



# Circadian Rhythm Disruption and Osteoporosis in Postmenopausal Women: An Observational Study from a Tertiary Care Center in India

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## ABSTRACT

**Background:** Osteoporosis, a common bone disease among postmenopausal women, where bone is weak by diminished bone mineral density (BMD), increasing the fracture risk. Our body's natural rhythm, called the "circadian rhythm," which is controlled by the brain and body, helps in bone formation and also in breakdown, disruption of this rhythm may affect bone health. This study explores how problems with circadian rhythm might be linked with osteoporosis in postmenopausal women.

**Objective:** To assess the prevalence of osteoporosis among postmenopausal women and to see if it is related to changes in their body's daily sleep-wake cycle, "circadian rhythm," using a composite morningness-eveningness questionnaire (CMEQ) that groups people as morning, evening, or in between types.

**Materials and methods:** This cross-sectional observational study was conducted at Swaroop Rani Hospital, Prayagraj, India, between March 2024 and March 2025. This study included 109 postmenopausal women after applying strict inclusion/exclusion criteria. Each woman underwent clinical evaluation, anthropometric measurements, and biochemical testing. BMD by dual-energy X-ray absorptiometry (DEXA) scan at the lumbar spine with right and left femoral necks. To understand their sleep-wake pattern, "circadian rhythm" participants filled out a special questionnaire called the CMEQ, which groups them as morning, evening, or in between types. Data was analyzed using computer software (SPSS v25.0) to find patterns and differences.

**Results:** The prevalence of osteoporosis was 32.1% (35 among 109 women). Osteoporotic women had significantly lower weight ( $58.1 \pm 11.63$  vs  $64.3 \pm 13.65$  kg;  $p = 0.023$ ) and height ( $149.1 \pm 7.12$  cm vs  $153.0 \pm 7.08$  cm;  $p = 0.008$ ) compared to nonosteoporotic participants. Body mass index (BMI) was lower in the osteoporotic group ( $26.3$  vs  $28.1$ ), though not statistically significant ( $p = 0.093$ ). The mean composite M-E score did not have a significant value between osteoporotic and nonosteoporotic groups ( $44.8 \pm 3.55$  vs  $44.6 \pm 4.23$ ;  $p = 0.852$ ), indicating no significant association between circadian rhythm and osteoporosis.

**Conclusion:** About one-third of postmenopausal women in the study had osteoporosis. Although anthropometric differences were significant, no statistical significance was found between circadian rhythm and BMD. The findings suggest that circadian rhythm may affect bone health, but the questionnaires CMEQ used in this study may not be the best way to measure it. Future studies should use more accurate measures of taste, such as circadian hormone levels, and follow people over time to better understand this relationship.

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## INTRODUCTION

Osteoporosis is a skeletal disorder where bones become fragile and break easily because of a low bone mass and microarchitectural deterioration, thus resulting in increased bone fragility and susceptibility to fractures.<sup>1</sup> It is common in postmenopausal women due to estrogen drop, which accelerates bone resorption and compromises bone strength.<sup>2</sup> It is also called "silent disease" because it usually has no symptoms, and a fracture occurs suddenly, even on trivial trauma, most commonly at the vertebrae, hip, or wrist, leading to significant morbidity and mortality.<sup>3</sup> Globally, osteoporosis affects over 200 million people,

and it is predicted that about one-third of women over 50 years will experience osteoporotic fractures in their lifetime.<sup>4</sup>

Our bones constantly rebuild through a balanced action of resorption by osteoclasts and formation by osteoblasts, controlled by mechanical, hormonal, and increasingly appreciated circadian rhythm.<sup>5</sup> Our circadian rhythm is an inbuilt 24-hour cycle that controls a range of physiological activities in our body. These rhythms are controlled by a part of the brain, the suprachiasmatic nucleus (SCN) of the hypothalamus, and synchronized with environmental signals such as light and feeding times.<sup>6</sup> At the molecular level, circadian rhythms are governed by transcriptional-translational

feedback loops involving clock genes such as *BMAL1* (brain and muscle ARNT-like 1), *CLOCK*, *PER* (period), and *CRY* (cryptochrome). These genes not only maintain systemic circadian timing but are also expressed in osteoblasts, osteoclasts, and osteocytes, indicating that skeletal tissues are under circadian control.<sup>7</sup>

