

## Original Research Article

# A study of the association between hyperuricemia and knee osteoarthritis in the coastal Indian population

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**Received:** 03 July 2017

**Accepted:** 06 August 2018

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## ABSTRACT

**Background:** Hyperuricemia and knee osteoarthritis are common problems that affect the aging population and they have an increasing prevalence with obesity and hypertension. Epidemiologic and immunological studies have shown a possible relation between the two conditions. Uric acid is a common factor found in association with the evaluation and treatment of osteoarthritis. There are serious therapeutic implications, particularly in using traditional gout medications, for use in osteoarthritis treatment is to be explored in detail. Our diet contains a good amount of purine containing food stuffs. The common items which increase our uric acid levels are red meat, all alcoholic beverages, seafood and shellfish. Previous studies have shown an association between serum uric acid and generalized osteoarthritis, but with the limited studies on the evidence of association between serum uric acid and knee joint osteoarthritis. This study aims to know the association between serum uric acid levels and osteoarthritis of knee joint.

**Methods:** This is a Cross-sectional analytical study including eight hundred and thirty patients (461 males, 369 females) in a population screening during a patient education program on joint pains. Their serum uric acid level, total count, differential count, erythrocyte sedimentation rate (ESR), height, weight, blood pressure, BMI and standing radiographs of affected knees were obtained. The presence of radiographic osteoarthritis of the knee was analyzed using Kellgren-Lawrence system. The patients were divided into cohorts with hyperuricemia and osteoarthritis and compared with the subjects without either of the problems.

**Results:** Isolated knee joint osteoarthritis is present in 183 subjects (22%), hyperuricemia was present in 154 subjects (18.55%). There is a significant positive association present between isolated knee joint osteoarthritis and the highest level of serum uric acid (adjusted odd's ratio-2.24, 95% confidence interval-1.57-2.94). There is a significant positive association between high serum uric acid levels and progression of the knee joint osteoarthritis (highest level versus lowest level of serum uric acid odd's ratio-1.38, 95% confidence interval-0.96-2.74).

**Conclusions:** It is concluded that knee joint osteoarthritis and its progression are associated with hyperuricemia.

**Keywords:** Diet for hyperuricemia, Hyperuricemia, Knee joint, Osteoarthritis, Serum uric acid

## INTRODUCTION

Hyperuricemia is an abnormally high level of uric acid in the blood. In the pH conditions of body fluid, uric acid exists largely as urate, the ion form. The amount of urate in the body depends on the balance between the amount

of purines eaten in food, the amount of urate synthesised within the body (e.g. through cell turnover), and the amount of urate that is excreted in urine or through the gastrointestinal tract. In humans, the upper end of the normal range is 6mg/dL (360µmol/L) for women and 6.8mg/dL (400µmol/L) for men.

Osteoarthritis is the most common type of arthritis worldwide. The association of osteoarthritis with age, obesity, sex, and metabolic factors has been studied. All of these studies showed an association of osteoarthritis with different aspects like degeneration of body tissues with aging, body weight, female sex and different metabolic parameters like uric acid. Inflammatory arthritis causes progressive, immune mediated inflammatory disorder involving the entire joint structure including the synovial membrane, cartilage and subchondral bone and in advance cases deformity of joint develops. OA typically affects all the synovial joints, however, knee is affected most (41%) among all the joints.<sup>1,2</sup>

Gout is a crystal-induced arthritis caused by deposition of the monosodium uric acid crystal in joints and tendon attachments in long standing hyperuricemia. 5% of the middle-aged and elderly population worldwide is affected by this form of inflammatory arthritis.

