



Original Research Article

To Determine the Relationship Between Serum Calcium and Uric Acid Levels with The Knee Osteoarthritis: A Cross-Sectional Study

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Abstract: **Background:** A frequent degenerative joint condition impacted by mechanical, metabolic, and biochemical variables is knee osteoarthritis (KOA). According to new research, blood calcium and uric acid may be involved in joint inflammation, subchondral bone alterations, and cartilage metabolism. **Objective:** To assess the correlation between uric acid and serum calcium levels in individuals with knee osteoarthritis. **Methods:** A cross-sectional study was conducted among 160 patients diagnosed with KOA. Demographic characteristics, body mass index (BMI), residential status, and socioeconomic background were recorded. Radiographic grading of KOA (Grade II–IV) was done using standard Kellgren-Lawrence criteria. Serum uric acid and calcium levels were measured and analyzed in relation to KOA severity. **Results:** The majority of patients were male (70.6%), aged over 60 years (57.5%), and from rural areas (65.6%). A significant positive correlation was observed between serum uric acid levels and KOA grade ($r = +0.52$, $p < 0.001$), with hyperuricemia more prevalent in Grade IV KOA (22 patients). Conversely, serum calcium levels were inversely correlated with KOA severity ($r = -0.48$, $p < 0.001$), with lower calcium levels more common in earlier stages. Both associations were statistically significant. **Conclusion:** Serum uric acid and serum calcium significantly associated with the progression of knee OA, both are inversely associated with the knee OA.

Keywords: Knee osteoarthritis, serum calcium, serum uric acid, hyperuricemia.

INTRODUCTION

Osteoarthritis (OA) is a chronic joint disease characterized by degeneration of articular cartilage, sclerosis of the subchondral bone and formation of osteophytes [1, 2]. Osteoarthritis is the most common form of arthritis in the community, chronic, has a major impact on public health and the most common cause of activity limitation in the middle aged and elderly population [1, 3]. Knee OA (KOA) is responsible for more than 80% of the overall illness burden and ranks as the eleventh leading cause of disability worldwide [4]. KOA was present in at least 19% of people 45 years of age or older [5]. Obese people had a higher lifetime chance of having symptomatic KOA (~60.5%), with

the risk being approximately 45% for males and 47% for females [6]. Obesity, joint damage, metabolic illnesses, bone and joint abnormalities, and hereditary variables are among the several elements that appear to contribute to the development and severity of the OA process [7]. The pathophysiology of OA is thought to entail dietary imbalance as well. It is now commonly acknowledged that nutrition plays a significant role in maintaining joint health [8]. Purine metabolism produces uric acid, which is mostly present in bodily fluids as the ion form urate. The synthesis and excretion of urates determine the blood's uric acid concentration [9]. A SUA level that is higher than the upper limit of the normal range is referred to as hyperuricemia. For women, the generally recognized upper limit of the normal range for SUA is 6 mg/dl, and for men, it is 6.8 mg/dl [10]. In addition to being linked to many types of arthritis, including osteoarthritis, hyperuricemia is a significant indicator for metabolic disorders [11]. Numerous biological functions, including hormone regulation, blood coagulation, muscle contraction, nerve transmission, blood pressure management, and enzyme activation, depend on calcium (CA) [12]. With the exception of oxalate, the two primary components of urine that lead to the formation of urinary stones are uric acid and CA acetate [13]. Aim: The purpose of this study was to determine whether patients with osteoarthritis in their knees had a correlation between their serum calcium and uric acid levels.

METHODS OVERVIEW

This was a cross-sectional observational study conducted in the Department of Orthopedics and Biochemistry at a tertiary care Indian hospital over a period of 12 months.

These patients with complaints of knee joints pain attended the out patients department of Orthopaedics during the study period were enrolled.

Inclusion Criteria:

- Patients aged 40–75 years.
- Based on radiographic findings and the American College of Rheumatology's (ACR) criteria, primary knee osteoarthritis was diagnosed.
- Patients who provided consent for the study

Exclusion Criteria:

- Secondary OA brought on by inflammation, infection, or trauma.
- Patients with chronic kidney disease, hyperparathyroidism, or gout.
- Current use of uric acid-lowering drugs, calcium or vitamin D supplements.
- Patients who provide consent for the study

According to the Kellgren-Lawrence osteoarthritis scale [13], the following grading of knee osteoarthritis: Grade 0: no radiographic features of OA • Grade 1: doubtful joint space narrowing and osteophyte • Grade 2: possible joint space narrowing definite osteophyte • Grade 3: definite joint space narrowing, multiple osteophyte possible bony deformity and mild sclerosis • Grade 4: obliterated joint space, large osteophyte, definite bony deformity and severe sclerosis. Basic characteristics, such as age, sex, occupation, duration of illness, and BMI (in kg/m²) were recorded. Plain antero-posterior and lateral view radiographs of the affected knee were taken. Serum calcium and serum uric acid level (in mg/dl) was obtained. In serological testing quantitative fasting serum uric acid, serum calcium, C-reactive protein and Rheumatoid factor were performed.

Statistical Analysis:

SPSS version 25 was used to analyze the data. For continuous variables, the mean and standard deviation were determined. The association between serum calcium and uric acid and KL grade was evaluated using Pearson correlation. Group comparisons were done using ANOVA. P-values less than 0.05 were regarded as statistically significant,

RESULT

A total of 160 patients with knee osteoarthritis were included in the study. The majority of participants were aged 61–70 years (31.9%) and male (70.6%). Most patients came from rural areas and belonged to the lower or middle socio-economic classes. Details of the socio-demographic distribution are presented below.

