

Research

Burden of Osteomalacia in Premenopausal Women in a Tertiary Care Hospital

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Abstract:

Background: Osteomalacia is a metabolic bone disorder characterized by defective mineralization of osteoid, commonly associated with abnormalities in vitamin D, calcium, and phosphate metabolism. Premenopausal women presenting with nonspecific musculoskeletal symptoms may remain undiagnosed, highlighting the importance of early clinical and biochemical evaluation.

Objective: To determine the burden of osteomalacia among premenopausal women attending a tertiary care hospital and to evaluate relevant clinical, biochemical, and radiological findings.

Methods: This hospital-based observational study included 151 premenopausal women attending the Orthopaedics Outpatient Department with complaints suggestive of osteomalacia. Participants underwent detailed clinical examination and biochemical assessment of serum 25-hydroxyvitamin D, alkaline phosphatase, calcium, and inorganic phosphorus. Relevant radiographs were obtained when clinically indicated. Data were analysed using descriptive and inferential statistics, with $p < 0.05$ considered statistically significant.

Results: Among 151 participants, 112 (74.17%) were diagnosed with osteomalacia, while 39 (25.83%) had no osteomalacia. Most affected women (77.68%) were aged 31–40 years, with no significant age difference between groups ($p = 0.670$). Myalgia (25.0%), tiredness (17.0%), and generalized weakness (12.5%) were common complaints, with a significant difference in clinical presentation between groups ($p = 0.041$). Women with osteomalacia had significantly higher alkaline phosphatase (174.11 ± 80.43 vs. 111.09 ± 23.47 IU/L; $p = 0.011$) and significantly lower serum calcium ($p = 0.027$), inorganic phosphorus ($p = 0.038$), and 25-hydroxyvitamin D levels ($p = 0.001$) compared with women without osteomalacia.

Conclusion: Osteomalacia constituted a substantial burden among symptomatic premenopausal women. Early recognition of clinical symptoms and comprehensive biochemical evaluation may facilitate timely diagnosis and management of this potentially preventable metabolic bone disorder.

Keywords: Osteomalacia, Premenopausal women, Vitamin D, Alkaline phosphatase, Metabolic bone disease.

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1 | Introduction

Osteomalacia is a metabolic bone disease characterized by defective mineralization of mature osteoid after closure of the growth plates, resulting in reduced skeletal strength and increased susceptibility to bone pain, deformity, and fractures.^[1,2] Nutritional

vitamin D deficiency is the most common cause; however, abnormalities in calcium or phosphate homeostasis, malabsorption, chronic kidney or liver disease, and certain medications may also impair bone mineralization.^[3,4] The condition may be clinically underrecognized because its symptoms often overlap

with osteoporosis and other musculoskeletal disorders.^[3,5]

Globally, vitamin D deficiency remains a major public health concern. A pooled analysis including approximately **7.9 million participants from 81 countries** estimated that **15.7%** of the population had serum 25-hydroxyvitamin D [25(OH)D] concentrations below 30 nmol/L, while **47.9%** had concentrations below 50 nmol/L^[6–8]. Females were identified as a particularly vulnerable population. The true global burden of osteomalacia, however, remains difficult to determine because definitive diagnosis may require specialized investigations and the disorder is frequently underdiagnosed or misclassified as osteoporosis.^[9–11]

The clinical manifestations of osteomalacia are often nonspecific and include diffuse bone pain, skeletal tenderness, fatigue, proximal muscle weakness, and difficulty walking or climbing stairs.^[12,13] Progressive disease may result in waddling gait, insufficiency fractures, and characteristic pseudofractures or Looser's zones. These manifestations can substantially impair physical functioning and quality of life.^[14,15]

Diagnosis requires integration of clinical findings with biochemical and radiological evaluation. Serum **25(OH)D** is an important indicator of vitamin D status, while elevated **alkaline phosphatase**, abnormalities in serum **calcium**, and reduced **inorganic phosphate** may support impaired bone mineralization. Radiographs may reveal reduced bone density, cortical changes, or Looser's zones in established disease.^[16,17]

Although osteomalacia is often associated with older individuals, **premenopausal women may also be susceptible**, particularly in the presence of inadequate nutritional intake, limited sunlight exposure, or underlying metabolic abnormalities.^[13] Osteomalacia in this population is clinically important because persistent musculoskeletal symptoms may remain undiagnosed or be attributed to other conditions.^[18]

The present study was therefore undertaken to assess the burden of osteomalacia among premenopausal women attending a tertiary care hospital, using clinical examination, biochemical markers, and relevant radiological investigations.

