

RELATIONSHIP BETWEEN SERUM CALCIUM, URIC ACID, AND KNEE OSTEOARTHRITIS: A CROSS-SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Knee osteoarthritis (KOA) is a common chronic musculoskeletal disorder that causes pain, disability, and progressive structural changes, particularly in older adults. Metabolic factors may contribute to the development and progression of osteoarthritis. Serum uric acid and calcium have been proposed as potential biochemical markers associated with osteoarthritis, but their relationship with radiological severity remains incompletely understood.

Aim: To evaluate the association of serum uric acid and serum calcium levels with the radiological severity of knee osteoarthritis.

Materials and Methods: This observational study was conducted in the Department of Orthopaedics, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, from May 2025 to February 2026. Patients of either sex aged >40 years with persistent knee pain for more than one month, insidious onset of symptoms, and knee crepitus were enrolled after obtaining written informed consent. Patients with non-osteoarthritic joint diseases, known hyperuricaemia, generalized osteoarthritis, or age <40 years were excluded. Demographic and clinical parameters, including age, sex, occupation, duration of illness, and body mass index, were recorded. Serum uric acid, serum calcium, C-reactive protein, and rheumatoid factor were estimated. Radiological severity was assessed using the Kellgren–Lawrence grading system, and patients with grade II or higher KOA were included. Serum uric acid was categorized into <5 mg/dL, 5.1–7 mg/dL, and >7 mg/dL. Statistical analysis was performed using appropriate tests, with $p < 0.05$ considered statistically significant.

Results: A total of 238 patients with knee osteoarthritis were analyzed. Males constituted 166 (69.7%) and females 72 (30.3%) of the study population. The largest proportion of patients belonged to the 61–70-year age group (30.3%). Regarding socioeconomic status, 41.2% belonged to the lower socioeconomic group. Normal BMI was observed in 42.4%, while 38.7% were overweight. Serum uric acid demonstrated a significant positive association with radiological severity of knee osteoarthritis. Patients with higher serum uric acid levels had greater odds of advanced KOA compared with those in the lowest uric acid category. The association remained significant after adjustment for age and sex. Increasing serum uric acid levels were also associated with progression from lower-grade to higher-grade radiological disease. The relationship between serum calcium levels and KOA severity was also assessed.

Conclusion: Higher serum uric acid levels were significantly associated with greater radiological severity of knee osteoarthritis. Serum uric acid may therefore have potential as a biochemical marker associated with disease severity. Further prospective studies are required to clarify the role of serum uric acid and calcium in the progression and pathogenesis of knee osteoarthritis.

Keywords: Knee osteoarthritis; Serum uric acid; Serum calcium; Kellgren–Lawrence grading; Hyperuricaemia; Radiological severity; Biomarker.

How to cite this article: Ajith Kumar C, Vankamaddi Vishnuvardhan, Lavanya. RELATIONSHIP BETWEEN SERUM CALCIUM, URIC ACID, AND KNEE OSTEOARTHRITIS: A CROSS-SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL. Int J Drug Deliv Technol. 2026;16(79s):822-824. DOI: 10.25258/ijddt.16.79s.148

Introduction

Osteoarthritis (OA) is one of the most prevalent musculoskeletal disorders and a major cause of pain, disability, and reduced quality of life, particularly among older adults. Knee osteoarthritis (KOA) is one of the most frequently affected joint sites and contributes substantially to the global burden of disability. The Global Burden of Disease

Study estimated approximately 364.6 million prevalent cases of knee OA worldwide in 2019, with the burden increasing with advancing age and being higher among women.[1] OA is a multifactorial joint disorder involving mechanical, biological, metabolic, and inflammatory mechanisms rather than simply an age-related process. Structural changes include progressive cartilage degradation, subchondral bone remodeling and sclerosis,

osteophyte formation, synovial alterations, and changes in the joint capsule and periarticular tissues.[2]

In India, knee OA represents an important public health problem because of the ageing population, increasing obesity, occupational loading, and other metabolic risk factors. A community-based Indian study involving 5,000 individuals reported a prevalence of knee OA of 28.7%, with age, female sex, obesity, and sedentary occupation identified as important associated factors.[3] A systematic review and meta-analysis among elderly Indians has subsequently reported a substantial pooled prevalence of knee OA, further highlighting the increasing burden of this condition in the country.[4] Therefore, identification of potentially modifiable biochemical and metabolic factors associated with KOA may contribute to improved understanding of its pathogenesis and risk stratification.