Research shows that bone rebuilding follows the daily pattern. For example, certain markers of resorption, specifically c-terminal telopeptide of type I collagen (CTX), peak in the early morning hours.<sup>8</sup> Change in these rhythms is common in shift workers, individuals with irregular sleep patterns, or those exposed to non-natural light at night, which is linked with impaired bone metabolism and risk of osteoporosis.<sup>9</sup>

Hormones such as melatonin, released at night by the brain's pineal gland, play an essential role in circadian rhythm control and have been found to directly support bone health by encouraging bone building and reducing bone breakdown. It increases matrix formation and mineralization. Melatonin enhances osteoblast proliferation and differentiation while inhibiting osteoclastogenesis through modulation of RANKL/OPG signaling. Lower melatonin levels, as seen in individuals with circadian disruption or aging, are associated with increased bone loss. High cortisol value in the early morning exerts catabolic effects on bone by reducing osteoblast activity and promoting osteoclast activity. Chronic circadian impairment, such as in shift workers, exaggerates glucocorticoid exposure and enhances bone resorption.<sup>10</sup> Animal studies have shown that melatonin supplementation improves bone mineral

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density and microarchitecture in rats in which ovaries are removed, mimicking postmenopausal osteoporosis.<sup>11</sup>

Additionally, melatonin levels drop as we age and are even lower in individuals with poor sleep quality or disrupted daily rhythms, both of which correlate with lower bone mineral density (BMD) and increased fracture risk.<sup>12</sup> These findings suggest that a disrupted circadian rhythm is a modifiable risk factor in osteoporosis pathogenesis. Furthermore, giving medications at the right time of day may improve their effectiveness and could offer a new way to treat these diseases.<sup>13</sup>

As people age and more of them experience sleep problems, it becomes important to understand how the daily body rhythm, "circadian rhythm," affects bone health. Understanding and addressing the effect of circadian rhythms on skeletal metabolic processes could help in developing better ways to prevent and treat osteoporosis. Public health efforts and clinical guidelines must evolve to start including the impact of these body rhythms when assessing the risk of osteoporosis and planning treatment.<sup>14</sup>

## AIM AND OBJECTIVES

### Aim

To study the prevalence of osteoporosis among postmenopausal women and to see if it is related to changes in their body's daily sleep–wake cycle, "circadian rhythm."

### Objective

- To estimate the prevalence of osteoporosis in postmenopausal women using BMD assessment.
- To assess circadian rhythm patterns in postmenopausal women using a composite morningness–eveningness questionnaire (CMEQ).
- To examine the association between circadian rhythm disorganization and osteoporotic status.

## MATERIALS AND METHODS

### Study Design and Setting

This cross-sectional observational study was carried out in the Department of Medicine at SRN Hospital, affiliated with Moti Lal Nehru Medical College, Prayagraj, Uttar Pradesh (March 2024–March 2025).

### Sample Size

A total of 415 postmenopausal females expressed willingness to participate after providing informed consent. Following the application of exclusion criteria, 269 postmenopausal females were excluded.

Thus, 146 postmenopausal females were finally included in the study. Among them, 109 postmenopausal females completed the questionnaire and underwent dual-energy X-ray absorptiometry (DEXA) scanning.

### Inclusion Criteria

Postmenopausal females confirmed by clinical history who were willing to undergo BMD assessment and participate in circadian rhythm evaluation.