2 | Patients and Methods

Study Design and Setting

This was a hospital-based observational study conducted at the Teerthanker Mahaveer Medical

College and Research Centre (TMMC & RC), Moradabad, Uttar Pradesh, India. The study was conducted after obtaining approval from the College Research Committee and Institutional Ethics Committee, over a period of 18 months.

Study Participants

Premenopausal women aged 20–40 years attending the Orthopaedics Outpatient Department with clinical features suggestive of osteomalacia were included in the study. Participants presenting with musculoskeletal pain, muscle weakness, tiredness, muscle spasms, myalgia, arthralgia, or spinal, limb, or pelvic deformities suggestive of previous metabolic bone disease were evaluated.

Women with known hepatic or renal disorders, malignancy, or those receiving medications known to affect bone metabolism were excluded from the study.

Study Procedure

A detailed clinical history was obtained from all eligible participants, including relevant menstrual history, followed by a comprehensive clinical examination. Plain radiographs were performed when clinically indicated to identify radiological features suggestive of osteomalacia or other skeletal abnormalities.

Blood samples were collected for biochemical evaluation, including serum 25-hydroxyvitamin D, alkaline phosphatase, serum calcium, and inorganic phosphorus levels.

Outcome Measures

The diagnosis of biochemical osteomalacia was based on the diagnostic criteria specified in the study protocol. In women without underlying renal or hepatic disease, osteomalacia was considered when abnormalities were identified in at least two relevant biochemical parameters, including low serum 25-hydroxyvitamin D, elevated alkaline phosphatase, low serum calcium, and/or low inorganic phosphorus levels.

The primary outcome was the burden of osteomalacia among premenopausal women attending the Orthopaedics OPD, determined through clinical assessment, biochemical evaluation, and relevant radiological findings.

Sample Size Estimation

The sample size was calculated using the formula $n = Z^2 \times P \times Q / d^2$, where $Z_{\alpha/2} = 1.96$ at a 95% confidence

level, $P = 33\%$, $Q = 100 - P = 67\%$, and the allowable error (d) was 7%. Based on these assumptions, the calculated minimum sample size was 151 participants.

Statistical Analysis

The collected data were compiled and analysed using appropriate statistical methods. Quantitative variables were expressed as mean $\pm$ standard deviation, while qualitative variables were presented as frequency and percentage. Appropriate inferential statistical tests were applied to assess associations between study variables, and a p-value of <0.05 was considered statistically significant.

3 | Results

A total of **151** premenopausal women were included in the study. Of these, 112 (74.17%) were diagnosed with osteomalacia, while 39 (25.83%) did not meet the diagnostic criteria for osteomalacia. The demographic distribution, clinical presentation, and biochemical characteristics of participants are presented in Tables 1–3.

As shown in Table 1 and Figure 1, among the 151 study participants, 112 (74.17%) were diagnosed with osteomalacia. The majority of women with osteomalacia (77.68%) belonged to the 31–40-year age group, while 22.32% were aged 20–30 years. A similar age distribution was observed among women without osteomalacia, with 82.05% belonging to the 31–40-year age group. The mean age was comparable between women with and without osteomalacia (33.13 ± 5.00 vs. 32.69 ± 5.65 years; $p=0.670$), indicating no statistically significant association between age and osteomalacia status.

