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Review article

A systematic review and *meta*-analysis examining the role of zinc supplementation in ameliorating physical and psychological manifestations of premenstrual syndrome in young females

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ABSTRACT

Background and objectives: Zinc has been associated with a reduction in symptoms severity in females with Premenstrual syndrome (PMS) in recent trials. This meta analysis of randomized clinical trials (RCTs) was performed to assess the efficacy of zinc supplements in alleviating the physical and psychological symptoms of PMS.

Methods: A thorough search of electronic repositories was meticulously undertaken until May 2023. Studies that observed the influence of zinc on symptoms severity pertaining to PMS in females were included. A threshold of significance was set at a p-value of 0.05 with 95% confidence intervals (CIs) across all estimates. All statistical analysis was carried out using software Review Manager v.5.4.

Results: This analysis encompassed five studies. Compared to the placebo group, females with PMS who received zinc supplements showed significant improvement in physical health (MD: 3.69, CI: 1.65 – 5.74, P: 0.0004), and physical symptoms (MD: −0.79, CI: −1.39 – −0.20, P: 0.009). Regarding the subdomains of PMS symptoms assessed using the Premenstrual Symptoms Screening Tool (PSST) scale, zinc supplementation was associated with a significant decrease in anger (P: 0.005), anxiety (P: 0.04), and tearfulness (P: < 0.0001). In the interest-related domain, zinc supplementation significantly decreased lack of interest in work activities (P: 0.005) and social activities (P: 0005). Within the cognitive domain, zinc supplementation was associated with a significant decrease in difficulty concentrating ($p = 0.02$). Significant decreases were found for insomnia ($p < 0.00001$), hypersomnia ($p = 0.006$), feeling overwhelmed ($p = 0.05$), and overeating ($p = 0.0003$).

Conclusion: The results of this meta analysis posit zinc as an effective remedy for alleviating symptoms of PMS in young females.

Introduction

Women's well-being is a key focus of global health efforts, as it is closely tied to their overall quality of life, social participation, and economic contributions. Understanding how various health conditions impact women's daily activities is crucial for improving health outcomes. For instance, many challenges that women face in daily life are linked to their menstrual cycle, particularly in relation to premenstrual syndrome (PMS). This condition affects both physical and psychological well-being, often leading to discomfort and reduced quality of life for those experiencing it. Given the complexity of these symptoms, finding effective treatments has been a focus of ongoing research. In this context, recent studies have explored the potential of zinc supplementation as a promising approach to help alleviate both the physical and psychological symptoms of PMS. This systematic review examines the role of zinc in reducing the physical and psychological manifestations of PMS in young females.

PMS is a disorder characterized as a combination of physical, affective, and behavioral symptoms that manifests during the luteal phase of the menstrual cycle, lasts for a few days after the onset of menstruation, and dramatically impairs work performance, social relationships, and quality of life [1–3]. It is estimated that approximately 70–90 % of women in their reproductive years experience at least one of the PMS symptoms [4]. The most common symptoms associated with PMS are

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anxiety, irritability, altered appetite, sleep disturbances, and low mood, headache, joint pain, and myalgia, nausea, vomiting, diarrhea, fluid retention, breast tenderness, acne, and fatigue [5,6].

Although the exact etiology of PMS remains unclear, several mechanisms have been identified. It is hypothesized that sex hormone levels during the menstrual cycle have more fluctuations in women with PMS [7]. However, few studies opposed this, as no difference was found in hormone levels among healthy and PMS females [8,9]. Another important theory is the alteration in progesterone and its metabolite allopregnanolone, a gamma-aminobutyric acid-A (GABA-A) agonist, during the luteal phase [10] which may cause oxidative stress, hormonal imbalance, and an altered GABAergic system, perpetuating PMS symptoms [11].