### Exclusion Criteria

Patients who had not attained menopause, a history of parathyroid disease or any metabolic bone disease, vitamin D deficiency, liver disease, chronic kidney disease, malignancy, chronic drug use (such as antiepileptic agents, steroids), diagnosed psychiatric illness, or neurodegenerative disorders affecting sleep. Shift workers or those with irregular sleep–wake cycles due to occupational demands or a history of calcium or vitamin D supplementation within 1 year. Patients who were unwilling to undergo study-related diagnostic procedures were excluded from the study.

### Data Collection Tools and Procedures

#### Clinical Evaluation

Detailed medical history, including menopausal duration, physical activity, dietary calcium intake, and relevant comorbidities, was recorded.

#### Anthropometric Measurements

Measurements such as height, weight, and body mass index (BMI) were obtained using standard protocols.

#### Bone Mineral Density Assessment

Bone mineral density was measured using DEXA scan at three anatomical sites as of lumbar spine, the right femur neck, and the left femur neck. WHO T-score criteria were used to classify osteoporosis (T-score  $\leq -2.5$  SD).

#### Circadian Rhythm Assessment

The composite CMEQ was used to assess circadian rhythm. The questionnaire depicted in Table 1 includes 13 items that help in evaluating preferred sleep–wake times, alertness, and diurnal activity levels.<sup>15</sup> Scores were categorized as:

- Morning type with score  $>44$ .
- Intermediate type with score 23–43.
- Evening type with score  $\leq 22$ .

#### Laboratory Investigations

Blood samples were collected to measure serum total calcium, serum phosphorus, serum alkaline phosphatase, and 25-hydroxy vitamin D.

### Statistical Analysis

Data were analyzed on a computer using SPSS software (version 25.0). The association between circadian rhythm types and osteoporosis was evaluated using statistical methods such as Chi-square test and analysis of variance (ANOVA) as suitable. A  $p$ -value  $< 0.05$  is considered statistically significant.

## RESULTS

The above Table 2 and Figure 1 represent the distribution of study participants based on their osteoporotic status. Out of the total 109 participants, 74 individuals (67.9%) were categorized as nonosteoporotic, while 35 individuals (32.1%) were identified as osteoporotic, indicating that approximately one-third of the study population had osteoporosis.

The above Table 3 and Figure 2 represent a comparison of anthropometric parameters age, weight, height, and BMI, between osteoporotic and nonosteoporotic individuals. The mean age of the osteoporotic group was higher (62.7 years) as compared to the nonosteoporotic group (59.9 years), but the difference was not statistically significant ( $p = 0.153$ ). The distribution of osteoporosis varied markedly with age. Among women aged 41–50 years, osteoporosis was observed in 5 out of 21 cases (23.8%), while osteopenia and normal bone mass were seen equally (38.1%) each. In the 51–60 years age group, osteoporosis was found in 10 out of 37 cases (27%), and osteopenia in 29.7%, indicating that nearly 57% of women already had compromised bone health by this decade. The 61–70 years age group demonstrated the highest burden of osteoporosis, affecting 12 out of 29 women (41.4%), a prevalence equal to the proportion of normal bone density (41.4%), with only 17.2% having osteopenia. In women aged 71–80 years, osteoporosis persisted in 8 out of 20 cases (40%), while normal bone density declined further to 35%, and osteopenia comprised 25%. In the