Table 1. Age Distribution of Participants According to Osteomalacia Status

Age group (years)	With osteomalacia (n=112) n (%)	Without osteomalacia (n=39) n (%)	P-value
20–30	25 (22.32)	7 (17.95)	
31–40	87 (77.68)	32 (82.05)	
Mean age $\pm$ SD (years)	33.13 $\pm$ 5.00	32.69 $\pm$ 5.65	0.67

Figure 1. Burden of Osteomalacia Among Study Participants

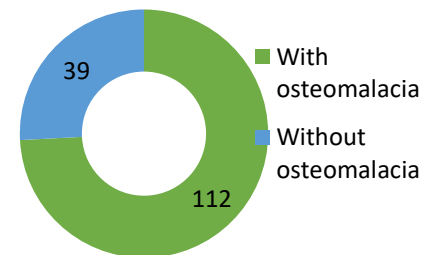


Table 2 demonstrates a statistically significant difference in the distribution of chief complaints between women with and without osteomalacia ($p=0.041$). Among women with osteomalacia, myalgia (25.0%) was the most common complaint, followed by tiredness (17.0%), generalized weakness (12.5%), and musculoskeletal pain (10.7%). In contrast, among women without osteomalacia, myalgia and musculoskeletal pain were the most frequently reported complaints, each affecting 28.2% of participants. Generalized weakness and muscle spasms were observed exclusively among women with osteomalacia, supporting their clinical relevance in the identification of affected patients.

Table 2. Distribution of Chief Complaints According to Osteomalacia Status

Chief complaint	With osteomalacia (n=112) n (%)	Without osteomalacia (n=39) n (%)
Cervical pain	7 (6.3)	4 (10.3)
Generalized weakness	14 (12.5)	0 (0.0)
Low backache	7 (6.3)	4 (10.3)
Low backache radiating to bilateral lower limbs	3 (2.7)	4 (10.3)
Musculoskeletal pain	12 (10.7)	11 (28.2)
Myalgia	28 (25.0)	11 (28.2)
Muscle spasm	10 (8.9)	0 (0.0)

Pain over bilateral upper limbs	2 (1.8)	1 (2.6)
Pain over multiple joints	10 (8.9)	1 (2.6)
Tiredness	19 (17.0)	3 (7.7)
Statistical test	Chi-square = 1.190	p=0.041

As shown in **Table 3**, all evaluated biochemical parameters differed significantly between women with and without osteomalacia. Women diagnosed with osteomalacia had significantly higher serum alkaline phosphatase levels (174.11 ± 80.43 vs. 111.09 ± 23.47 IU/L; $p=0.011$) and significantly lower serum calcium (6.17 ± 2.33 vs. 9.26 ± 0.28 mg/dL; $p=0.027$), inorganic phosphorus (1.20 ± 1.20 vs. 3.57 ± 0.43 mg/dL; $p=0.038$), and 25-hydroxyvitamin D levels (14.56 ± 10.66 vs. 26.69 ± 7.76 nmol/L; $p=0.001$). These findings demonstrate the characteristic biochemical profile of osteomalacia and support the diagnostic value of combined biochemical assessment.

Table 3. Comparison of Biochemical Parameters Between Women With and Without Osteomalacia

Biochemical parameter	With osteomala cia (n=112) Mean $\pm$ SD	Without osteomala cia (n=39) Mean $\pm$ SD	p- value
Serum alkaline phosphatase (IU/L)	174.11 $\pm$ 80.43	111.09 $\pm$ 23.47	0.011 *
Serum calcium (mg/dL)	6.17 $\pm$ 2.33	9.26 $\pm$ 0.28	0.027 *
Serum inorganic phosphorus (mg/dL)	1.20 $\pm$ 1.20	3.57 $\pm$ 0.43	0.038 *
Serum 25-hydroxyvita min D (nmol/L)	14.56 $\pm$ 10.66	26.69 $\pm$ 7.76	0.001 *

4 | Discussion

The present study assessed the burden of osteomalacia among 151 premenopausal women attending the Orthopaedics OPD of a tertiary care hospital. A total of 112 women (74.17%) fulfilled the predefined

clinical and biochemical criteria for osteomalacia, indicating a substantial burden among symptomatic women seeking tertiary care. This proportion should be interpreted in the context of the selected study population rather than as a community prevalence. **Minisola S et al.**^[17] emphasized that the true prevalence of osteomalacia is difficult to determine because the condition is frequently underdiagnosed and diagnostic definitions vary across studies.