Zinc (Zn) metabolism has been foregrounded as one of the important mechanisms related to PMS due to its antioxidant activity, role in progesterone binding, gonadal and prolactin secretion, opiate response, and regulatory effects on the menstrual cycle [12]. Low levels of zinc in the body due to insufficient intake are linked to increased glucocorticoid production, resulting in neurologic and psychologic features such as irritability, emotional instability, and depression, frequent in PMS [13]. It has been speculated that inflammation has a role in the development of PMS, or premenstrual symptoms [14]. There is an increase in inflammatory mediators during the menstrual cycle in women of reproductive age [15] and this inflammatory response has been suggested to aggravate symptoms of PMS, such as elevated C-reactive protein (CRP) levels, which have been shown to exacerbate pain and mood symptoms in PMS [16]. Being an anti-inflammatory agent, Zn adjusts levels of certain inflammatory markers, including high-sensitivity CRP, which has been reported to mitigate PMS symptoms [17]. Furthermore, Zn also enhances gene expression of certain neurotrophic factors owing to its antidepressant action [18]. Multiple pieces of evidence have appeared over recent years supporting improvement in PMS symptoms after zinc supplementation in human-based clinical settings [17,19,20–22]. Accordingly, we aimed to systematically accumulate evidence from these studies and produce well-powered results regarding the efficacy of zinc supplementation in the management of PMS.

Methods

Analysis registration

The measures outlining the specific steps for this research have been documented and registered with the "PROSPERO (International Prospective Register of Systematic Reviews)" database, where it has been assigned the unique identifier of protocol number CRD42023428758.

Strategy for literature search

Literature search was conducted according to the instructions elucidated in the March 2020 version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [23]. Two researchers autonomously conducted thorough searches in the digital repositories of scholarly literature, including Medline, Embase, Scopus, and Cochrane Library. The pertinent publications were meticulously investigated and deemed suitable. During the process of analysis and evaluation, the conflicting perspective regarding the incorporation of specific studies was effectively resolved by the intervention of the alternate researcher. In the pursuit of an exhaustive search strategy, the following terms were utilized from the beginning until May 2023: premenstrual syndrome, physical symptoms, psychological symptoms, premenstrual symptoms, young females, young women, zinc, zinc gluconate, and zinc sulfate. The conjunction "and" was employed for the purpose of connecting clusters, while within the same grouping, the terms were combined using the conjunction "or." The aggregate of search outcomes from all authors was consolidated to remove duplicate articles. The search strategy had no language restrictions. We also did not use filters for study design or set any specific time limits for the studies included. In addition, the review encompassed an assessment of research papers obtained from the reference citations, with the aim of identifying potential avenues for supplementary study.

Study selection

The adoption of the PICOS model facilitated the retrieval of pertinent literature, emphasizing studies that juxtaposed the effectiveness of zinc supplementation as opposed to placebo in ameliorating the somatic and psychological manifestations experienced by adolescent females afflicted with premenstrual syndrome [24]. We undertook a meticulous and exhaustive exploration, scouring literature for articles that precisely targeted the specific demographic of adolescent girls dealing with the debilitating effects of premenstrual syndrome. The articles delved into the utilization of zinc supplements as an interventional approach and juxtaposed it with a placebo group that refrained from consuming zinc supplements. The outcomes investigated encompassed a broad spectrum, including the assessment of physical symptoms, physical well-being, and psychological manifestations. The studies included in the review adhered to rigorous design criteria, specifically randomized investigations. The parameters employed for ascertaining the admissibility of investigations in the *meta*-analysis were as delineated below: (1) randomized trials; (2) restriction to young women within the age range of 18 to 35 years who encounter premenstrual syndrome (PMS); (3) participants diagnosed with PMS based on established criteria or self-reported symptoms of PMS; (4) incorporation of studies where zinc was integrated as an interventional modality. We eliminated any studies that encompassed individuals with concomitant medical conditions or disorders that could exert a substantial influence on PMS manifestations (e.g., endocrine disorders, psychiatric disorders); studies concentrating on pregnant or postpartum females; participants with a past medical record of zinc insufficiency or additional particular nutritional insufficiencies; studies encompassing individuals who have utilized hormonal contraceptives or other pharmaceutical agents that might impact PMS symptoms; studies involving participants who have formerly undergone zinc supplementation for PMS. Trials that compared different interventions or failed to disclose a pertinent outcome, proceedings from academic conferences, written correspondences, and specific clinical cases were not included in the analysis. A detailed list of excluded studies and the reasons for their exclusion is provided in Appendix Table 1. To delineate the appraisal and categorization procedures of the exploration, a PRISMA schematic representation was deployed (Fig. 1).