Epidemiologic and immunological studies have shown a possible relation between uric acid and osteoarthritis. Aging and obesity are significant risk factors shared by both OA and gout and may confound the association between both conditions.<sup>3</sup> The pathological links between these two common conditions remains to be further explored. Whether gout promotes the development or progression of osteoarthritis is particularly relevant to osteoarthritis research. Despite the high prevalence, individual impact of disability, and high societal cost of osteoarthritis, there is no drug categorically approved for structural protection of the joint or prolongation of joint life in OA. Therefore, if there is an association between hyperuricemia and osteoarthritis, effective treatment for gout might potentially be useful for preventing and treating osteoarthritis.

In the western coastal population of India, where there is significant number of meat eaters, the prevalence of hyperuricemia is also high. There is a paucity of information regarding the association with age, gender,

comorbidities like diabetes and hypertension, and knee osteoarthritis. In this study, we try to observe the possible associations and pathological mechanisms between hyperuricemia and knee osteoarthritis.

**METHODS**

We collected data from 830 patients above, 35 years of age, attending a joint pain awareness medical camp at Ernakulam by anthropometric measurements, laboratory and clinical examination and interviewing about their diet habits. Their serum uric acid level, total count, differential count, erythrocyte sedimentation rate (ESR), height, weight, blood pressure, BMI, standing radiographs of affected knees were obtained. The presence of radiographic osteoarthritis of the knee was analyzed using Kellgren-Lawrence system. Those with grade 2 and above knee osteoarthritis were selected for the study. The subjects were divided into three groups based on serum uric acid levels. Group 1: serum uric acid less than 4mg/dl, Group 2: serum uric acid levels between 4.1-7mg/dl, Group 3: serum uric acid levels more than 7mg/dl.

The patients were divided into cohorts with hyperuricemia and osteoarthritis. This was then adjusted for age, sex, body mass index (BMI). The cohorts with hyperuricemia and knee osteoarthritis were compared with the subjects without either of the problem and statistically analysed for odd's ratio and adjusted odd's ratio to look for association between hyperuricemia and osteoarthritis and its progression.

**RESULTS**

In our study, out of 830 subjects who participated in the study, 461 males (55.6%) and 369 females (45.6%), hyperuricemia was found in 154. Knee osteoarthritis was seen in 183 persons of which 131 were males (71.6%) and 52 were females (28%). Of the 154 patients with hyperuricemia, 121 were male (78%) and 33 were female (22%).

**Table 1: Descriptive data.**

Patients	Total number, (n= 830)	Mean Age (years)	Knee joint arthritis, (n= 183)	Hyperuricemia (n = 154)
Males	461 (55.6%)	56.8±14.2	131 (71.6%)	121 (78%)
Females	369 (45.6%)	45.3±13.9	52 (28.4%)	33 (22%)

**Table 2: The relationship expressed as odds ratio. the crude odds ratio for the relationship between knee osteoarthritis and high uric acid was 1.38 (95% CI, 0.96-2.74).**

Disease	Uric acid group	Crude odd's ratio (95% confidence interval)	Odd's ratio adjusted for age, sex, BMI (95% confidence interval)
Knee osteoarthritis (n=187)	<4 mg/dL	1.00 (reference)	1.00 (reference)
	4-7 mg/dL	1.05 (0.51 - 2.06)	1.26 (0.98-1.66)
	>7 mg/dL	1.00 (0.53 - 1.86)	2.24 (1.57-2.94)

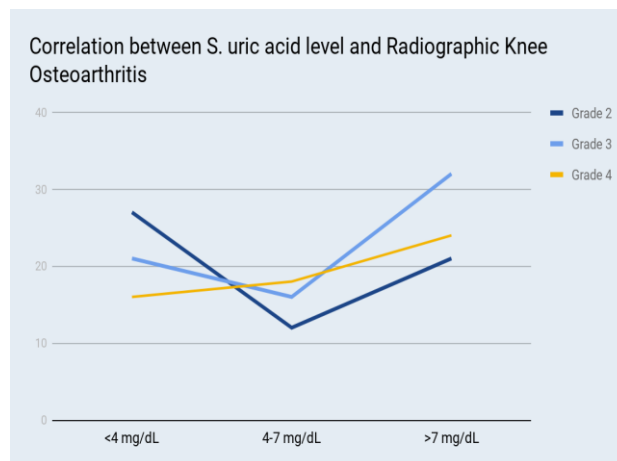
Authors report the overall prevalence rate of hyperuricemia as 18.55%, with higher proportion of

males having elevated SUA compared to females. Additionally, we found that >30% of the subjects with

T2DM with or without HTN had HU. The proportion of diabetic subjects with HU (33.6%) was much higher in our study as compared to previously published literature where around 25% of T2DM patients were reported to have elevated SUA levels.

