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Comparative Analysis of Serum Uric Acid Levels and Bone Mineral Density Among Elderly Individuals

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ABSTRACT

Osteoporosis is a major public health concern, particularly in aging populations. Emerging evidence suggests that serum uric acid (SUA) may influence bone mineral density (BMD) due to its antioxidant properties. However, the relationship between SUA levels and BMD remains controversial. **Objectives:** To compare BMD among individuals with low and high SUA levels and to determine the association between SUA and osteoporosis prevalence. **Methods:** This cross-sectional-comparative study was done at Liaquat University Hospital, Hyderabad, from March 2022 to August 2022. A total of 182 participants (≥50 years old) who underwent DEXA scan for BMD assessment were included using a purposive sampling technique.Participants were categorized into low SUA (<5.5 mg/dL) and high SUA (>5.5 mg/dL) groups. BMD at the lumbar spine, total hip, and femoral neck was recorded. Statistical analysis was performed using SPSS v.24, with t-tests, chi-square tests, and Pearson's correlation applied. A p-value of <0.05 was considered significant. **Results:** Participants with high SUA levels had significantly higher BMI (p=0.01). Lumbar spine BMD was significantly lower in the high SUA group (p=0.04), but no significant differences were observed for total hip and femoral neck BMD. Pearson's correlation showed a positive association between SUA and lumbar BMD (r=0.32, p=0.015). **Conclusions:** It was concluded that higher SUA levels were associated with lower osteoporosis prevalence but paradoxically lower lumbar BMD.

INTRODUCTION

The prevalence of osteoporosis increases with age. In Pakistan, where the aging population is steadily growing, osteoporosis and osteoporotic fractures have become a significant public health concern. The burden of osteoporosis is particularly high among postmenopausal women and elderly men, contributing to increased healthcare costs, disability, and mortality [1]. Osteoporotic fractures, particularly hip and vertebral fractures, can lead to severe pain, prolonged immobilization, reduced quality of life, and even death [2]. According to a systematic review, hip fractures in the elderly are associated with a one-year mortality rate of approximately 30%, highlighting the urgent need for effective prevention and management strategies [3]. Additionally, data suggest that osteopenia, a precursor to osteoporosis, significantly increases fracture risk and should also be aggressively managed to prevent future fractures [4]. Uric acid, a byproduct of purine metabolism, has been widely studied for its role in metabolic disorders such as gout, chronic kidney disease, and cardiovascular disease [5]. While hyperuricemia has traditionally been considered a risk factor for metabolic syndrome and inflammatory diseases [6], recent evidence

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suggests that uric acid also has antioxidant properties that may influence bone metabolism [7]. As a potent scavenger of free radicals, uric acid contributes to the body's overall antioxidant defense by neutralizing peroxyl radicals and chelating iron [8]. Since oxidative stress plays a crucial role in bone resorption and osteoporosis, some studies have proposed that higher serum uric acid (SUA) levels may be associated with higher bone mineral density (BMD) and a lower risk of fractures [9]. However, the relationship remains controversial, with some studies reporting no association or even an inverse correlation [10, 11]. Furthermore, much of the existing research has been conducted on women, with limited data available on men. In Pakistan, where malnutrition, vitamin D deficiency, and poor healthcare access contribute to a high prevalence of osteoporosis, understanding metabolic factors that influence bone health is crucial. Body weight and body mass index (BMI) have long been recognized as protective factors against BMD decline, with fat-free mass (FFM) having a stronger association with BMD than body fat mass (BFM) [12]. Some studies suggest that SUA may be positively correlated with both BMD and skeletal muscle mass index (SMI), indicating a potential indirect role in bone health through muscle mass preservation [12, 13]. However, research on the association between SUA and skeletal muscle mass remains limited and inconsistent, particularly in developing countries like Pakistan, where lifestyle and dietary habits differ significantly from Western populations [14].

This study aims to evaluate the relationship between serum uric acid levels and bone mineral density among elderly individuals in Pakistan.