With respect to age, the majority of women with osteomalacia in the present study (77.68%) belonged to the 31–40-year age group, with a mean age of 33.13 ± 5.00 years. However, the mean age did not differ significantly from women without osteomalacia (32.69 ± 5.65 years; $p=0.670$). These findings suggest that, within this symptomatic premenopausal population, osteomalacia was not significantly associated with age. **Harinarayan et al.**^[19], in their study of Indian women of reproductive and postmenopausal age, also demonstrated the importance of assessing vitamin D status and bone health among women before menopause. Similarly, **Ray et al.**^[20] reported a greater susceptibility to biochemical osteomalacia among females, particularly in association with low vitamin D status, inadequate dietary calcium intake, and reduced sunlight exposure. The clinical presentation in our study was predominantly nonspecific. Among women with osteomalacia, myalgia was the most common complaint (25.0%), followed by tiredness (17.0%), generalized weakness (12.5%), and musculoskeletal pain (10.7%). Importantly, the overall distribution of clinical complaints differed significantly between women with and without osteomalacia ($p=0.041$). Generalized weakness and muscle spasms were observed only among women diagnosed with osteomalacia. These findings are consistent with **Minisola S et al.**^[5], who identified diffuse musculoskeletal pain, proximal muscle weakness, and fatigue as common but frequently nonspecific manifestations of osteomalacia.

Similarly, **Uday and Högler**^[4] reported that adults with osteomalacia commonly present with fatigue, malaise, muscle weakness, and nonspecific musculoskeletal symptoms, while characteristic radiological findings may occur only in more advanced disease. **Bhadada et al.**^[21] also described backache, joint pain, bony deformities, and fractures as common manifestations among patients with

hypophosphataemic osteomalacia. Therefore, the predominance of myalgia and generalized weakness in our study supports the importance of biochemical evaluation in women presenting with otherwise nonspecific musculoskeletal complaints.

The most important finding of the present study was the characteristic biochemical profile observed among women with osteomalacia. Mean serum alkaline phosphatase was significantly higher in affected women (174.11 ± 80.43 IU/L) compared with those without osteomalacia (111.09 ± 23.47 IU/L; $p=0.011$). Conversely, women with osteomalacia had significantly lower serum calcium (6.17 ± 2.33 vs. 9.26 ± 0.28 mg/dL; $p=0.027$), inorganic phosphorus (1.20 ± 1.20 vs. 3.57 ± 0.43 mg/dL; $p=0.038$), and 25-hydroxyvitamin D levels (14.56 ± 10.66 vs. 26.69 ± 7.76 nmol/L; $p=0.001$).

This biochemical pattern is strongly consistent with the established pathophysiology of nutritional osteomalacia. Minisola S et al.^[4] described progressive vitamin D deficiency as being associated with increased alkaline phosphatase followed by declining calcium and phosphate levels in more advanced disease. Similarly, Marya et al.^[22] demonstrated hypocalcaemia and elevated alkaline phosphatase among North Indian women with biochemical evidence supporting osteomalacia. Harinarayan et al.^[23] and Krishnamoorthy et al.^[24] also reported the relationship between reduced vitamin D status and adverse alterations in calcium-phosphate metabolism and alkaline phosphatase.

Furthermore, Sofi N et al.^[25] reported vitamin D deficiency in 88% of women of reproductive age in North India, highlighting the vulnerability of this population to disturbances in bone and mineral metabolism. The significantly lower 25-hydroxyvitamin D concentration observed in our osteomalacia group therefore provides an important biological explanation for the accompanying abnormalities in calcium, phosphorus, and alkaline phosphatase.

5 | Conclusion

The present study demonstrated a **high burden of osteomalacia (74.17%)** among symptomatic premenopausal women attending a tertiary care hospital. Myalgia, tiredness, and generalized weakness were common clinical manifestations, while affected women showed significantly higher alkaline phosphatase and lower serum calcium, inorganic

phosphorus, and 25-hydroxyvitamin D levels. These findings highlight the importance of early clinical and biochemical evaluation for timely diagnosis and management of osteomalacia in premenopausal women.

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