

**Original research article**

## **Correlation between serum calcium and uric acid levels with the knee osteoarthritis patients**

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### **Abstract**

**Background:** Osteoarthritis is the most common form of arthritis over all. Serum uric acid (SUA) and serum calcium level are an important biomarker for metabolic diseases and it is related to many forms of arthritis including osteoarthritis (OA).

**Objectives:** The purpose of the study was to explore the association of serum uric acid and serum calcium levels with clinical and radiological severity of knee osteoarthritis.

**Methods:** Patients diagnosed with knee OA attending OPD of orthopaedics department during the study period were enrolled in this study. Basic socio-demographics data and BMI (kg/m<sup>2</sup>) were recorded. In serological testing quantitative fasting serum uric acid, serum calcium, C-reactive protein and Rheumatoid factor were performed.

**Results:** Majority of them (69.7%) were male, 30.3% were 61-70 year of age, 41.2% belong to lower socio-economic class and 42.4% had normal BMI. Serum uric acid level was significantly associated with the grading of the knee OA. Severity of knee OA increases with the uric acid level. 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).

**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 OA, serum uric acid, serum calcium, hyperuricemia

### **Introduction**

Osteoarthritis (OA) is one of the most prevalent conditions resulting to disability particularly in elderly population. OA is the most common articular disease of the developed world and a leading cause of chronic disability, mostly as a consequence of the knee OA and/or hip OA <sup>[1]</sup>. Osteoarthritis is a primary localized degenerative disorder of multi-factorial etiology characterized by loss of articular cartilage, hypertrophy of bone at the margins, subchondral sclerosis and a range of biochemical and morphological alternatives of the synovial membrane and joint capsule. Late-stage osteoarthritis shows softening ulceration and focal disintegration of the articular cartilage <sup>[2]</sup>. In India, many studies have reported osteoarthritis as the second most common rheumatologic problem and the most frequently occurring joint disease <sup>[3]</sup>. It is well known that serum uric acid (SUA) is a biological product of purine metabolism. SUA is a useful antioxidant in the human blood, and helps maintain antioxidant stress (1). However, elevated SUA can lead to a series of diseases, such as hyperuricemia, gout, hypertension, obesity, diabetes, coronary disease and chronic kidney disease <sup>[4-5]</sup>. Calcium (CA) plays a vital role in several biological processes, such as hormone regulation, blood clotting, muscle contraction, nerve transmission, blood pressure regulation, and enzyme activation <sup>[6]</sup>. Uric acid and CA acetate are the two main elements in urine that contribute to the development of urinary stones, except for oxalate <sup>[7]</sup>. However, the relationship between total CA and SUA remains unclear. Observational studies have suggested that total CA levels are associated with SUA in adults, lacking evidence and remaining unclear <sup>[8-9]</sup>.

**Aims & Objectives:** Present study was done to find the association between serum calcium and serum uric acid level with knee osteoarthritis patients.

### **Materials & Methods**

This study was a cross sectional observational study, conducted in the department of orthopedics in a tertiary care center at India. A total of 238 patients of knee osteoarthritis were enrolled in this study. These patients with complaints of knee joints pain attended the out patients department of Orthopaedics

during the study period were enrolled.

**Inclusion criteria**

- Patients age more than forty years with either sex.
- Patients having persistent knee pain more than one month.
- Pain is insidious in onset and having crepitus during movement of knee joint.
- Patients who provide consent for the study.

**Exclusion criteria**

- Patients age less than forty years.
- Non-OA joint disease; known cases of hyperuricaemia; and patients with generalized OA.
- Patients who provide consent for the study.

All included patients provided written informed consent. Basic characteristics, such as age, sex, occupation, duration of illness, and BMI (in kg/m<sup>2</sup>) were recorded. Plain antero-posterior and lateral view radiographs of the affected knee were taken 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.

The serum uric acid levels were divided into tertiles.

**Group 1:** Serum uric acid level less than 5 mg/dl.

**Group 2:** Serum uric acid level between 5.1 mg/dl-7 mg/dl.

**Group 3:** Serum uric acid level greater than 7 mg/dl.

In this study patients suffering from knee osteoarthritis of grade 2 or more (according to Kellgren-Lawrence osteoarthritis scale) are included [13]. This system has 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.