Data retrieval and quality assessment

The data extraction endeavor was undertaken by a pair of self-directed investigators, operating in a state of complete autonomy. For every manuscript included intricate particulars including the primary author, nation of provenance, study design, age cohort, publication year, number of participants within the zinc and placebo cohorts, amalgamated sample magnitude, as well as the outcome measures, were assimilated within a meticulously tailored Excel spreadsheet. The limited number of studies in this *meta*-analysis precluded the execution of a funnel plot to assess publication bias. The application of the Cochrane Collaboration's apparatus for appraising the propensity towards bias was enacted to segregate randomized studies into either substandard or elevated quality categories [25].

Statistical analysis and outcome appraisal

The application of the inverse variance tool was enacted to ascertain the mean differences (MD) pertaining to continuous data sequences. Across all scenarios, a threshold of statistical significance was set at a p-value of 0.05, accompanied by the provision of a 95 % confidence interval (CI) for all estimations. The determination of heterogeneity

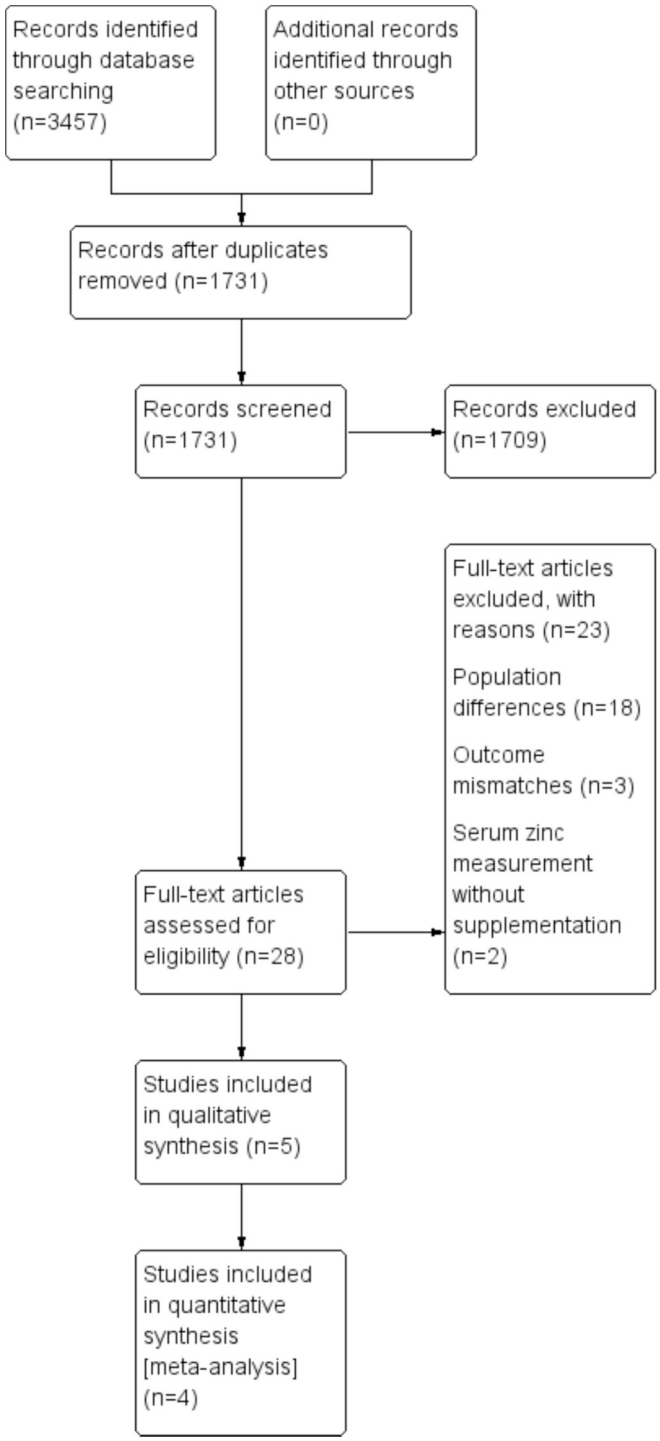

Fig. 1. Schematic representation of literature appraisal process.

encompassed the application of the Higgins I^2 statistic, wherein a conspicuous heterogeneity was indicated by an I^2 value surpassing 50 % [26]. We also performed a sensitivity analysis, progressively removing one study at a time, to determine whether any individual study had a substantial impact on the overall results. The estimate of publication bias remained indeterminable due to the paucity of pertinent publications as there were fewer than 10 studies [27]. Consequently, a meticulous evaluation of sensitivity was undertaken through the deliberate elimination of specific publications at intermittent intervals, aiming to identify any disproportionately influential investigations that might have affected the observed outcomes. To carefully examine each result separately, we adopted a random-effects framework. In order to ensure a thorough review of the data, the rigorous analysis process included the precise use of post-intervention metrics for both the zinc and control cohorts. Through the implementation of application Review Manager v.5.4, the statistical analysis was meticulously executed with utmost precision [28]. Outcome measures included physical health, physical symptoms, and various subdomains of PMS symptoms assessed using the Premenstrual Symptoms Screening Tool (PSST) scale.