METHODS

This cross-sectional comparative study was conducted at the Department of Orthopedics and Medicine OPD of Liaquat University Hospital, Hyderabad. The study was conducted from March 2022 to August 2022. Men and women aged 50 years and older who had undergone dual-energy X-ray absorptiometry (DEXA) scans for bone mineral density (BMD) assessment were selected through purposive sampling. A 5cc sample of fasting intravenous blood was collected to measure serum uric acid levels using the enzymatic colorimetric method in a standardized laboratory. Both BMD and serum uric acid levels were assessed on the same day. Patients with known metabolic bone diseases, chronic kidney disease, or conditions affecting uric acid metabolism were excluded from the study. The study was approved via the REC of Liaquat University of Medical and Health Sciences vide letter NO.LUMHS/REC/-046. Informed written consent was taken from each participant before enrollment in the study. The study sample included a total of 182 participants, equally divided into two groups: low serum uric acid levels (<5.5 mg/dl) and high serum uric acid levels (>5.5 mg/dl). Sample size was calculated via the Open Epi Sample Size Calculator (mean difference) by taking the mean BMD at the Lumbar spine in the Low Uric Acid group as 1.097±0.152 g/cm2 and in the High Uric Acid group as 1.161 ± 0.156 g/cm2 [15]. Power of study was 80%, and CI was taken as 95%. BMD was assessed at the lumbar spine (L1–L4), total hip, and femoral neck using a DEXA. Osteoporosis was diagnosed based on the World Health Organization (WHO) criteria, with a T-score ≤ -2.5 indicating osteoporosis and a T-score between -1.0 and -2.5 indicating osteopenia. Clinical and demographic data, including age, sex, BMI, smoking status and physical activity, were collected through structured questionnaires and medical records. Statistical analysis was conducted using SPSS v.24. The normality of the data was assessed via the Shapiro-Wilk test. The data were found to be normally distributed, so parametric tests were applied. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Independent t-tests and chi-square tests were used to compare variables between groups. Pearson's correlation analysis was conducted to assess the relationship between SUA levels and BMD. A p-value of <0.05 was considered statistically significant.

RESULTS

The mean age of participants was comparable between the low uric acid and high uric acid groups (65.3 ± 7.1 vs. 64.8 ± 6.9 years, p=0.65), with a nearly equal distribution of males and females in both groups. However, BMI was significantly higher in the high uric acid group (26.5 ± 4.1 kg/m^2) compared to the low uric acid group (23.1 ± 3.5 kg/m^2, p=0.01), suggesting a possible association between higher uric acid levels and increased body weight. No significant differences were observed in smoking status (p=0.51) or physical activity levels (p=0.32) between the groups.The demographic and clinical characteristics of the study population are presented in Table 1.

Table 1: Demographic and Clinical Characteristics of the Study Population

Variables	Low Uric Acid (n=91)	High Uric Acid (n=91)	p-value
Mean Age (Years)	65.3 ± 7.1	64.8 ± 6.9	0.65
Male	45 (49.5%)	47 (51.6%)	0.75
Female	46 (50.5%)	44 (48.4%)	0.80
Mean BMI (kg/m^2)	23.1 ± 3.5	26.5 ± 4.1	0.01*
Smoking	30 (33.0%)	35 (38.5%)	0.51
Physical Activity	51 (56.0%)	58 (63.7%)	0.32

Participants with high uric acid levels had significantly lower lumbar spine BMD (0.85 ± 0.12 g/cm^2) compared to those with low uric acid levels (0.93 ± 0.15 g/cm^2, p = 0.04). However, BMD differences at the total hip (p=0.25) and

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femoral neck (p=0.67) were not statistically significant. Bone mineral density (BMD) measurements are given in Table 2.

Table 2: Bone Mineral Density (BMD) by Uric Acid Levels

BMD Site	Low Uric Acid (n=91)	High Uric Acid (n=91)	p-value
Lumbar Spine (g/cm^2)	0.93 ± 0.15	0.85 ± 0.12	0.04*
Total Hip (g/cm^2)	0.78 ± 0.16	0.86 ± 0.11	0.25
Femoral Neck (g/cm^2)	0.72 ± 0.9	0.81 ± 0.14	0.67

A significantly higher proportion of osteoporotic patients were found in the low uric acid group (41.8%) compared to the high uric acid group (23.1%, p=0.02). Meanwhile, osteopenia was relatively balanced between the two groups (44.0% vs. 47.3%: p=0.18), while normal BMD was more common in the low uric acid group (29.6% vs. 14.2%: p=0.056). These findings further support the hypothesis that higher uric acid levels might be associated with better bone health and lower osteoporosis risk. The prevalence of osteoporosis and osteopenia across uric acid groups is shown in Table 3.

