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Vitamin D Deficiency and Mastalgia: A Prospective Controlled Study on Prevalence and the Therapeutic Impact of Supplementation

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ABSTRACT

Objective: To investigate the relationship between vitamin D deficiency and mastalgia and assess the effectiveness of vitamin D supplementation in alleviating mastalgia symptoms.

Materials and Methods: A prospective investigational study conducted in an Indian tertiary teaching centre. Participants were included if the presented with mastalgia and controls without mastalgia were also were recruited. Exclusion criteria were malignant pathology; fibroadenoma; other benign breast diseases; or recent therapeutic vitamin D supplementation. Vitamin D deficiency was classified as <20 ng/mL. Women in the mastalgia group with deficiency received 60,000 IU weekly oral vitamin D for eight weeks. Symptom severity was evaluated using a visual analog scale (VAS) at baseline and follow-up intervals of 4, 8, and 12 weeks. Difference in serum vitamin D levels between groups and changes in VAS scores post-supplementation was assessed.

Results: A total of 200 women, including 100 with mastalgia and 100 without (control group), were recruited over two years.The mean serum vitamin D level was significantly lower in the mastalgia group (25.29±7.7 ng/mL) compared to controls (31.46±8.5 ng/mL, p<0.0001). Vitamin D deficiency was more prevalent in the mastalgia group (26% *vs.* 9%, p = 0.001). Post-supplementation, 46% of deficient patients in the mastalgia group reported symptom improvement, with 21% achieving complete resolution. However, 54% reported persistent symptoms despite achieving sufficient vitamin D levels.

Conclusion: Vitamin D deficiency is more prevalent in Indian women with mastalgia, and supplementation provides symptomatic relief for some patients. However, a significant proportion of patients continue to experience symptoms, suggesting other underlying factors contributing to mastalgia. Further research is needed to explore these factors and optimize management strategies.

Keywords: Mastalgia; vitamin D deficiency; serum vitamin D levels; vitamin D supplementation; prospective study; randomized controlled study; symptom relief; visual analog scale

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Key Points

- This work investigates the association between vitamin D deficiency and mastalgia and explores the therapeutic potential of supplementation in alleviating symptoms, aiming to bridge critical gaps in our understanding of this prevalent condition.

Introduction

Mastalgia, or breast pain, is one of the most frequently reported breast complaints among women, affecting up to 70% at some point in their lives (1-3). Despite its prevalence, the etiology of mastalgia remains enigmatic, with treatments often yielding inconsistent results. Various hormonal, anatomical, and lifestyle factors have been implicated, but none provide a comprehensive explanation or solution (2). Recently, attention has focused on the potential role of vitamin D deficiency in mastalgia, driven by its established link to musculoskeletal and nonspecific chronic pain (4). This connection is particularly intriguing given the widespread prevalence of vitamin D deficiency globally and its known role in modulating inflammation, immune response, and hormonal balance (5, 6). While studies have investigated the impact of vitamin D supplementation on breast pain, these largely focus on patient populations without robust comparisons to the general population, leaving a significant gap in understanding whether vitamin D levels truly differ in mastalgia patients (4, 7, 8).

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In this first study we aimed to assess whether vitamin D deficiency is disproportionately associated with mastalgia as compared to those in the general population and if supplementation would offer symptomatic relief.

Materials and Methods

This prospective, investigational, controlled study was conducted at a tertiary teaching centre in central India from November 2023 to August 2024. Ethics approval was obtained from the Institutional Ethics Committee Netaji Subhash Chandra Bose Medical College (IEC/2022/8629-129, date: 26.08.2022) and study was registered with the clinical trials registry of India (CTRI/2023/11/059708).

Patient eligibility and selection: all female patients presenting with the complaint of breast pain reporting to our department were identified. All patients were evaluated as per protocol and underwent a triple assessment that included complete clinical examination, ultrasonography and/or X-ray mammography of bilateral breasts and fine needle aspiration cytology or core needle biopsy, if indicated. All unwilling females, or those with malignant pathology, fibroadenomas, patients taking oral contraceptive pills, pregnant females, recent surgery, trauma, abscess, other benign breast disease or recent therapeutic vitamin D supplementation were excluded from the study. Healthy controls were recruited using convenience sampling from the same outpatient clinic, ensuring comparable demographic characteristics including age, body mass index (BMI), menopausal status, and parity. All participants provided informed consent after receiving detailed information about the study.