Results

Baseline attributes

This extensive evaluation encompasses a combined total of five publications [17,19,20–22]. The participants were university-going females between the ages of 18 and 35. Studies that were included in quantitative analysis intervention duration ranged from 84 days to 168 days [17,19,20,22]. Included studies administered oral zinc supplements either as zinc sulfate [19,22] or zinc gluconate [17,20]. Table 1 depicts the baseline attributes. The outcomes stemming from the assessment of bias risk were presented in the supplementary documentation, specifically encapsulated in Appendix Figs. 1 and 2. Within the supplementary documentation, Appendix Table 2 depicts a thorough presentation of the standards that were employed to ascertain which individuals were suitable for enrollment and which were disqualified from participation in each trial. The majority of the included studies implemented specific controls to minimize the influence of other treatments, ensuring that the effects of zinc supplementation were assessed in isolation [17,19,20,21], as depicted in Appendix Table 3.

Outcomes

The quantitative analysis included four studies, all of which had a follow-up period of twelve weeks [17,19,20,22]. However, one particular study conducted by Ahmadi et al had the longest follow-up duration of 24 weeks [19]. To ensure the utmost precision in our aggregated analysis, we considered the statistics presented in the same publication for various follow-up durations as distinct occurrences [19].

Physical health: According to the pooled analysis, people who consumed zinc supplements had significantly improved physical health than those in the control cohort (MD: 3.69, CI: 1.65 – 5.74, I2 = 62 %, P: 0.0004) (Fig. 2).

Physical symptoms: In accordance with the quantitative analysis, those who consumed zinc demonstrated a significant decline in physical symptoms than those in the placebo group (MD: −0.79, CI: −1.39 – −0.20, I^2 = 94 %, P: 0.009) (Fig. 3).

PSST subdomains: The analysis offers insights into the assessment of Premenstrual Syndrome (PMS) symptoms using the PSST scale. The PSST scale is designed to measure the severity of PMS symptoms in various subdomains. The analysis comprised a total of 13 items from the PSST scale, encompassing a wide range of PMS symptoms (Fig. 4). Among emotional symptoms, a significant decrease in anger (MD: −0.97, CI: −1.66 – −0.28, I^2 = 87 %, P: 0.005), anxiety (MD: −0.95, CI: −1.88 – −0.02, I^2 = 93 %, P: 0.04), and tearfulness (MD: −0.49, CI: −0.72 – 0.26, I^2 = 0 %, P: < 0.0001) was observed. In the mood-related domain, a non-significant association in depressed mood was noted (MD: −0.48, CI: −1.02 – 0.06, I^2 = 69 %, P: 0.07). However, overeating (MD: −0.63, CI: −0.96 – −0.3, I2 = 39 %, P: 0.0003), insomnia (MD: −1.01, CI: −1.45 – −0.57, I2 = 72 %, P: < 0.00001), and hypersomnia (MD: −1.07, CI: −1.84 – −0.31, I^2 = 88 %, P: 0.006) exhibited significant decreases within the eating and sleep-related domains respectively. Interest-related symptoms demonstrated a substantial decrease in the lack of interest specifically towards work activities (MD: −0.89, CI: −1.50 – −0.28, I^2 = 82 %, P: 0.005) and social activities (MD: −0.44, CI: −0.68 – −0.2, I^2 = 0 %, P: 0.0005). While no significant effects were observed for home activities (MD: −0.45, CI: −0.95 – 0.05, I^2 = 71 %, P:

Table 1
Baseline attributes of included studies.