Serum uric acid (SUA) is the final product of purine metabolism in humans and has both antioxidant and pro-oxidant properties depending on its concentration and biological environment. Although uric acid may contribute to antioxidant capacity under physiological conditions, elevated SUA levels and hyperuricemia are associated with several metabolic and cardiovascular disorders, including obesity, hypertension, diabetes mellitus, chronic kidney disease, and gout.[5] Increasing evidence has also suggested a possible relationship between uric acid metabolism and OA. Uric acid crystals and soluble uric acid may influence inflammatory pathways and oxidative stress, potentially contributing to cartilage and subchondral bone changes. A large cross-sectional study found that higher serum uric acid concentrations and hyperuricemia were positively associated with knee osteophytes, particularly among women, although the relationship with joint-space narrowing was less consistent.[6] These findings suggest that SUA may have a potential association with specific structural manifestations of KOA.

Calcium is an essential mineral involved in numerous physiological processes, including neuromuscular transmission, muscle contraction, blood coagulation, cellular signaling, and maintenance of skeletal mineralization. Disturbances in calcium homeostasis may influence bone remodeling and the interaction between subchondral bone and articular cartilage.[7] Emerging evidence has investigated the relationship between circulating calcium concentrations and OA. A Mendelian randomization study reported an inverse association between genetically predicted serum calcium levels and the risk of overall, hip, and knee OA, suggesting that calcium metabolism may have a potential role in OA susceptibility.[8] However, the biological mechanisms underlying this association remain incompletely understood.

The relationship between serum calcium, SUA, and the severity of KOA is therefore of clinical and research interest. Although previous studies have

independently examined uric acid or calcium in relation to OA, limited evidence is available regarding their combined association with knee OA, particularly in the Indian population. Evaluation of these readily measurable biochemical parameters in patients with KOA may help identify metabolic associations and generate further hypotheses regarding disease pathogenesis. Hence, the present study was undertaken to evaluate the association of serum calcium and uric acid levels with knee osteoarthritis and to determine their relationship with the clinical and/or radiological severity of the disease.

Aim

To evaluate the association of serum calcium and uric acid levels with knee osteoarthritis and determine their relationship with the severity of the disease.

Objectives

1. To estimate the serum calcium levels in patients with knee osteoarthritis.
2. To estimate the serum uric acid levels in patients with knee osteoarthritis.
3. To assess the radiological severity of knee osteoarthritis using the Kellgren–Lawrence grading system.

Materials and Methods

This observational study was conducted in the Department of Orthopaedics, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, during the period from May 2025 to February 2026. Patients of either sex aged more than 40 years who presented with persistent knee pain for more than one month were considered for inclusion. Patients with insidious-onset knee pain and crepitus during movement of the knee joint were included after obtaining written informed consent.

Patients aged less than 40 years, those with non-osteoarthritic joint diseases, known hyperuricaemia, or generalized osteoarthritis were excluded from the study. All eligible participants provided written informed consent before enrolment.

Baseline demographic and clinical characteristics, including age, sex, occupation, duration of symptoms, and body mass index (BMI), were recorded using a structured data collection proforma. Clinical evaluation was followed by radiological and biochemical assessment.

Plain anteroposterior and lateral weight-bearing radiographs of the affected knee were obtained and evaluated according to the Kellgren–Lawrence (KL) grading system. Patients with radiographic knee osteoarthritis of KL grade 2 or higher were included in the analysis.[13]

Blood samples were collected after an appropriate period of fasting for quantitative estimation of serum uric acid, serum calcium, C-reactive protein (CRP), and rheumatoid factor (RF) using standard laboratory methods. Serum uric acid levels were categorized into three groups for analysis: Group 1: <5 mg/dL; Group 2: 5.1–7.0 mg/dL; and Group 3: >7 mg/dL.

Serum calcium levels were recorded as continuous variables and assessed in relation to the severity of radiographic knee osteoarthritis. The relationship between serum uric acid and calcium levels and radiological severity of KOA was subsequently evaluated.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using appropriate statistical software. Continuous variables were expressed as mean $\pm$ standard deviation (SD) for normally distributed data or median with interquartile range where appropriate, while categorical variables were presented as frequency and percentage.

The distribution of continuous variables was assessed for normality before statistical testing. Differences in serum calcium and uric acid levels across different Kellgren–Lawrence grades and uric acid categories were assessed using one-way ANOVA for normally distributed data or the Kruskal–Wallis test for non-normally distributed data.

The association between categorical variables was assessed using the chi-square test or Fisher's exact test, as appropriate. The correlation between serum calcium, serum uric acid, and radiological severity of knee osteoarthritis was assessed using Pearson's correlation coefficient for normally distributed variables or Spearman's rank correlation coefficient for non-parametric data.

Where appropriate, multivariable analysis may be performed to assess whether serum calcium and uric acid levels are independently associated with radiological severity after adjusting for potential confounders such as age, sex, BMI, and duration of illness.

A two-tailed p-value <0.05 was considered statistically significant.