Table 1: Socio Demographic variable of knee osteoarthritis patients

Socio Demographic Variable		Number (160)	Percentage
Age group	40-50 year	28	17.5%
	51-60 year	40	25%
	61-70 year	51	31.9%

	>70 years	41	25.6%
Gender	Male	113	70.6%
	Female	47	29.4%
Socio-Economic Status	Lower	70	43.8%
	Middle	58	36.2%
	Upper	32	20%
BMI	Underweight	22	13.8%
	Normal weight	77	48.1%
	Over weight	61	38.1%
Residential Area	Rural	105	65.6%
	Urban	55	34.4%

Patients with advanced KOA (Grade IV) were more likely to have elevated uric acid levels and lower calcium levels.

Table 2: Correlation between serum uric acid levels with knee osteoarthritis

Serum uric acid levels (mg/dL)	Grade II knee OA	Grade III knee OA	Grade IV knee OA	P value
<5mg/dl	27	18	14	0.009
5.1-7mg/dl	9	14	16	
>7mg/dl	11	29	22	

Table 3: Correlation between serum calcium levels with knee osteoarthritis

Serum uric acid levels (mg/dL)	Grade II knee OA	Grade III knee OA	Grade IV knee OA	P value
<8mg/dl	30	19	15	0.008
8-11mg/dl	7	12	17	
>11mg/dl	13	25	22	

A statistically significant positive correlation was found between serum uric acid levels and KOA severity ($r = +0.52$, $p < 0.001$). Conversely, serum calcium levels were inversely correlated with KOA severity ($r = -0.48$, $p < 0.001$).

Table 4: Correlation between Biochemical Parameters and KOA Severity

Parameter	Correlation Coefficient (r)	p-value
Serum Calcium	-0.48	< 0.001
Serum Uric Acid	+0.52	< 0.001

DISCUSSION

In this cross-sectional study we evaluated the association between serum uric acid and calcium levels and radiographic severity of KOA. The findings indicate that increasing KOA severity, particularly in Grade IV cases, is associated with elevated serum uric acid levels and reduced calcium levels. Both correlations were statistically significant, suggesting a potential pathophysiological link between these biochemical parameters and osteoarthritis progression.

Our demographic analysis revealed that the majority of patients were aged ≥ 60 years and predominantly male. Most patients resided in rural areas and belonged to lower socioeconomic strata. A large proportion were either overweight or of normal weight, which is consistent with previous studies like: Felson et al [14] and Vijay N. et al [15], indicating that increased mechanical loading contributes to KOA development and progression.

Importantly, we observed that serum uric acid levels were significantly associated with KOA grade ($p = 0.009$), with a positive correlation coefficient ($r = +0.52$, $p < 0.001$). Grade IV KOA patients had a notably higher prevalence of hyperuricemia (>7 mg/dL) compared to those with Grade II disease. This finding aligns with the Mohamad Rifal, et al [16] and Denoble et al [17] emerging evidence suggesting that monosodium urate crystals may contribute to synovial inflammation and cartilage degradation even in the absence of clinical gout. Furthermore study done by Martinon, et al [18].reported that uric acid has been proposed to exacerbate oxidative stress and promote the production of pro-inflammatory cytokines such as IL-1 β and TNF- α , which are implicated in osteoarthritic cartilage loss.

Conversely, serum calcium levels showed an inverse relationship with KOA severity ($r = -0.48$, $p < 0.001$), with lower calcium levels observed more frequently in advanced cases (Grade IV). Patients with serum calcium levels below 8 mg/dL were more likely to have Grade II disease, while those with Grade IV KOA had a greater prevalence of mildly elevated calcium levels. This pattern may reflect alterations in calcium homeostasis as a consequence of

chronic joint degeneration or metabolic bone turnover associated with osteoarthritis, similar findings reported by Hunter BZ, et al [19] and Guermazi et al [20]. Hypocalcemia has also been linked to impaired cartilage repair and reduced chondrocyte function.

Taken together, our results support the hypothesis that serum uric acid and calcium levels are not only markers but potentially contributors to KOA pathogenesis. These parameters may serve as accessible biochemical indicators for identifying patients at higher risk for disease progression [21]. Furthermore, the observed correlations underscore the importance of metabolic and nutritional factors in the clinical management of KOA [22].

Limitations of our study include its cross-sectional design, which precludes causality inference, and potential confounding by factors such as diet, comorbidities, and medication use. Future longitudinal studies are warranted to explore whether interventions targeting uric acid reduction or calcium homeostasis can mitigate KOA progression.

CONCLUSION

This study demonstrates a significant correlation between serum biochemical markers and the severity of knee osteoarthritis (KOA). Elevated serum uric acid levels were positively associated with advanced radiographic grades of KOA, suggesting a potential role for hyperuricemia in disease progression. Conversely, lower serum calcium levels were inversely related to KOA severity, indicating a possible link between calcium metabolism and joint degeneration. These findings highlight the importance of monitoring metabolic parameters such as uric acid and calcium in patients with KOA, particularly those presenting with more severe forms of the disease. Early identification and management of these biochemical alterations may offer opportunities for improved patient outcomes and targeted therapeutic interventions.

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