Study ID	Sangestani G 2015	Siahbazi S 2017	Jafari F 2020 March	Jafari F 2020 September	Ahmedi M 2022
Study population	Female university students with primary dysmenorrhea over the course of the past 3 menstrual cycles. (spanning from 21 to 35 days)	Females exhibiting a regular menstrual cycle occurring within a duration of 21–35 days, BMI between 19.8–26 kg/m2, aged between 20–35 years, with premenstrual syndrome.	Unmarried, female university students exhibiting a regular menstruation occurring within a span of 21–35 days, BMI between 18.5 and 24.9, aged between 18–30 years, diagnosed with premenstrual syndrome.	Unmarried, female university students exhibiting a regular menstruation occurring within a span of 21–35 days, BMI between 18.5 and 24.9, aged between 18–30 years, diagnosed with premenstrual syndrome.	Female university students aged between 18–35 years with premenstrual syndrome.
Study design	RCT	RCT	RCT	RCT	RCT
Sample size	66	142	60	60	69
Intervention duration	4 days	12 weeks	12 weeks	12 weeks	24 weeks
Intervention	oral zinc supplements (50 mg) twice daily (n = 34)	oral zinc sulfate supplements (50 mg) (n = 71)	oral zinc gluconate supplements (30 mg) (n = 30)	oral zinc gluconate supplements (30 mg) (n = 30)	oral zinc sulfate supplements (50 mg) (n = 33)
Control	Not specified (n = 32)	sucrose 220 mg (n = 71)	Not specified (n = 30)	starch (n = 30)	Not specified (n = 36)
Age (years) mean ± SD	21.5 ± 2.5 (intervention group) 21.7 ± 2.2 (control group)	22.4 ± 3 (intervention group) 22.6 ± 2.2 (control group)	23.04 ± 2.97 (intervention group) 22.53 ± 1.85 (control group)	23.04 ± 2.97 (intervention group) 22.53 ± 1.85 (control group)	25.64 ± 0.53 (intervention group) 24.38 ± 0.51 (control group)
BMI (kg/m^2) mean ± SD	Not specified	21.8 ± 1.6 (intervention group) 21.8 ± 1.2 (control group)	21.39 ± 2.00 (intervention group) 21.03 ± 1.90 (control group)	21.39 ± 2.00 (intervention group) 21.03 ± 1.90 (control group)	NR
Age at menarche (years)	13.2 ± 1.0 (intervention group) 13.6 ± 1.3 (control group)	13.3 ± 1.7 (intervention group) 13.5 ± 1.2 (control group)	12.10 ± 1.21 (intervention group) 12.26 ± 1.36 (control group)	12.10 ± 1.21 (intervention group) 12.26 ± 1.36 (control group)	NR
Cycle length (days)	28.26 ± 2.6 (intervention group) 27.66 ± 2.8 (control group)	29 ± 1.7 (intervention group) 28.8 ± 1.5 (control group)	27.73 ± 2.53 (intervention group) 27.56 ± 2.92 (control group)	27.73 ± 2.53 (intervention group) 27.56 ± 2.92 (control group)	NR
Duration of menstruation (days)	6.15 ± 1.3 (intervention group) 5.62 ± 1.3 (control group)	6.06 ± 1.01 (intervention group) 6 ± 1.08 (control group)	6.56 ± 0.77 (intervention group) 6.23 ± 1.19 (control group)	6.56 ± 0.77 (intervention group) 6.23 ± 1.19 (control group)	NR
Outcomes assessed	Duration of menstruation, Interval between menses, Severity of bleeding, Severity of dysmenorrhea, Premenstrual symptoms (headache, vertigo, nausea, vomiting, diarrhea, constipation, urinary urgency, muscular pain, weakness, disability in performing daily activities), Rate of doctor visit, Rate of medication use, Tendency to use thermotherapy	PMS symptoms and their degree of interference with daily activities according to the PSST, QOL scores (physical and mental components)	Physical symptoms of PMS, Psychological symptoms of PMS, Serum zinc, TAC, BDNF and hs-CRP levels	Zinc serum level, Sleep quality, QOL domains (environmental aspect of life, physical health, social and personal relationships, and psychological health.)	PSST subdomains (anger, depressed mood, relationship with friends/family, anxiety, tearful, decrease interest in home activities/work activities/social activities, fatigue, difficulty in concentration, hypersomnia, work efficiency, insomnia, overeating, social life activity, feeling overwhelmed, physical symptoms, and home responsibilities.