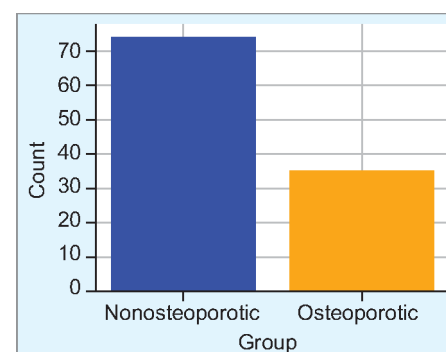


Fig. 1: Distribution of study participants based on osteoporotic status

**Table 1:** The composite morningness–eveningness questionnaire

*Directions: Please check the response for each item that best describes you*

1. Considering only your own “feeling best” rhythm, at what time would you get up if you were entirely free to plan your day?  
5:00 AM–6:30 AM (5)  
6:30 AM–7:45 AM (4)  
7:45 AM–9:45 AM (3)  
9:45 AM–11:00 AM (2)  
11:00 AM–12:00 noon (1)
2. Considering your only “feeling best” rhythm at what time would you go to bed if you were entirely free to plan your evening?  
8:00 PM–9:00 PM (5)  
9:00 PM–10:15 PM (4)  
10:15 PM–12:30 AM (3)  
12:30 PM–1:45 AM (2)  
1:45 AM–3:00 AM (1)
3. Assuming normal circumstances, how easy do you find getting up in the morning?  
Not at all easy (1)  
Slightly easy (2)  
Fairly easy (3)  
Very easy (4)
4. How alert do you feel during the first half hour after having awakened in the morning? (Check one)  
Not at all alert (1)  
Slightly alert (2)  
Fairly alert (3)  
Very alert (4)
5. During the first half hour after having awakened in the morning, how tired do you feel?  
Very tired (1)  
Fairly tired (2)  
Fairly refreshed (3)  
Very refreshed (4)
6. You have decided to engage in some physical exercise. A friend suggests that you do this one hour twice a week, and the best time for him is 7:00 AM–8:00 AM. Bearing in mind nothing else but your own “feeling best” rhythm, how do you think you would perform?  
Would be in good form (4)  
Would be in reasonable form (3)  
Would find it difficult (2)  
Would find it very difficult (1)
7. At what time in the evening do you feel tired and, as a result, in need of sleep?  
8:00 PM–9:00 PM (5)  
9:00 PM–10:15 PM (4)  
10:15 PM–12:30 AM (3)  
12:30 AM–1:45 AM (2)  
1:45 AM–3:00 AM (1)
8. You wish to be at your peak performance for a test, which you know is going to be mentally exhausting and lasting for 2 hours. You are entirely free to plan your day, and considering only your own “feeling best” rhythm, which one of the four testing times would you choose?  
8:00 AM–10:00 AM (4)  
11:00 AM–1:00 PM (3)  
3:00 PM–5:00 PM (2)  
7:00 PM–9:00 PM (1)
9. One hears about “morning” and “evening” types of people. Which ONE of these types do you consider yourself to be?  
Definitely a morning type (4)  
More of a morning than an evening type (3)  
More of an evening than a morning type (2)  
Definitely an evening type (1)
10. When would you prefer to rise (provided you have a full day’s work—8 hours) if you were totally free to arrange your time?  
Before 6:30 AM (4)  
6:30 AM–7:30 AM (3)  
7:30 AM–8:30 AM (2)  
8:30 AM or later (1)
11. If you always had to rise at 6:00 AM, what do you think it would be like?  
Very difficult and unpleasant (1)  
Rather difficult and unpleasant (2)  
A little unpleasant but no great problem (3)  
Easy and not unpleasant (4)
12. How long, a time, does it usually take before you “recover your senses” in the morning, after rising from a night’s sleep?  
0–10 minutes (4)  
11–20 minutes (3)  
21–40 minutes (2)  
More than 40 minutes (1)
13. Please indicate to what extent you are a morning or evening active individual.  
Pronounced morning active (morning alert and evening tired) (4)  
To some extent, morning active (3)  
To some extent, evening active (2)  
Pronounced evening active (morning tired and evening alert) (1)

