PDSR = PMS Daily Symptom Record; GHQ-28 = General Health Questionnaires-28; COPE = Calendar of Premenstrual Experiences; PSST = Premenstrual Syndrome Screening Tool; IU = International Unit.

the others did not mention anything (8,10–12,14,23–26,28), except for one study (27) that assessed the intake of dairy products only. Among interventional studies, based on the Jadad scale, 3 studies (8,12,23) ranked as high-quality and 2 as low (10,11). Among 8 observational studies, 5 (13,15–17,26) were identified as high-, 5 as moderate- (14,18,25,27,28) and 1 (24) as low-quality, respectively. Characteristics of included studies are illustrated in Table 1.

Findings from the systematic review

The efficacy of vitamin D supplementation on PMS

The efficacy of vitamin D supplementation in patients with PMS was examined in 3 randomized clinical trials (8,12,23) and 2 quasi-experimental studies (10,11).

In the first study, Bahrami et al. assessed the effects of vitamin D supplementation on dysmenorrhea and PMS in adolescents. In this study, 897 adolescent girls (12–18 years old) were first categorized as follows: those with only PMS; individuals with only dysmenorrhea; subjects with both PMS and dysmenorrhea; and normal subjects and then received 9 high doses of vitamin D (50000 IU/week) for 9 weeks. The prevalence of PMS fell from 14.9% to 4.8% ($p < 0.001$). Also, vitamin D supplementation was associated with reduction in some PMS symptoms such as backache and tendency to cry easily ($p < 0.05$) (10).

In 2018, Karimi et al. investigated the effects of calcium plus vitamin D supplementation among subjects with PMS. In this study, 40 females (aged 22–48) were recruited and then divided into 4 groups in order to receive cognitive-behavioral therapy, supplements (500 mg calcium plus 200 IU vitamin D twice daily), a combination of cognitive-behavioral therapy and supplements, or placebo. Intervention groups compared to controls revealed a significant reduction in PMS score after 2 months of treatment ($p < 0.05$) (11).

Another study evaluated the effects of vitamin D supplementation through an RCT. Eighty-six women (14–45 years old) were randomly assigned to two intervention groups and one control group to receive either 200 mg of vitamin D, 100 mg of vitamin E, or placebo daily for 2 months. Although PMS scores of all groups (vitamin D, vitamin E, placebo) decreased significantly after the intervention ($p < 0.05$), there were no significant differences between intervention groups as compared to placebo regarding to reduction in PMS score ($p > 0.05$) (23).

In 2009, Khajehei et al. conducted a double-blind RCT to compare the effects of dydrogesterone and calcium plus vitamin D in women with severe PMS. In this study, 180 university students (18–26 years old) were enrolled and randomly assigned to receive either 5 mg of dydrogesterone, 500 mg of calcium plus 200 IU of vitamin D, or a placebo twice a day. Results of this study revealed that dydrogesterone and calcium plus vitamin D had the same lessening effect on symptom severity ($p > 0.05$) and that both were more effective than placebo ($p < 0.05$) (12).

In the last study, Tartagni et al. assessed the hypothesis that administration of vitamin D (200,000 IU at first, followed by 25,000 IU every 2 weeks) for a 4-month period could lessen PMS-related complications, including anxiety, irritability, crying easily, sadness, and disturbed relationships. One hundred fifty-eight females (15–21 years old) with PMS-related symptoms and low serum 25-hydroxycholecalciferol (25-OH-D3) levels ($\leq$ 10 ng/mL) were recruited and randomly assigned to group 1 (vitamin D) or group 2 (placebo). After 4 months of intervention, all of the PMS-related complications improved significantly in group 1 as compared to placebo ($p < 0.001$) (8).

The association between serum vitamin D status and PMS

The association between serum vitamin D and PMS was investigated in 7 cross-sectional (13–15,18,25–27) and 4 case-control studies (16,17,24,28). Among these, 7 articles