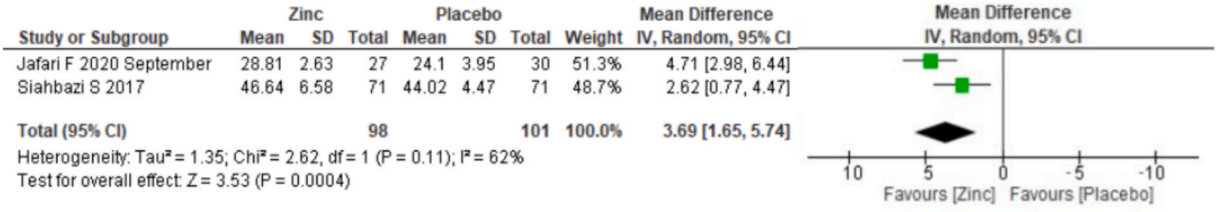

Fig. 2. Forest plot of physical health domain in females with PMS contrasting zinc consumption with placebo.

0.07) and fatigue (MD: −0.76, CI: −1.56 – 0.04, I2 = 94 %, P: 0.06). Difficulty concentrating exhibited a significant association (MD: −1.24, CI: −2.26 – −0.22, I^2 = 93 %, P: 0.02) within the cognitive domain. Feeling overwhelmed displayed a significant decrease (MD: −0.71, CI: −1.42 – 0.00, I^2 = 83 %, P: 0.05) within the general well-being domain.

Discussion

Premenstrual syndrome (PMS) encompasses a wide array of physiological and psychological manifestations encountered by women throughout the luteal phase of their menstrual cycle that resolve spontaneously within a few days after the start of menses [29]. Some of the

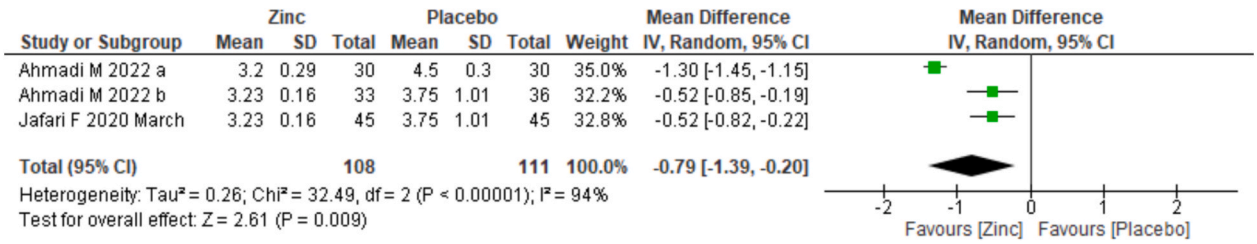

Fig. 3. Forest plot of physical symptoms domain in females with PMS contrasting zinc consumption with placebo.

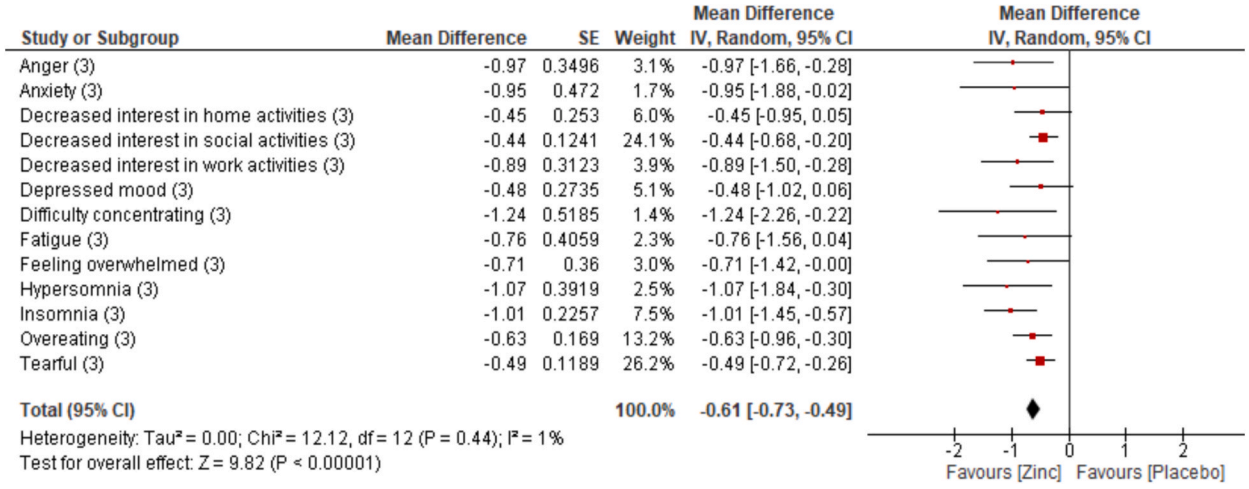

Fig. 4. Forest plot of subdomains of PSST comparing zinc and placebo.