**Table 2:** Distribution of study participants based on osteoporotic status

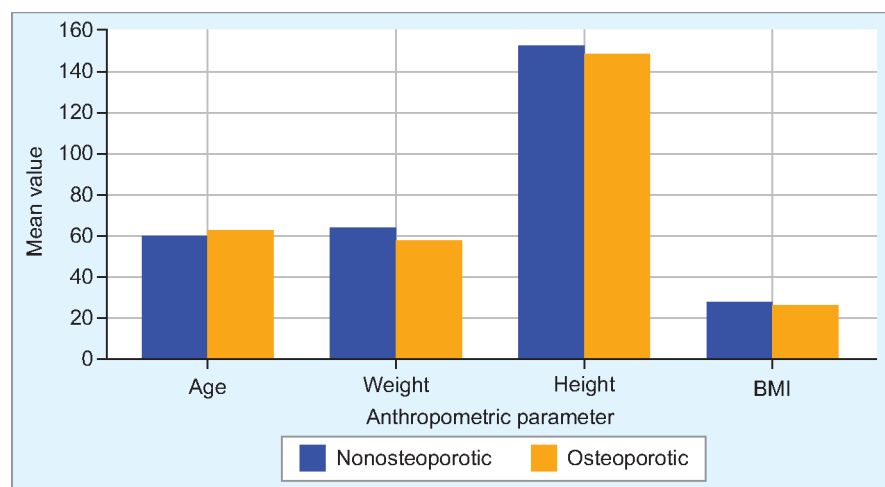
Group	Participants	% of total
Nonosteoporotic	74	67.9
Osteoporotic	35	32.1

**Table 3:** Comparison of anthropometric parameters between osteoporotic and nonosteoporotic individuals

Variable ( $\pm 2$ SD)	Nonosteoporotic (N = 74)	Osteoporotic (N = 35)	p-value
Age (year)	59.9 $\pm$ 9.9	62.7 $\pm$ 9.45	0.153
Weight (Kg)	64.3 $\pm$ 13.65	58.1 $\pm$ 11.63	0.023
Height (meter)	1.53 $\pm$ 0.0708	1.49 $\pm$ 0.0712	0.008
BMI (kg/m <sup>2</sup> )	28.1 $\pm$ 5.02	26.3 $\pm$ 5.59	0.093

**Table 4:** Comparison of composite M-E scoring between osteoporotic and nonosteoporotic groups

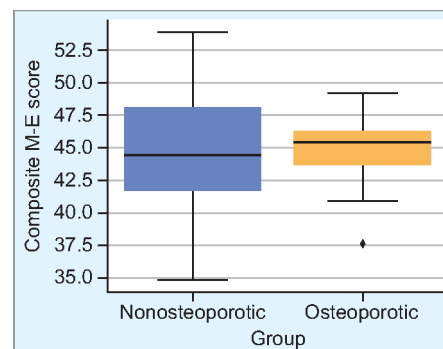
Variable	Nonosteoporotic (N = 74)	Osteoporotic (N = 35)	p-value
Composite M-E scoring	44.6 $\pm$ 4.23	44.8 $\pm$ 3.55	0.852

**Fig. 2:** Comparison of anthropometric parameters between osteoporotic and non-osteoporotic individuals

81–90 years age group, no women out of two cases had normal bone density, and 100% demonstrated low bone mass (osteopenia 100%, osteoporosis 0%), reflecting advanced skeletal fragility in extreme age. This study shows a significant difference in weight, with the nonosteoporotic group having a higher mean weight (64.3 kg) than the osteoporotic group (58.1 kg), with a *p*-value of 0.023. Similarly, the mean height was statistically significant, with a greater mean height in the nonosteoporotic group (1.53 m) compared to the osteoporotic group (1.49 m), with a *p*-value of 0.008. Although the mean BMI was slightly higher in the nonosteoporotic group (28.1) than in the osteoporotic group (26.3), this was not statistically significant (*p* = 0.093).

The above Table 4 and Figure 3 represent a comparison of composite M-E scoring between osteoporotic and nonosteoporotic groups. The mean score in the nonosteoporotic group (*n* = 74) was 44.6 with a median of 45, standard deviation of 4.23, and standard error of 0.495. In the osteoporotic group (*n* = 35), the mean was 44.8 with a median of 45, standard deviation of 3.55, and standard error of 0.6. The *p*-value of 0.852 suggested that there was no statistically significant correlation in the composite M-E scoring between the osteoporotic and nonosteoporotic groups.