Table 3: Osteoporosis and Osteopenia Prevalence among Groups

Bone Status	Low Uric Acid (n=91) (<5.5 mg/dl)	High Uric Acid (n=91) (>5.5 mg/dl)	p-value	CI (95%)
Osteoporosis	38 (41.8%)	21 (23.1%)	0.02*	0.01 to 0.16
Osteopenia	40 (44.0%)	43 (47.3%)	0.18	-0.07 to 0.03
Normal BMD	27 (29.6%)	13 (14.2%)	0.056	-0.04 to 0.06

The correlation analysis presented a significant positive correlation between serum uric acid levels and lumbar spine BMD (r=0.32, p=0.015), reinforcing the previous findings of a protective effect of uric acid on bone mass. However, no significant correlation was observed between uric acid levels and total hip BMD (r=0.35, p=0.65) or femoral neck BMD (r=0.40, p=0.08), suggesting site-specific effects of uric acid on bone density, as shown in Table 4.

Table 4: Correlation Between Serum Uric Acid Levels and BMD

Variables	p-value		CI (95%)
Uric Acid vs Lumbar BMD	0.32	0.015*	0.06 to 0.52
Uric Acid vs Hip BMD	0.35	0.65	-0.18 to 0.62
Uric Acid vs Femoral BMD	0.40	0.08	-0.04 to 0.67

DISCUSSION

The present study aimed to analyze the association between serum uric acid levels and bone mineral density (BMD) among osteoporotic and non-osteoporotic patients. Our findings indicate that higher serum uric acid levels are associated with significantly lower lumbar spine BMD (p=0.04), while no significant differences were observed at the total hip or femoral neck BMD sites.Several studies have investigated the potential protective effect of uric acid on bone metabolism.A meta-analysis by Kim *et al.*, suggested that higher serum uric acid levels were associated with greater BMD and lower fracture risk in older adults [16].This was attributed to the antioxidant properties of uric acid, which may reduce oxidative stress and subsequent bone loss. However, our study does not fully support this hypothesis, as lumbar BMD was significantly lower in the high uric acid group, contrary to expectations. Our findings are more aligned with the study by Robles-Rivera *et al.*, which found that elevated uric acid levels were not consistently associated with improved BMD across all skeletal sites [17].They reported that uric acid might exert different effects depending on bone location, which aligns with our observation that lumbar BMD was significantly affected while hip and femoral neck BMD were not. Interestingly, our results showed a significantly higher BMI in the high uric acid group (p=0.01).Obesity and higher BMI are well-documented protective factors against osteoporosis due to the mechanical loading effect on bones and increased estrogen production from adipose tissue [18].Therefore, it is possible that higher BMI rather than uric acid levels contributed to bone health in our study population, making it difficult to isolate the direct effect of uric acid on BMD.This observation is supported by Tu *et al.*, who reported that higher BMI was more strongly correlated with increased BMD than uric acid levels alone [19].In contrast, a study conducted by Tanaka *et al.*, found that hyperuricemia was associated with increased BMD in postmenopausal women [20].Previous research has highlighted that estrogen plays a crucial role in regulating bone remodeling and that postmenopausal women may experience different responses to uric acid compared to men or premenopausal women [21].Our study population included both males and females, which could have influenced the results differently from studies that focused solely on postmenopausal women. Regarding osteoporosis prevalence, our findings indicated that osteoporosis was significantly more common in the low uric acid group (41.8%) than in the high uric acid group (23.1%, p=0.02).This aligns with a study by Yan *et al.*, which reported that low serum uric acid levels were associated with a higher risk of osteoporosis and fractures [22].However, unlike their study, our research found that lumbar BMD was lower in individuals with high uric acid levels, adding complexity to the relationship between uric acid and bone health

CONCLUSIONS

It was concluded that our study provides mixed evidence on the association between serum uric acid levels and bone health. While osteoporosis prevalence was lower in individuals with high uric acid levels, lumbar spine BMD was paradoxically lower in this group, suggesting a complex and site-specific relationship between uric acid and bone metabolism. Additionally, BMI differences between the groups may have confounded the observed associations.

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All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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