The distribution of the patients in different uric acid groups is shown in Table 2. It showed a greater number of patients with advanced osteoarthritis in the higher uric acid groups.

There is significant association between knee osteoarthritis and hyperuricemia (SUA>7mg/dL). Adjusted odd's ratio 2.24, 95% confidence interval 1.57-2.94. There is a significant positive association between serum uric acid and progression of knee joint osteoarthritis. Highest uric level group versus lowest uric acid level group odd's ratio-2.02, 95% confidence interval 1.01-3.66 (Table 3).



**Figure 1: Correlation between serum uric acid and radiographic grade of osteoarthritis.**

**Table 3: The relationship between serum uric acid groups and progression of osteoarthritis expressed as odd's ratio with 95% confidence interval.**

Serum uric acid group (mg/dL)	Patients with grade II knee osteoarthritis	Patients with grade III and IV knee osteoarthritis	Crude Odd's ratio (95% confidence interval)	Odd's ratio adjusted for age, sex, BMI (95% confidence interval)
<4 mg/dL	26	36	1.00 (reference)	1.00 (reference)
4-7 mg/dL	11	33	0.88 (0.54-1.47)	0.82 (0.49-1.35)
>7 mg/dL	21	56	2.24 (1.02-3.74)	2.02 (1.01-3.66)

## DISCUSSION

The prevalence of HU varies with age and gender. Our study showed similar prevalence of HU as documented in previous studies from different population.<sup>4,5</sup> In the previous literature, SUA levels were reported to increase with advancing age.<sup>6,7</sup> In the US study conducted from 1959 to 1960, the SUA values in males rose rapidly to a peak level at 20-24 years followed by a slight decline and a rise at 55 to 59 years. In females, the SUA levels rose to a minor peak at 15-19 years followed by a decline and levelling at approximately 40 years and reached peak levels at 50-54 years and 60-64 years, due to a decline in the production of estrogen due to menopausal conditions.<sup>6</sup>

In 1999, Culleton et al, in the Framingham Heart Study, also reported that there is a gradual increase in SUA levels in females from the fourth to the seventh decades of life.<sup>7</sup> In our study as well, the proportion of HU subjects increased with progression in age; maximum subjects were evident in the age category of >50 years followed by 31-50 years and ≤30 years. Our findings were contrary to the earlier reported results of Lin CS et al, where the highest prevalence of HU was reported in 20-39 years of age category, with a subsequent decline in

the proportion of HU subjects with age in cases of essential HTN.<sup>8</sup>

Various studies have reported higher SUA levels in males than females.<sup>9,10</sup> This may be due to the presence of estrogen in premenopausal females, which enhances renal urate clearance or excretion by inhibition of renal urate reabsorption via organic ion transporter, resulting in low SUA levels. The results of our study were in concordance with the earlier published data. We also observed a higher proportion of males to have HU than females (27.5% versus 22.3%). However, when the data was split by T2DM and HTN alone, a higher proportion of females had HU than males (38.4% versus 33.3%), this may be due to more severe condition of the patient or low estrogen production, leading to a decrease in tubular excretion of UA.