In our study, we correlated the composite morningness–eveningness (CME) score to body measurements such as BMI and blood levels of a few important nutrients, such as vitamin D and serum calcium, using a statistical test called Pearson's correlation coefficient. First, we checked if there is any link between CME score and BMI; the result showed a very weak negative connection (*r* = −0.0208), and the *p*-value (0.830) was quite high, which means this result is not significant, suggesting CME score and BMI do not seem to be related in our study group. Thereafter, we looked at the CME score and serum calcium; the correlation was very weak (*r* = 0.0489), and the *p*-value (0.657) was again high, which is statistically not significant, showing that there is no clear relation between them either. Lastly, we checked the relationship between CME score and vitamin D levels. This showed a slightly better positive correlation (*r* = 0.1256), but still, the *p*-value (0.248) was not statistically significant. Overall, in our Indian postmenopausal female population, no strong or significant connection between CME score and BMI, vitamin D, or serum calcium levels was found which indicated that changes in these values are not clearly linked to changes in CME scores.

**Fig. 3:** Comparison of composite M-E scoring between osteoporotic and non-osteoporotic groups

## DISCUSSION

In this study, we looked at how common osteoporosis is in postmenopausal women and whether it is related to their daily body rhythm (circadian rhythm) and metabolic factors. We compared our findings with other similar Indian studies to ensure accuracy and relevance.

In this study, as shown in the (Fig. 4) total of 415 postmenopausal females expressed willingness to participate after providing informed consent. Following the application of exclusion criteria, 269 women were excluded due to conditions such as history of parathyroid or metabolic bone disease, vitamin D deficiency, liver disease, chronic kidney disease, malignancy, long-term use of drugs such as antiepileptics or steroids, psychiatric or neurodegenerative illnesses affecting sleep, history of calcium or vitamin D supplementation within the last year, or unwillingness to undergo the required diagnostic procedures. Thus, 146 participants were finally included in the study. Among them, 109 women completed the questionnaire and underwent DEXA scanning, while 37 filled out the questionnaire but declined DEXA scanning at a later stage. Based on DEXA results, 74 participants (67.9%) were categorized as nonosteoporotic, and 35 participants (32.1%) were classified as osteoporotic. Both groups completed the CMEQ, with nonosteoporotic women obtaining a mean score of 44.6  $\pm$  5.55 and osteoporotic women scoring 44.6  $\pm$  4.23.