Result:

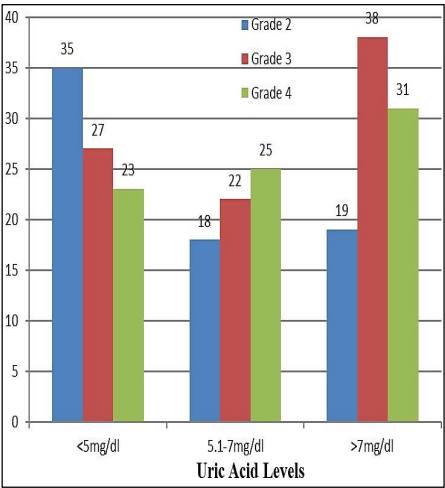
A total of 238 patients diagnosed with Knee joint osteoarthritis were enrolled and analysed. Majority of them (69.7%) were male, and 30.3% was females. Most of OA patients (30.3%) were 61-70 year of age, 41.2% belong to lower socio-economic class and 42.4% had normal BMI [table: 1].

Table 1: Sociodemographic variable of knee osteoarthritis patients

Sociodemographic variable		Number (n=238)	Percentage
Gender	Male	166	69.7%
	Female	72	30.3%
Age group	40-50 year	39	16.4%
	51-60 year	63	26.4%
	61-70 year	72	30.3%

	>70 years	64	26.9%
Socio-economic status	Lower	98	41.2%
	Middle	75	31.5%
	Upper	65	27.3%
BMI	Underweight	45	18.9%
	Normal weight	101	42.4%
	Overweight	92	38.7%

Association of serum uric acid level with knee osteoarthritis according to the Kellgren–Lawrence osteoarthritis scale was shown in figure: 1. Serum uric acid level was significantly associated with the grading of the knee OA. Severity of knee OA increases with the uric acid level.



Graph 1: Distribution of Knee Osteoarthritis according to Serum uric acid levels and Kellgren-Lawrence osteoarthritis scale

Table 2: Correlation between serum uric acid levels and serum calcium levels with knee osteoarthritis progression expressed as odds ratio (OR)

	Se ru m ur ic ac id le ve ls (m g/ d L)	P ati ent s wit h gra de II kne ee OA	Pa tie nt s wi th gra de II and grade IV knee OA	Odds ratio	O d d s r a t i o a d j u s t e d f o r a g e, a n d se x
Seru m uric aci d lev	<5mg /dl	35	50	1.00(r eferen ce)	1.00(ref erence)
	5.1- 7mg/d l	18	47	0.84	0.83

els (mg /dL)	>7mg /dl	19	69	2.25	2.07
S er u m ca lc iu m le v els (m g/ d L)	<8mg /dl	38	54	1.00 (refer ence)	1.00 (referen ce)
	8- 11mg/ dl	13	41	0.65	0.74
	>11m g/dl	21	70	2.17	2.12

There is a strong association present between osteoarthritis of knee joint and the highest tertile of serum uric acid level [adjusted odds ratio - 2.31 and adjusted odds ratio-3.27 respectively). Also, we found a positive association of increasing serum uric acid with progression of the knee joint osteoarthritis (highest tertile in comparison to lowest tertile of serum uric acid odds ratio-2.07.

Discussion

The present study evaluated the association of serum uric acid and serum calcium levels with the radiological severity of knee osteoarthritis among 238 patients. The study population showed a male predominance, with 166 (69.7%) males and 72 (30.3%) females. The largest proportion of participants belonged to the 61–70-year age group (30.3%), followed by those aged >70 years (26.9%). This age distribution is consistent with the established relationship between advancing age and the development and progression of knee osteoarthritis, as cumulative cartilage degeneration, subchondral bone remodeling, and other structural changes become more prominent with increasing age.[9]

In the present study, 41.2% of patients belonged to the lower socioeconomic group, while 31.5% and 27.3% belonged to the middle and upper socioeconomic groups, respectively. Regarding BMI, 42.4% of participants had normal weight, whereas 38.7% were overweight and 18.9% were underweight. These findings indicate considerable heterogeneity in the metabolic and demographic characteristics of patients with knee OA. Obesity and increased mechanical loading are established risk factors for KOA; however, the presence of OA among participants with normal BMI indicates that

factors other than mechanical loading, including age, metabolic abnormalities, inflammation, and genetic susceptibility, may also contribute to disease development.[10]

A major finding of the present study was the positive association between serum uric acid levels and the radiological severity of knee osteoarthritis. Patients with higher serum uric acid concentrations demonstrated a greater likelihood of having advanced KOA. The highest tertile of serum uric acid was associated with substantially increased odds of more severe knee OA, and the association persisted after adjustment for age and sex. Furthermore, increasing serum uric acid levels were associated with progression from lower-grade to higher-grade radiological disease. These findings are consistent with previous research suggesting a relationship between serum uric acid and structural manifestations of knee OA. Sun et al. reported that higher serum uric acid and hyperuricaemia were associated with knee osteoarthritis and particularly with osteophyte formation.[11]

The biological basis for this association may involve the pro-inflammatory and oxidative effects of uric acid. Although uric acid has antioxidant properties at physiological concentrations, increased levels may promote oxidative stress, endothelial dysfunction, and inflammatory signaling. Soluble uric acid may influence chondrocyte metabolism and synovial inflammation, while monosodium urate deposition can activate inflammatory pathways. However, because the present study is observational, the association should not be interpreted as proof that elevated uric acid directly causes progression of knee OA.