Blood samples were collected from all participants to measure serum vitamin D levels using an electrochemiluminescence method. Vitamin D levels were classified as sufficient (30–100 ng/mL), insufficient (20–29 ng/mL), and deficient (<20 ng/mL). Patients in the mastalgia group with vitamin D deficiency received 60,000 IU oral weekly vitamin D supplementation for eight weeks in accordance with established guidelines (9). A visual analog scale (VAS) scores for mastalgia severity was recorded for all patients in the mastalgia group at baseline, and at 4,8, and 12 weeks. Patients were considered to have complete response in terms of pain if their VAS score fell below 3/10 and a partial response if VAS fell to 4 or 5/10 (10). Patients were followed up at 4, 8 and 12 weeks.

Sample Size

Based on literature review (4, 11) approximately 40 to 50% in the general population and 60 to 80% among those with mastalgia have Vitamin D deficiency. Assuming that 50% of the subjects in the reference population have the factor of interest, the study would require a sample size of 91 for each group to achieve a power of 80% for detecting a difference in proportions of 0.20 between the two groups (test - reference group) at a two sided p-value of 0.05. Assuming a 10% drop out rate, a total sample size of 200 (equal group sizes) was taken (12).

Statistical Analysis

Data were entered and analyzed using MedCalc online statistical software (https://www.medcalc.org/calc/). Descriptive statistics were used to summarize demographic characteristics, vitamin D levels, and symptom scores for the mastalgia group. Continuous variables, such as serum vitamin D levels and VAS scores, were expressed as means with standard deviations, while categorical variables were presented as frequencies and percentages.

Comparative analysis was performed using independent t-tests to evaluate the difference in mean serum vitamin D levels between the mastalgia and control groups. The association between vitamin D levels and the presence of mastalgia was further analyzed using chi-square tests for categorical comparisons. McNemar's test was employed to compare pre- and post-supplementation symptom improvement in the mastalgia group (https://www.sciencedirect.com/topics/medicine-and-dentistry/mcnemar-test). A p-value of <0.05 was considered statistically significant for all analyses.

Results

A total of 200 women participated in the study, with 100 women in the mastalgia group and 100 women in the control group. The mean age of participants, BMI, menopausal status and parity were comparable between the two groups (Table 1). The mean serum vitamin D level in the mastalgia group was 25.29±7.7 ng/mL, while in the control group, it was 31.46±8.5 ng/mL (p<0.0001). The mastalgia group exhibited a higher proportion of participants with vitamin D deficiency (26% *vs.* 9%, p = 0.001). The proportion of women with vitamin D insufficiency was comparable between the two groups. The number of Vitamin D sufficient women was higher in control group compared to the mastalgia group (35% *vs.* 57%, p = 0.001) (Table 2).

Within the mastalgia group, 54% had cyclical and 46% had non-cyclical type of pain. Participants with vitamin D deficiency (n = 26) received Vitamin D supplementation, but two patients were lost to follow-up. After supplementation, 46% of patients reported symptomatic improvement based on VAS scores. Of these, 21% experienced complete resolution of symptoms, while 25% reported partial improvement. However, 54% of patients reported no response despite

Table 1. Baseline clinical and demographic profile

Factor	Patients n = 100	Controls n = 100	p
Age (mean ± standard deviation)	29.99±8.14	28.67±6.0	0.19
Body mass index (mean ± standard deviation)	21.2±3.5	22.0±4.0	0.13
Menopausal Status, n (%)			
Pre-menopausal	91 (91)	88 (88)	0.5
Post-menopausal	9 (9)	12 (12)	
Parity			
Nulliparous	35 (35)	48 (48)	0.06
Multiparous	65 (65)	52 (52)	

Table 2. Status of vitamin D nutrition in women with mastalgia and controls

Vitamin D status	Patients	Control	p
Deficient	26	9	0.001
Insufficient	39	34	0.46
Sufficient	35	57	0.001

achieving sufficient serum vitamin D levels post-supplementation (Table 3). The resolution of mastalgia between patients with sufficient vitamin D levels (12/35, 34.3%) and those with Vitamin D deficiency (11/24, 45.8%) was not statistically significant (p = 0.53). Subgroup analysis showed no significant difference in Vitamin D levels between cyclical (54%) and non-cyclical (46%) mastalgia patients (p = 0.39). Symptom improvement post-supplementation was similar in both groups.

Discussion and Conclusion

In this first study, the relationship between vitamin D levels and mastalgia was explored in an Indian population, comparing the serum vitamin D levels of women with mastalgia to those in the general population. Moreover, the therapeutic effects of vitamin D supplementation in women with mastalgia and vitamin D deficiency on mastalgia symptoms were investigated. Serum vitamin D levels were generally lower in the mastalgia group compared to the control group and vitamin D supplementation resulted in symptomatic improvement in many women with mastalgia. However, there was no response to supplementation in most deficient women.