In this study, 109 participants were categorized based on their BMD status as



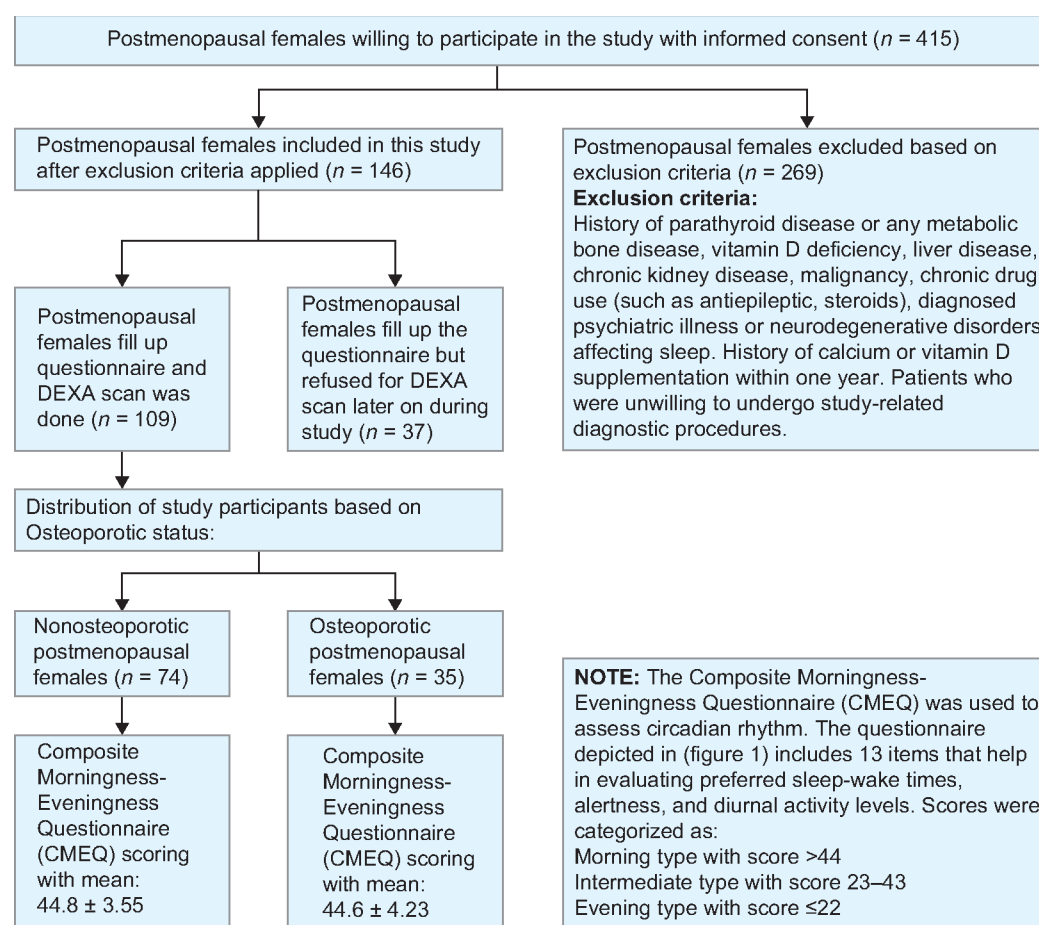


Fig. 4: A flowchart detailing recruitment of participants

osteoporotic and nonosteoporotic, out of which approximately one-third of the study population had osteoporosis. This prevalence is consistent with findings from various Indian studies like Sharma et al.,<sup>16</sup> who highlighted that an osteoporosis prevalence of 30–40% among postmenopausal women in North India, while a study by Marwaha et al.<sup>17</sup> also observed a similar trend in urban Indian populations, attributing it to nutritional deficiencies and hormonal changes after menopause. On the international front, the World Health Organization (WHO) estimates that globally one-third of women above the age of 50 years will suffer an osteoporotic fracture during their lifetime.

This study also compared anthropometric parameters between osteoporotic and nonosteoporotic individuals. We observed that the mean age in the osteoporotic group was  $62.7 \pm 9.45$  years, which was higher than the nonosteoporotic group ( $59.9 \pm 9.9$  years), but the difference was not statistically significant ( $p = 0.153$ ). However, weight shows a statistically significant difference ( $64.3 \pm 13.65$  kg in nonosteoporotic vs  $58.1 \pm 11.63$  kg in osteoporotic;  $p = 0.023$ ) and also the height ( $1.53 \pm 0.0708$  vs  $1.49 \pm 0.0712$  m;

$p = 0.008$ ). The BMI was higher in the non-osteoporotic group (28.1 vs 26.3), but the difference was not statistically significant ( $p = 0.093$ ). These anthropometric associations resonate with findings from the study by Prasad et al.<sup>18</sup> Similarly, Pan et al.<sup>19</sup> reported an average BMI of 26.4 in diabetic osteoporotic women, showing a comparable reduction in BMI, which aligns with our osteoporotic group. The mean age in their cohort was 63.7 years, nearly identical to our osteoporotic mean value. Li et al.<sup>20</sup> reported lower BMI and height in osteoporotic patients without diabetes as well, suggesting anthropometry's universal role irrespective of glycemic status. Lastly, Dimitrova and Hristozov<sup>21</sup> found a mean height of 151.2 cm in osteoporotic postmenopausal women, which approximates our osteoporotic group (149.1 cm), supporting a strong inverse relationship between stature and osteoporosis.