most common manifestations include mood swings, depression, anxiety, bloating, abdominal pain, back aches and breast tenderness. These symptoms can be a source of significant distress for women and may cause impairment in daily life activities [29,30]. The primary objective of PMS management is to relieve the symptoms and improve daily functioning. Mild symptoms can be managed by lifestyle changes such as dietary modifications, exercise, and stress management [31]. However, symptoms that do not respond to non-pharmacologic measures require drug therapy. At present, selective serotonin reuptake inhibitors (SSRIs) are used as the first-line pharmacologic treatment for PMS. Oral contraceptive pills (OCPs), gonadotropin-releasing hormone (GnRH) agonists, and cognitive behavioral therapy (CBT) are some of the alternative treatment options that are being used for the management of moderate to severe symptoms [30,32].

Over the years, several vitamins and minerals have been suggested as potential therapeutic options for the management of PMS, but little scientific research has been done in this regard. In 2019, a systematic review concluded that increasing dietary intake of calcium and vitamin D can help alleviate PMS symptoms [33]. Other studies have reported the beneficial impact of vitamin B6 and magnesium, alone and in combination, in reducing premenstrual complaints [34–36]. In recent years, increasing evidence has emerged in the form of several randomized clinical trials (RCTs) supporting the beneficial role of zinc supplementation in PMS patients [17,19,20–22]. These vitamins and minerals, if proven in their efficacy, can serve as a simple and cheap remedy for managing mild symptoms of PMS alongside lifestyle modifications.

Investigation into a possible relationship between PMS and zinc began as early as 1994, when two separate studies were conducted comparing serum zinc and copper concentrations between PMS patients and healthy subjects [37,38]. Both studies independently reported the same findings: women with PMS had significantly lower plasma zinc levels during the luteal phase in comparison with the follicular phase. In addition, the plasma zinc-to-copper ratio was notably reduced in individuals with PMS during the luteal phase in comparison with healthy individuals (controls). These findings suggested that low plasma zinc concentration may be a contributing factor for PMS, and subsequently, zinc supplementation may be helpful in alleviating the symptoms associated with PMS.

The above hypothesis was put to the test in 2017, when Siahbazi et al. conducted a randomized control trial involving women diagnosed with PMS [22]. Participants in the intervention group were given supplements containing 50 mg of elemental zinc from day 16 of the menstrual cycle until day 2 of the subsequent cycle for 3 months. The study reported a significant reduction in the prevalence of moderate to severe PMS and improvement in all components of PSST in the experimental group. Additionally, there was notable improvement in both physical and mental domains of health-related quality of life after 3 months of intervention [22]. In 2020, Jafari et al. also reported improvement in somatic dimensions pertaining to the overall well-being of females with PMS after 12 weeks of zinc supplementation (30 mg) [20].

In 2022, Ahmadi et al. reported that the provision of a supplement incorporating 220 mg of zinc for 24 weeks resulted in a substantial decrease in both somatic symptoms (mastalgia, headache, myalgia, bloating, and weight gain) as well as psychological symptoms (anger, anxiety, and depression) of PMS [19]. Moreover, there was a significant improvement in social relationships in the group receiving zinc in comparison with placebo [19]. Jafari et al., in their RCT, also reported a noteworthy reduction in both somatic and psychosomatic manifestations of PMS after a 12-week regimen of supplementing with 30 mg of zinc gluconate [17]. Similarly, Sangestani et al. also found a significant improvement in premenstrual complaints such as vertigo, myalgia, generalized weakness, and impairment in daily life functioning after supplementation with 50 mg zinc [21].