This study showed a significant positive association between serum uric acid and progression of osteoarthritis. Adjusted odd's ratio 2.24, 95% confidence interval 1.57-2.94. This positive association between serum uric acid and radiographic severity of knee joint osteoarthritis as measured by Kellgren-Lawrence grading system was as reported previously by Srivastava S et al.<sup>11</sup> We also found an association between hyperuricemia and progression of

knee osteoarthritis as reported by Hart et al and Al Afraj et al.<sup>12,13</sup>

The limitation of this study was that it was not a prospective study, but a cross sectional analytical study of the data collected from ongoing healthcare clinics. Hence, the scope of finding the association between the SUA levels and different patient characteristics, including weight or BMI, antihypertensive or antidiabetic or other medications, systolic and diastolic BP, diet, smoking status, alcohol consumption, different stages of HTN, other comorbidities etc. was limited.

## CONCLUSION

In conclusion, the overall prevalence of HU in patients attending the screening programs was 18.55%. There was an increasing trend in the prevalence of HU with age. We found a positive association between elevated uric acid levels and progression of radiographic osteoarthritis of the knee joint in our cross-sectional analysis. Thus, there is a need to do prospective case control studies in Indian population to corroborate the results of the current study and to determine if early screening of SUA levels may help to reduce the risk of comorbidities and its further complications.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Di Cesare P, Abramson S, Samuels J. Pathogenesis of osteoarthritis. In: Firestein GS, Kelley WN, eds. Kelley's Textbook of Rheumatology. 8th ed. Philadelphia, Pa: Saunders Elsevier; 2009:1525-40.
2. King LK, March L, Anandacoomarasamy A. Obesity and osteoarthritis. Indian J Med Res. 2013;138:185-93.
3. Smith E, March L. Global Prevalence of Hyperuricemia: A Systematic Review of Population-Based Epidemiological Studies. Arthritis Rheumatol. 2015;67(suppl 10).
4. Ogbera AO, Azenabor AO. Hyperuricaemia and the metabolic syndrome in type 2 DM. Diabetology and metabolic syndrome. 2010 Dec;2(1):24.
5. Tuomilehto J, Zimmet P, Wolf E, Taylor R, Ram P, King H. Plasma uric acid level and its association with diabetes mellitus and some biologic parameters in a biracial population of Fiji. Am J Epidemiol. 1988 Feb;127(2):321-36.
6. Mikkeksen WM, Dodge HJ, Valkenburg H. The distribution of serum uric acid values in a population unselected as to gout or hyperuricemia. Tecumseh, Michigan, 1959-1960. Am J Med. 1965;39:242-51.
7. Culleton BF, Larson MG, Kannel WB, Levy D. Serum uric acid and risk for cardiovascular disease and death: the Framingham Heart Study. Ann Intern Med. 1999;131:7-13.
8. Lin CS, Lee WL, Hung YJ, Lee DY, Chen KF, Chi WC, et al. Prevalence of hyperuricemia and its association with antihypertensive treatment in hypertensive patients in Taiwan. Inter J Cardiology. 2012 Apr 5;156(1):41-6.
9. Mundhe SA, Mhasde DR. The study of prevalence of hyperuricemia and metabolic syndrome in type 2 diabetes mellitus. Int J Adv Med. 2016;3:241-49.
10. Remedios C, Shah M, Bhasker AG, Lakdawala M. Hyperuricemia: a reality in the Indian obese. Obes Surg. 2012;22:945-48.
11. Srivastava S, Saksena AK, Kumar S. Association of serum uric acid and severity of osteoarthritis of Knee. Inter J Curr Res. 2016;8(5):30620-3.
12. Hart DJ, Doyle DV, Spector TD. Association between metabolic factors and knee osteoarthritis in Women: the Chingford Study. J Rheumatol. 1995;22:1118-23.
13. Al-Afraj AS. Serum uric acid and radiographic osteoarthritis. J Pak Med Assoc. 2003;53(5):187-9.

**Cite this article as:** Jos S, Anand R, Nazar N, Jose R. A study of the association between hyperuricemia and knee osteoarthritis in the coastal Indian population. Int J Res Med Sci 2018;6:3076-9.