Mastalgia is a common clinical complaint among women, significantly impacting their quality of life. Despite the high prevalence of this condition, its etiopathogenesis remains poorly understood, often resulting in empirical treatments with variable outcomes. Our findings suggest that vitamin D deficiency may play a contributory role in the pathogenesis of some mastalgia, potentially through its effects on inflammatory pathways, muscle metabolism, and nociceptive signaling. The lower serum vitamin D levels observed in the mastalgia group and pain relief in many patients after supplementation align with prior studies, reinforcing the biological plausibility of this association (4, 13). The controlled design of the present study enables a clearer delineation between vitamin D deficiency and mastalgia compared to earlier uncontrolled studies. In addition, the longitudinal follow-up design allows for assessment of short and mid-term effects of supplementation, providing insights into treatment duration and sustained impact.

Vitamin D plays a crucial role in musculoskeletal function, immune modulation, and pain regulation (14). Its deficiency has been linked to increased inflammatory cytokines levels, altered nociceptive signaling, and estrogen imbalance, all of which may contribute to mastalgia (15). Furthermore, vitamin D receptors are expressed in breast tissue, suggesting a potential role in breast pain modulation (16). These mechanisms provide a plausible link between vitamin D deficiency and mastalgia, reinforcing the rationale for supplementation in affected individuals.

However, our study is not without limitations. The lack of a blinded, placebo-controlled design limits the ability to attribute symptom improvement solely to vitamin D supplementation, as a placebo effect cannot be ruled out. The reliance on convenience sampling for controls may introduce selection bias. Furthermore, the lack of a placebo-controlled design limits conclusions regarding the causal role of vitamin D. Mastalgia often improves without intervention, and a 54% non-response rate suggests multifactorial causes beyond vitamin D deficiency. Another potential limitation of our study is that we did not stratify vitamin D levels based on seasonal variations. Given the known impact of seasonal sun exposure on vitamin D synthesis, future studies should assess whether seasonal fluctuations influence the prevalence of vitamin D deficiency in mastalgia patients. Furthermore, while our study was powered adequately to detect a significant difference between groups, larger multicenter studies with a greater sample size are needed to confirm the generalizability of the results. However, the strengths of our study include its prospective design and inclusion of a control group with similar demographics to the study group, which enhances the validity of our findings. The use of standardized tools such as electrochemiluminescence for serum vitamin D measurements and VAS for symptom assessment enhances the data collection, analysis and reliability of the results. By focusing on a population with diverse demographic and socioeconomic backgrounds, our study offers valuable insights into the relationship between vitamin D levels and mastalgia, and the broader applicability of vitamin D supplementation as a potential intervention for mastalgia. However, further research is needed to confirm these findings. Future studies should consider larger sample sizes, randomized controlled designs, and longer longitudinal follow-ups to assess the long-term benefits of vitamin D supplementation. Despite its limitations, our study adds to the growing body of evidence suggesting that vitamin D deficiency may be an important, modifiable factor in the management of mastalgia. Given the observed partial response to supplementation, a combination approach addressing other potential contributors to mastalgia, including stress management and hormonal modulation, may enhance therapeutic outcomes.

Vitamin D deficiency was more prevalent in Indian women with mastalgia, and supplementation provided symptomatic relief for many patients. Given that a significant proportion of women are vitamin D deficient, addressing this deficiency through supplementation could also alleviate other symptoms and conditions increasingly attributed to vitamin D deficiency. Such supplementation, which is both cost-effective and safe, has the potential to offer broad health benefits without causing any harm. However, a significant proportion of patients continue to experience symptoms, suggesting other underlying factors contributing to mastalgia. A randomized, placebo-controlled trial would better establish the therapeutic efficacy of vitamin D supplementation for the treatment of mastalgia.

Table 3. Impact of Vitamin D nutrition supplementation on mastalgia

Group	Vitamin D status post-intervention		No response (VAS >6/10)	p
Deficient (n-24)	Sufficient (n-24) (100%)	Complete response (VAS <3/10) n = 5 (21%) Partial response (VAS = 4 or 5/10) n = 6 (25%)	n = 13 (54%)	<0.0001

VAS: Visual analog scale

Presentation: This study was presented in best oral award category during Asian Society of Mastology annual conference, Dehradun, India, November 2023.