The growing pool of evidence supporting the impact of zinc on improving PMS symptoms prompted us to perform this *meta*-analysis so as to aggregate data from different studies and yield robust conclusions

about the role of zinc in the management of PMS. The results of our analysis showed that taking zinc supplements causes a significant reduction in the physical symptoms of PMS and an improvement in overall physical health. Analysis of the PSST components showed marked improvement in the non-physical manifestations of PMS as well, such as anger, anxiety, tearfulness, difficulty concentrating, work-related lack of interest, overeating, feeling overwhelmed, and sleep issues. The exact mode of action is not known, however, several mechanisms have been proposed. First of all, zinc has both anti-inflammatory and antioxidant properties [39]. These effects are thought to be responsible for reducing the physical symptoms associated with PMS. Jafari et al. found in their study that 12 weeks of supplementation with zinc significantly raised the total antioxidant capacity in women with PMS [17]. Secondly, zinc modulates serotonin levels, and a deficiency of serotonin is thought to be responsible for many of the manifestations of PMS [40]. Moreover, zinc is also needed for the synthesis of GABA and melatonin [41,42] both of which regulate the function of dopamine, which has an important role in the pathogenesis of PMS [43].

The included studies primarily aimed to assess the effects of zinc supplementation on PMS symptoms while minimizing the influence of other treatment modalities. Four studies [17,19,20,21] implemented strict controls to ensure that participants did not use additional medications or supplements during the study period. However, a study conducted by Sangestani et al. restricted symptom relief methods to mefenamic acid or local thermotherapy [22]. Overall, while prior treatment history was not consistently documented across all studies, the study designs largely sought to minimize confounding variables by controlling concurrent treatments and standardizing participant conditions. This approach enhances the reliability of the findings, ensuring that any observed effects on PMS symptoms can be primarily attributed to zinc supplementation. However, caution is warranted when interpreting these results, as the extent of prior treatment use was not always explicitly detailed, and individual variations in treatment history could still influence outcomes. Future studies should consider systematically documenting participants' previous PMS treatments to further refine the assessment of zinc's independent effects.

The limitations of our research are confined to the studies that have been included in the final analysis. Firstly, a notable limitation is the predominant representation of studies from Iran. While our search strategy was comprehensive and encompassed multiple databases without any specific timeframe or regional restrictions, it appears that relevant studies from other regions are limited or possibly underrepresented in the databases we accessed. This geographical bias might influence the generalizability of our results to a global context. The concentration of studies from a single region raises the possibility of publication bias, as research findings from other parts of the world may not be equally available or indexed in the databases searched. Additionally, cultural, dietary, and genetic differences could influence the response to zinc supplementation, potentially affecting the applicability of our findings to diverse populations. Future research should aim to include studies from a broader range of geographical locations to enhance the external validity of conclusions regarding zinc supplementation for PMS symptom management.

Secondly, in several studies, PMS symptoms were reported by the participants based on their memory, so there is a risk of recall bias. Small sample sizes and short durations of intervention in a few studies can be some additional limitations. Furthermore, the heterogeneity associated with the outcomes and any ongoing clinical trials that are yet to be published can also potentiate the risk of bias. In spite of these limitations, our *meta*-analysis substantiates the beneficial impact of zinc supplementation on PMS patients. Zinc can serve as a safe, cost-effective, and convenient remedy for alleviating the symptoms of PMS and improving the quality of life for women of reproductive age.

Conclusion

Our analysis indicates that zinc supplementation is associated with a significant reduction in the physical symptoms of PMS and improvements in psychological well-being, including anger, anxiety, mood disturbances, cognitive difficulties, and sleep-related issues. However, these findings should be interpreted with caution due to the relatively small sample sizes, variability in zinc dosage and supplementation duration, and the absence of long-term follow-up in the included studies.

While zinc appears to be a promising and accessible option for PMS symptom management, the current evidence is insufficient to establish definitive recommendations regarding the optimal dose and duration of supplementation. Further well-designed, large-scale studies with standardized protocols and extended follow-up are needed to confirm these findings and assess the long-term safety and efficacy of zinc supplementation. In the meantime, zinc may be considered as an over-the-counter supplement, for individuals seeking additional support in managing PMS symptoms.

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Data sharing

Access to the data outlined in the analytic code, manuscript, and code book will be granted following a request process that is subject to approval.

CRediT authorship contribution statement

Samna Haider: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation. **Mariam Sajjad:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Data curation, Conceptualization. **Mariyam Zahid:** Writing – original draft, Investigation, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2025.114082.

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