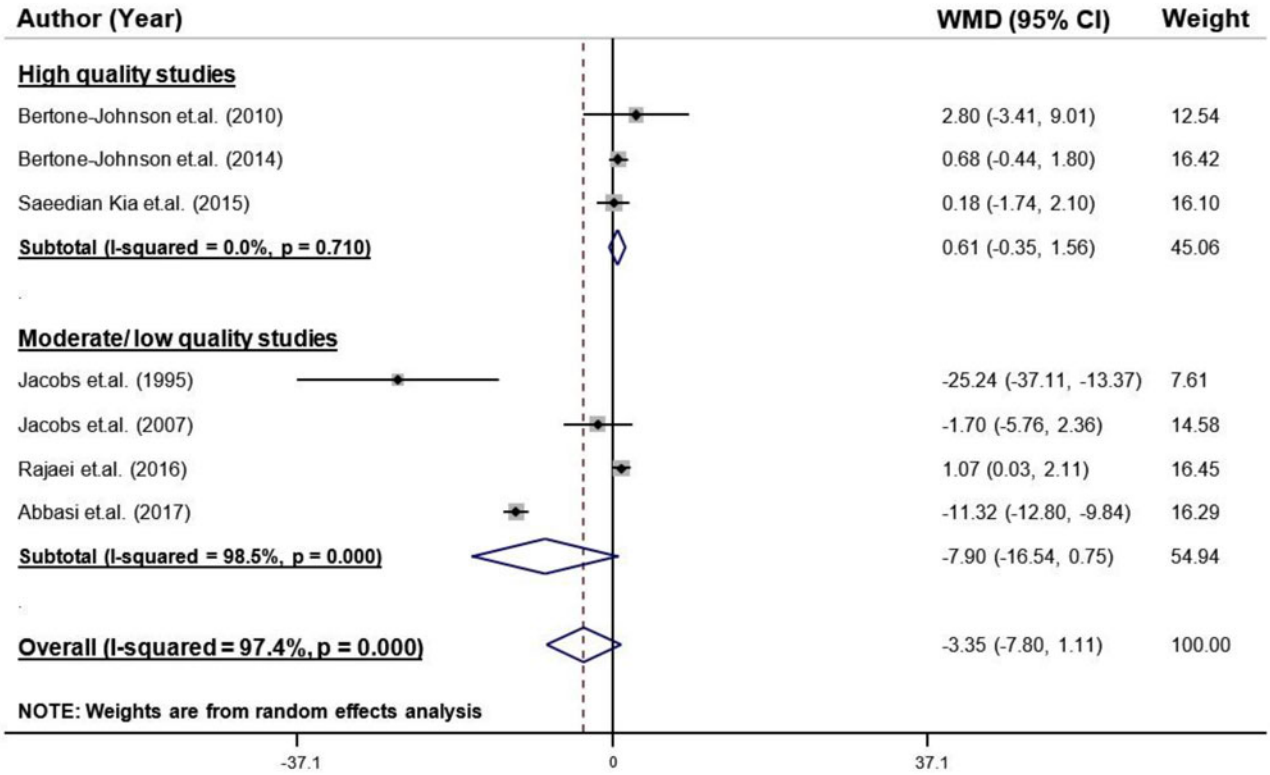

Figure 2. Forest plot of the association between the serum 25(OH)D in premenstrual syndrome and healthy subjects.

met our inclusion criteria and were included in the meta-analysis, and the remaining articles were reported in the systematic review.

In the first study, Jarosz et al. established a cross-sectional study to determine whether vitamin D status is associated with PMS. In this study, 998 women aged 20 to 29 years were recruited and categorized as having adequate ($\geq$ 20 ng/dl) or inadequate (<20 ng/dl) serum 25(OH)D levels. As compared to the participants with adequate vitamin D status, those with inadequate vitamin D status had an increased risk of experiencing the following mild symptoms: confusion and desire to be alone, as well as the following moderate/severe symptoms: cramps, fatigue, anxiety, confusion, and sexual desire ($p > 0.05$) (13).

Another study assessed the relationship between PMS symptoms and serum 25(OH)D among adolescent girls. In this cross-sectional study, 897 high school–aged girls (12–18 years old) were recruited and categorized based on serum 25(OH)D as deficient ($\leq$ 15ng/ml) and nondeficient ($>$ 15 ng/ml). There were no significant associations between vitamin D and PMS symptoms ($p > 0.05$) (26).

In 2012, Obeidat et al. conducted a cross-sectional study to explore the possible association between vitamin D and PMS. A total of 177 female students (18–24 years old) participated and were divided into a healthy group and those having PMS. There was no evident association between prevalence of PMS and its symptoms and vitamin D status ($p > 0.05$) (27).

The last study trying to look into the association between serum levels of vitamin D and PMS included 117 healthy adult women (19–47 years old). There were no significant associations between serum levels of vitamin D and PMS prevalence ($p > 0.05$) (25).

Findings from meta-analysis

Seven studies with 1344 participants examined the association between serum 25(OH)D and PMS among subjects with and without PMS (14–18,24,28). There was no significant association between serum 25(OH)D and PMS (WMD = −3.35; 95% CI, −7.80 to 1.11; $p = 0.14$). There was evidence of heterogeneity between the effect sizes of the included studies (I^2=98.1%; $p < 0.001$), so subgroup analysis was carried out to find the source of heterogeneity based on quality (high vs moderate/low), location (Asia vs America), and design (cross-sectional vs case-control) of the included studies. The heterogeneity decreased significantly in the subgroup of high-quality studies (I^2 = 0.0%; $p = 0.71$), but there was no significant result as well (WMD = 0.61; 95% CI, −0.35 to 1.56; $p = 0.21$) in this subgroup. No evidence of publication bias was found (Begg's test: $p = 0.099$, Egger's test: $p = 0.59$; Figure 2).