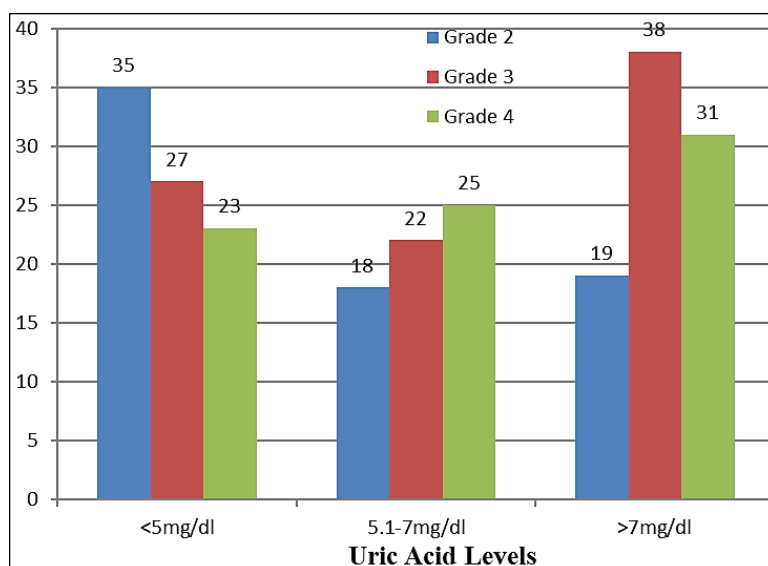
**Results**

A total of 238 patients diagnosed with Knee joint osteoarthritis were enrolled and analysed. Majority of them (69.7%) were male, and 30.3% were 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)

	Serum uric acid levels (mg/dL)	Patients with grade II knee OA	Patients with grade III and grade IV knee OA	Odds ratio	Odds ratio adjusted for age, and sex
Serum uric acid levels (mg/dL)	<5mg/dl	35	50	1.00(reference)	1.00(reference)
	5.1-7mg/dl	18	47	0.84	0.83
	>7mg/dl	19	69	2.25	2.07
Serum calcium levels (mg/dL)	<8mg/dl	38	54	1.00 (reference)	1.00 (reference)
	8-11mg/dl	13	41	0.65	0.74
	>11mg/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**

In our study epidemiologic results particularly about greater prevalence of hyperuricemia among male are very much comparable with other previous studies this study also showed an association between hyperuricemia and generalized osteoarthritis as described by various previous studies [10]. This may be explained by the pro-inflammatory effect of the elevated serum uric acid [11]. In a study done by Anna E. Denoble *et al.* [12] the strong association of synovial fluid uric acid level with severity of osteoarthritis of knee joint was advocated. In his study he quantified severity of osteoarthritis radiographically and scintigraphically and concluded that uric acid is a marker of disease severity. He also described strong possibility that uric acid may act as a promoting factor in the pathological process of osteoarthritis by activating the cascade of inflammation. Other possible explanatory mechanisms for the association between high serum uric acid levels and knee OA include genetic predisposition, and endogenous hormonal environment. Etiology of osteoarthritis is still doubtful but there are many physiological and clinical factors that may contribute to the risk and progression of osteoarthritis. These factors include obesity, joint deformity, trauma, age and female sex [13]. The increase in both hyperuricemia and osteoarthritis in women after menopause indicate towards any possible hormonal mechanisms. Another Indian study by Mishra *et al.* [14] described correlation of elevated serum uric acid levels with laboratory and anthropometric parameters of various metabolic syndromes. They suggested that this may be due to high caloric diet, sedentary habits and greater prevalence of obesity unfortunately in our study we were unable to find any co-relation in dietary pattern and life style with the elevated serum uric acid level. A co-relation between rise in uric acid level and progression of knee osteoarthritis was also found in present study which is comparable to result of various previous studies [15-16]. Our study also showed the correlation of serum uric acid level with radiographic severity in knee joint osteoarthritis as measured by Kellgren-Lawrence osteoarthritis scale has been previously reported by Anna E. Denoble *et al.* [12].

Yazmalar *et al.* [17] found that serum calcium levels were not significantly different between knee osteoarthritis patients and controls. Our study found inverse relationship between serum calcium concentration and OA of the knee; similar finding also reported by Valhmu WB *et al.* [18] and Kuznetsov G *et al.* [19]. Another reason for the observed association of uric acid level with osteoarthritis of knee joint and generalized osteoarthritis in present study may be that we did not excluded patients already having diabetes and medications including diuretics which have been shown to be associated with osteoarthritis.

## Conclusion

This study supports a possible correlation between hyperuricemia and osteoarthritis. Serum calcium concentration has an inverse relationship with OA of the knee. Various confounding factors such as endogenous hormonal environment, insulin resistance, and genetic predisposition exist, to affect the possible association between hyperuricemia and osteoarthritis. To validate this issue a large sample size multifactorial study is recommended.

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