In our study, composite M-E scoring was not statistically significant between osteoporotic and nonosteoporotic ( $p = 0.852$ ), and findings are similar to Prasad et al.<sup>18</sup> who pointed out that standard scoring systems and DEXA parameters underestimate fracture risk. Viggers<sup>22</sup> also pointed out the inadequacy of

the composite tool in predicting bone fragility. Dimitrova and Hristozov et al.<sup>21</sup> found that fracture risks are independent of BMD scoring alone, supporting our non-significant M-E scoring difference.

## CONCLUSION

The osteoporosis prevalence in this study was 32.1%, with 67.9% being nonosteoporotic, indicating that nearly one-third of postmenopausal females had compromised bone health. Participants with osteoporosis were older (mean age: 62.7 years) than nonosteoporotic individuals (mean age: 59.9 years), but the age difference was not statistically significant ( $p = 0.153$ ). Osteoporotic individuals had significantly lower body weight ( $58.1 \pm 11.63$  kg) compared to nonosteoporotic individuals ( $64.3 \pm 13.65$  kg), with  $p = 0.023$ , highlighting the influence of low body weight on bone density. Mean height was also significantly lower among osteoporotic participants (1.49 m) than their nonosteoporotic counterparts (1.53 m), suggesting a correlation between shorter stature and reduced bone mass ( $p = 0.008$ ). Composite M-E scoring did not

show statistical significance between the osteoporotic and nonosteoporotic groups ( $p = 0.852$ ), indicating limited diagnostic value in this study population.

## LIMITATIONS

The sample size of 109 participants, which is enough for preliminary analysis, limits the generalizability of the findings to a wider population, especially across different ethnic or regional groups within India. The cross-sectional nature of the study cannot prove cause and effect between osteoporosis and associated risk factors. There was a gender limitation as the study focused only on postmenopausal females, restricting applicability to other populations such as premenopausal women or men. A single-time-point BMD assessment might not reflect longitudinal changes or progression of osteoporosis over time. Variability in BMD measurement may arise due to dependency on a single anatomical site for diagnosis rather than multiple sites. Although some biochemical parameters were compared, markers of bone turnover (e.g., serum osteocalcin, CTX) were not included, limiting a proper understanding of bone metabolism. The study did not control for hormonal status or history of hormone replacement therapy, both of which can impact bone density in postmenopausal women.

## RECOMMENDATIONS

Older age was more frequently associated with osteoporosis, suggesting the need for early age-based screening in postmenopausal females, especially above 60 years. Significantly lower weight (58.1 kg) and height (149.1 cm) were observed in the osteoporotic group, indicating that low body mass and short stature could be potential anthropometric risk markers for osteoporosis and should be considered in routine assessments. BMI, although not statistically significant, was lower in osteoporotic individuals, supporting the role of maintaining a healthy body

composition to prevent bone loss. Composite M-E scoring did not significantly differ between osteoporotic and nonosteoporotic individuals, suggesting that subjective or quality-of-life-based assessments may not be sufficient to predict bone health.

## ETHICS APPROVAL

Proper Institutional Ethical Committee approval was taken from the institute's Moti Lal Nehru Medical College, Prayagraj (Ethics Committee Registration No. ECR/922/inst/UP/RR-22 issued under New Drugs and Clinical Trial Rules, 2019).

## WRITTEN CONSENT FOR PUBLICATION

We declare that this manuscript is original, has not been published before, and is not currently being considered for publication elsewhere, and we give consent to be published in your journal 'JAPI'.

## AUTHORS' CONTRIBUTIONS

AS and PG chose the topic and planned the execution. AKC, AS, PG, and MM wrote the main manuscript. AKC, PG, AS prepared tables and figures, and contributed in discussion. All authors reviewed the manuscript.

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