Ethics

Ethics Committee Approval: Ethics approval was obtained from the Institutional Ethics Committee Netaji Subhash Chandra Bose Medical College (IEC/2022/8629-129, date: 26.08.2022) and study was registered with the clinical trials registry of India (CTRI/2023/11/059708).

Informed Consent: Informed consent was obtained from all participants prior to inclusion in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.N.S., S.K.Y., D.B.S., D.S., S.S.; Concept: G.N.S., S.K.Y., D.B.S., D.S., S.S.; Design: G.N.S., S.K.Y., D.B.S., D.S., S.S.; Data Collection or Processing: G.N.S., S.K.Y., D.B.S., D.S., S.S.; Analysis or Interpretation: G.N.S., S.K.Y., D.B.S., D.S., S.S.; Literature Search: G.N.S., S.K.Y., D.B.S., D.S., S.S.; Writing: G.N.S., S.K.Y., D.B.S., D.S., S.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Barton MB, Elmore JG, Fletcher SW. Breast symptoms among women enrolled in a health maintenance organization: frequency, evaluation, and outcome. Ann Intern Med. 1999; 130: 651-657. (PMID: 10215561) [Crossref]
2. ElSherif A, Valente SA. Management of mastalgia. Surg Clin North Am. 2022; 102: 929-946. (PMID: 36335929) [Crossref]
3. Stachs A, Stubert J, Reimer T, Hartmann S. Benign breast disease in women. Dtsch Arztebl Int. 2019; 116: 565-574. (PMID: 31554551) [Crossref]
4. Sarkar DK, Khan M, Banerjee R, Jana D. P028. Vitamin D deficiency in mastalgia: is it a coincidence or an association? Eur J Surg Onc. 2019; 45: 893. [Crossref]
5. Holick MF. The vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord. 2017; 18: 153-165. (PMID: 28516265) [Crossref]
6. Ismailova A, White JH. Vitamin D, infections and immunity. Rev Endocr Metab Disord. 2022; 23: 265-277. (PMID: 34322844) [Crossref]
7. Shabanian S, Rozbeh A, Mohammadi B, Ahmadi A, Arjmand MH. The association between vitamin D deficiency and fibrocystic breast disorder. Curr Mol Med. 2024; 24: 899-905. (PMID: 37357512) [Crossref]
8. Alkhalaf Z, Kim K, Kuhr DL, Radoc JG, Purdue-Smithe A, Pollack AZ, et al. Markers of vitamin D metabolism and premenstrual symptoms in healthy women with regular cycles. Hum Reprod. 2021; 36: 1808-1820. (PMID: 33864070) [Crossref]
9. Płudowski P, Kos-Kudła B, Walczak M, Fal A, Zozulińska-Ziółkiewicz D, Sieroszewski P, et al. Guidelines for preventing and treating vitamin D deficiency: a 2023 update in Poland. Nutrients. 2023; 15: 695. (PMID: 36771403) [Crossref]
10. Verma A, Sharma DB, Yadav SK, Sharma D. Open-label three arm trial comparing ormeloxifene, gamma linolenic acid with methylcobalamine + vitamin C and placebo in mastalgia. Eur J Breast Health. 2022; 18: 248-251. (PMID: 35855192) [Crossref]
11. Vobecky J, Simard A, Vobecky JS, Ghadirian P, Lamothe-Guay M, Falardeau M. Nutritional profile of women with fibrocystic breast disease. Int J Epidemiol. 1993; 22: 989-999. [Crossref]
12. Dhand NK, Khatkar MS. Statulator: an online statistical calculator. Sample size calculator for comparing two independent proportions. Accessed: 20 December 2021. [Crossref]
13. Li E, Rizkalla N, Rai S, Brown H, Hoar F, Mirza M, et al. P045. Vitamin D deficiency treatment improves non-cyclical breast pain. Eur J Surg Onc. 2015; 41: S39-S40. [Crossref]
14. Shipton EA, Shipton EE. Vitamin D and pain: vitamin D and its role in the aetiology and maintenance of chronic pain states and associated comorbidities. Pain Res Treat. 2015; 2015: 904967. (PMID: 26090221) [Crossref]
15. Ao T, Kikuta J, Ishii M. The effects of vitamin D on immune system and inflammatory diseases. Biomolecules. 2021; 11: 1624. (PMID: 34827621) [Crossref]
16. Welsh J. Function of the vitamin D endocrine system in mammary gland and breast cancer. Mol Cell Endocrinol. 2017; 453: 88-95. (PMID: 28579119) [Crossref]