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis to evaluate the association between vitamin D and PMS in general populations. Considering the association between calcium supplementation and diets rich in dairy products and decreased PMS complications (29,30), it is hypothesized that vitamin D, as the most calcium-related nutrient (31), may influence the severity of PMS symptoms. In this review of 16 articles, 5 studies examined the efficacy of vitamin D supplementation on PMS complications and 11 observational studies investigated the association between plasma vitamin D and PMS symptoms.

However, we found limited significant results of this association.

In our study, we found no association between serum 25(OH)D and PMS, which is inconsistent with all interventional studies conducted so far. In the case of clinical studies, which all have indicated meaningful associations between vitamin D and PMS, some points should be noted. In one study (10), a very high dose of vitamin D (50000 IU/weekly) was administrated, which is recommended only for treatment of vitamin D deficiency (32). Furthermore, in this study there was no control group, and it is impossible to compare the effect of vitamin D supplementation with placebo effect on PMS severity. Another two studies assessed the effect of calcium plus vitamin D on PMS and gave the proven effects of calcium on relieving some PMS symptoms (12,33); it is difficult to obtain a firm conclusion on the mere effect of vitamin D from these studies. Furthermore, in clinical trials, only one study scored as high-quality, which should be considered when interpreting the results.

Observational studies regarding the association between serum 25(OH)D and PMS have yielded more consistent results from our study. Among the studies reporting higher serum vitamin D levels in subjects with PMS, only one study (16) had significant results in this regard. In this study, although vitamin D levels were not associated with the overall risk of PMS, a positive association was observed among women already experiencing PMS by the time of blood collection. One potential explanation for this unexpected result is that women with PMS may try to ameliorate their symptoms with multivitamins containing calcium and vitamin D or calcium/D supplements as commended by the American Congress of Obstetricians and Gynecologists (34,35).

In another study (15) enrolled in our meta-analysis, despite the inverse association between vitamin D intake based on Food Frequency Questionnaire and PMS symptoms, there was no relationship between serum 25(OH)D status and PMS severity. According to the author's opinion, this difference in the results for vitamin D intake vs serum vitamin D levels may be due to chance because of their relatively small study sample. In another study (28) which insignificantly showed higher levels of serum vitamin D in individuals with PMS, about 85% of participants were vitamin D–deficient, which can affect the results. It should be noted that only one of the observational studies with significant results regarding the association between vitamin D status and PMS scored high in quality assessment, and due to insufficient quality of studies, it is difficult to draw definitive conclusions.

Some possible reasons have been suggested for these discrepancies in the results. In addition to significant heterogeneity in the case of study population, geographic variation, methods of PMS assessment, seasonal variation in serum concentration of vitamin D, and ethnic heterogeneity of study populations, some points are noteworthy. All observational studies, except for 3 (13,16,27), evaluated the association of vitamin D with prevalence of PMS, not individual premenstrual symptoms. It is important to examine the effects on symptoms and symptom clusters separately because each somatic and affective symptom may have different etiologies, which could relate to their association with vitamin D status. In all clinical studies that proved the effectiveness of vitamin D supplementation on PMS severity, the intervention had effects on the severity of some symptoms, but not others. Also, the observational studies that indicated no association between serum vitamin D and PMS were conducted in populations with high rates of vitamin D deficiency (27,28), which may explain the lack of association, as differences in vitamin D status between those with and without PMS would be negligible. Thus, it is necessary to perform studies in participants with equal distribution of adequate and inadequate vitamin D statuses. Another issue is that none of the included studies considered the effect of vitamin D binding protein status, which may affect the bioavailability of vitamin D and thus the association between vitamin D and health outcomes (36).

As was noted, significant heterogeneity was observed in the included studies. Therefore, we assessed the studies stratified by location, quality score, and study design. Although in high-quality studies the heterogeneity decreased, still there was no association between vitamin D status and PMS in the overall subgroups.

The exact mechanisms of vitamin D's effect on decreased PMS severity are not completely discovered. The greatest relationship between vitamin D and PMS is through its effect on calcium metabolism (30), which has been demonstrated to relieve symptoms such as headache, irritability, and anxiety (33). Also, vitamin D has a proven effect on relieving chronic pain syndrome in PMS. In case of pain as one of the major manifestations of PMS, vitamin D by inhibiting cyclooxygenase and nitric oxide synthase results in decreased levels of prostaglandin and nitric oxide and finally declares pain modulatory effects (37). Another mechanism of vitamin D in pain amelioration in PMS is related to decreasing inflammatory cytokines such as the tumor necrosis factor α, which stimulate pain in the central nervous system (38). Also, it is established that vitamin D regulates production of adrenalin, noradrenaline, and dopamine through vitamin D receptors in the brain (39) and prevents depletion of dopamine and serotonin centrally (40). Hence, vitamin D modifies depression and mood disorders that share common features with PMS (16).