The present study also evaluated serum calcium in relation to knee OA severity. Evidence regarding this relationship remains inconsistent. Li et al., in a large cross-sectional study of 2,855 participants, reported an inverse association between serum calcium concentration and radiographic knee OA, with higher calcium concentrations associated with lower odds of radiographic disease after adjustment for major confounders.[12] Similarly, a Mendelian randomization study suggested an inverse causal association between genetically predicted serum calcium levels and knee OA.[13] These observations suggest that calcium homeostasis and subchondral bone metabolism may potentially influence OA pathogenesis. Nevertheless, serum calcium is tightly regulated by parathyroid hormone and vitamin D, and a single serum measurement may not accurately represent long-term calcium status.

The findings of the present study support the possibility that serum uric acid may serve as a metabolic marker associated with radiological severity of knee osteoarthritis, while the role of serum calcium requires further investigation. The study is strengthened by the use of the Kellgren–Lawrence grading system and assessment of

biochemical parameters. However, its observational design, single-centre setting, and inability to establish causality are important limitations. Larger prospective studies incorporating vitamin D, parathyroid hormone, renal function, inflammatory markers, dietary factors, and longitudinal radiological assessment are required to clarify the independent roles of serum uric acid and calcium in the progression of knee osteoarthritis.

Conclusion

The present study demonstrated a significant association between serum uric acid levels and the radiological severity of knee osteoarthritis. Higher serum uric acid levels were associated with an increased likelihood of advanced knee osteoarthritis according to the Kellgren–Lawrence grading system, and this association persisted after adjustment for age and sex. These findings suggest that elevated serum uric acid may serve as a potential biochemical marker of disease severity in knee osteoarthritis. The relationship between serum calcium levels and knee osteoarthritis requires further evaluation, as the available evidence remains inconsistent. Larger prospective and longitudinal studies are required to determine whether alterations in serum uric acid and calcium are causally involved in the progression of knee osteoarthritis.

References :

1. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional, and national burden of osteoarthritis, 1990–2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet Rheumatol*. 2023;5(9):e508–e522.
2. Hunter DJ, March L, Chew M. Osteoarthritis in 2020 and beyond: a Lancet Commission. *Lancet*. 2020;396(10264):1711–1712.
3. Pal CP, Singh P, Chaturvedi S, Pruthi KK, Vij A. Epidemiology of knee osteoarthritis in India and related factors. *Indian J Orthop*. 2016;50(5):518–522.
4. Daniel RA, Kalaivani M, Aggarwal P, Gupta SK. Prevalence of knee osteoarthritis among elderly persons in India: a systematic review and meta-analysis. *J Family Med Prim Care*. 2025;14(5):1675–1684.
5. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. *N Engl J Med*. 2008;359(17):1811–1821.
6. Sun Y, Miao J, Guo F, Zhang Y, Li Q, Liu J, et al. The associations of serum uric acid level and hyperuricemia with knee osteoarthritis. *Rheumatol Int*. 2016;36(5):713–718.
7. Peacock M. Calcium metabolism in health and disease. *Clin J Am Soc Nephrol*. 2010;5 Suppl 1:S23–S30.

8. Zheng J, et al. Causal relationship of serum nutritional factors with osteoarthritis: a Mendelian randomization study. *Rheumatology (Oxford)*. 2021;60(1):512-518.
9. Katz JN, Arant KR, Loeser RF. Diagnosis and treatment of hip and knee osteoarthritis: a review. *JAMA*. 2021;325(6):568-578.
10. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2010;18(1):24-33.
11. Sun Y, Miao J, Guo F, Zhang Y, Li Q, Liu J, et al. The associations of serum uric acid level and hyperuricemia with knee osteoarthritis. *Rheumatol Int*. 2016;36(5):713-718.
12. Li H, Zeng C, Wei J, Yang T, Gao SG, Li YS, et al. Serum calcium concentration is inversely associated with radiographic knee osteoarthritis: a cross-sectional study. *Medicine (Baltimore)*. 2016;95(6):e2838.
13. Zheng J, Chen J, Yang Y, et al. Causal relationship of serum nutritional factors with osteoarthritis: a Mendelian randomization study. *Rheumatology (Oxford)*. 2021;60(5):2383-2392. :::