To the best of our knowledge, this is the first systematic review and meta-analysis assessing the relationship between vitamin D status and PMS in observational and interventional studies. We performed a methodologically strict systematic review of the literature. Like all reviews, there are some potential limitations in our study. Considering great differences in the interventional studies in terms of statistical analyses or investigated exposures, our meta-analysis was restricted to observational studies, which usually yielded lower-quality evidence than RCTs. Also, most RCTs included in the systematic review had small sample sizes with short intervention periods. Among five trials, only one had treatment periods longer than 2 menstrual cycles. Another limitation that certainly affects the results is regarding the vitamin D binding protein concentrations and

Table 2. Characteristics of observational studies.

Author, Year	Location	Sample size	Age range	Study Design	DAM	PMSAM	Results	Adjustments	Quality score
Bertone-Johnson et al. 2010	USA	186	18–30	Cross-sectional	FFQ	COPE	Serum vitamin D is not different in PMS and healthy subjects	Age, season, BMI, smoking history, total calcium, and physical activity	8/10
Abbasi et al. 2017	Iran	85	18–28	Case control	–	–	Serum vitamin D is lower in subjects with PMS compared to healthy ones	–	3/10
Bahrami et al. 2018	Iran	897	12–18	Cross-sectional	–	COPE	The vitamin D deficient and non-deficient cases did not differ significantly with respect to PMS	–	7/10
Bertone-Johnson et al. 2014	USA	802	25–42	Case control	FFQ	COPE	Serum Vitamin D is not associated with PMS risk and also is not different in PMS and healthy subjects	Race/ethnicity, geographic region, BMI, physical activity, alcohol intake, smoking status, number of moles on leg, oral contraceptive use, maternal education, antidepressant use, significant childhood trauma, and vitamin B6 intake	9/9
Saeedian Kia et al. 2015	Iran	62	20–22	Case control	24-hour recall questionnaire	Utah PMS Calendar II	Serum Vitamin D is not different in PMS and healthy subjects	–	6/9
Obeidat et al. 2012	Jordan	177	18–24	Cross-sectional	Frequency of dairy intake	–	There was no association between presence of PMS and its symptoms and vitamin D status	–	6/10
Rajaei et al. 2016	Iran	82	18–45	Case control	–	PSST	Serum vitamin D is not different in PMS and healthy subjects	–	5/9
Azizieh et al. 2017	Kuwait	117	19–47	Cross-sectional	–	SRQ	There was no association between presence of PMS and its symptoms and vitamin D status	–	5/10
Jacobs et al. 1995	USA	12	28–45	Cross-sectional	–	PMS Diary	Serum vitamin D is lower in PMS subjects across the menstrual cycle and in midcycle compared to healthy ones	–	5/10
Jacobs et al. 2007	USA	115	26–31	Cross-sectional	Food record	PMS Diary	Serum vitamin D is not different in PMS and healthy subjects	–	6/10
Jarosz et al. 2018	Canada	998	20–29	Cross-sectional	FFQ	GHLQ	There was a significant association between PMS symptoms and vitamin D status	Ethnicity, BMI, physical activity, age, use of hormonal contraceptives or analgesics, season of blood draw, and total calcium intake	9/10

Note. DAM = Dietary Assessment Method; MSAM = Premenstrual Syndrome Assessment Method; PMS = premenstrual syndrome; COPE = Calendar of Premenstrual Experiences; PSST = Premenstrual Syndrome Screening Tool; SRQ = self-reported questionnaire; GHLQ = General Health and Lifestyle Questionnaire; FFQ = Food Frequency Questionnaire; IU = International Unit; BMI = body mass index.

vitamin D receptor polymorphisms, with none of the studies considering this issue. Furthermore, most included studies in the meta-analysis were performed in Iran and United States, so it is difficult to generalize the results to the population at large. Despite this, the results of our review provide an overall picture of the effect of vitamin D supplementation for PMS in populations with prevalent vitamin D deficiency.

Conclusion

Although our meta-analysis of observational studies did not show any significant association between serum vitamin D and PMS, current evidence from clinical studies indicates that vitamin D therapy can be proposed as a safe, effective, and convenient method for improving the quality of life of women with PMS. Based on the present findings, and with the limitations described above, additional well-designed clinical trials should be considered in future research to develop firm conclusions on the association between vitamin D and PMS (Table 2).

Conflict of interest

This manuscript has not been published elsewhere or submitted for publication elsewhere.

The authors have no conflicts of interests. Financial disclosure not declared to this review.

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