Original Article

Association of hyperuricemia and osteoarthritis knee in costal Indian population

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Abstract

Objectives: Previous studies have shown an association between serum uric acid and generalized osteoarthritis, but with the limited studies on evidence of association between serum uric acid and knee joint osteoarthritis. This study is to know the association between serum uric acid levels and osteoarthritis of knee joint. **Methods:** This is a prospective study including two hundred and seventy five patients (186 males, 89 females) with clinically diagnosed osteoarthritis of knee. Their serum uric acid level, Rheumatoid factor, standing radiographs of affected knees and hands were obtained. The presence of radiographic osteoarthritis of the knee was analyzed using Keligren-Lawrence system. Patients were divided into three groups basing on serum uric acid levels. Group 1: - serum uric acid less than 4mg/dl, Group 2: - serum uric acid levels between 4.1-7 mg/dl, Group 3: - serum uric acid levels more than 7 mg/dl. **Results:** Isolated knee joint osteoarthritis is present in 187 patients (68 %), generalized osteoarthritis is seen in 54 (19.6 %) patients, and Rheumatoid Factor, along with C-reactive protein is positive in 34 patients. There is a significant positive association present between isolated knee joint osteoarthritis, generalized osteoarthritis and the highest tertile of serum uric acid [adjusted odd's ratio- 2.25, 95% confidence interval- 1.58-2.95 and adjusted odd's ratio- 3.27, 95% confidence interval- 2.85-4.02 respectively). There is a significant positive association between high serum uric acid levels and progression of the knee joint osteoarthritis (highest tertile versus lowest tertile of serum uric acid odd's ratio- 2.03, 95% confidence interval-1.02-3.76). **Conclusion**: It is concluded that knee joint osteoarthritis, generalized osteoarthritis and there progression are associated with hyperuricemia.

Keywords: Osteoarthritis; Knee joint; Serum uric acid, hyperuricemia.

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INTRODUCTION

Osteoarthritis is the most common type of arthritis worldwide.[1] The association of osteoarthritis with age, obesity, sex, and metabolic factors has been studied.[2-7] All of these studies showed an association of osteoarthritis with obesity. Some of the studies on serum uric acid, showed no association between it and osteoarthritis.[3-5,7] Davis et al found a positive association between knee osteoarthritis and uric acid albeit a small one not reaching significant level.[2] Sun Ye et al study on serum uric acid relationship with osteoarthritis, concluded that although uric acid was associated with generalized osteoarthritis in patients undergoing hip replacement, there were no association with knee osteoarthritis or bilateral hip or bilateral knee osteoarthritis.[8] Acheson et al reported an association of serum uric acid with osteoarthritis of multiple joints.[9] This study was done in coastal region of Andhra Pradesh, to investigate the relationship between serum uric acid and osteoarthritis of knee and generalized osteoarthritis. Andhra Pradesh is one of the largest states in India with much higher usage of high value commodities (meat products) in total food expenditure especially in coastal region compared to other regions.[10] The prevalence of gout is high in urban Indian population and a study by Mishra et al showed correlation of elevated serum uric acid levels was due to high caloric diet, sedentary habits and greater prevalence of obesity.[11]

MATERIALS AND METHODS

This prospective study was conducted on two hundred and seventy five patients who attended department of Orthopaedics, from March 2012 to March 2013 in G.S.L medical college, one of the teaching institutes in costal India. Patients included in study, were with age more than forty years, persistent knee pain more than one month which is insidious in onset and with morning stiffness, having crepitus on knee movement and radiological evidence of osteoarthritis (defined as having grade 2 or more of the Kellgren-Lawrence grading system). This system has the following scheme: grade 0- normal, grade 1- small osteophytes of doubtful significance, grade 2- definite osteophytes, normal joint space, grade 3- definite osteophytes, moderate narrowing of joint space, grade 4- greatly reduced joint space, subchondral bone sclerosis and definite osteophytes. Generalized osteoarthritis was defined as the simultaneous presence of radiographic changes of osteoarthritis in knee and hand. Apart from radiographs of knee, hand, fasting serum uric acid levels, Rheumatoid factor, C-reactive protein were done. In case of bilateral knee joint involvement, more symptomatic knee was taken for radiographic grading. If symptoms are similar in both knees, the radiograph of right knee is taken into consideration. BMI calculated for all patients. Serum uric acid levels were divided into tertiles according to the observed distribution of values.

The serum uric acid values were classified into tertiles.

Group 1: Serum uric acid level less than 4 mg/dl.

Group 2: Serum uric acid level between 4.1 mg/dl-7 mg/dl.

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

Patients having knee joint radiological grades III and IV in each uric acid tertile were compared with to the patients having grade I and II in the same tertile. The patients in the higher second and third tertile were compared to first tertile (lowest) for presence of osteoarthritis of knee and generalized osteoarthritis. The crude odd ratio (OR) was calculated for the higher two tertiles in reference to the first (the lowest). This was then adjusted for age, sex, body mass index (BMI). The adjustment of odd ratio was done by using Mantel-Haenszel stratified analysis method.

RESULTS

Descriptive data: Out of 275 cases, 186 were males and 89 were females. Knee joint osteoarthritis is present in 187 patients (134 males, and 53 females). Generalized osteoarthritis was seen in 54 patients (38 males, and 16 females). Rheumatoid factor and C-reactive protein were positive in 34 patients. Their distribution among the different serum uric acid tertiles is outlined in Table 2.

Table 1: Descriptive data

Patients	Total number (n=275)	Mean Age in Years	Knee Joint Arthritis (n=187)	Generalized Osteoarthritis (n=54)	Rheumatoid Arthritis (n=34)
Males	186	54.3 ± 12.1	134	38	14
Females	89	47.1 ± 11.9	53	16	20

Table 2: Correlation between Serum uric acid and radiographic grade of osteoarthritis

Disease	Uric Acid Tertiles	Kellgren-Lawrence Radiological Grading System		
		Grade 2	Grade 3	Grade 4
Knee Joint Osteoarthritis (n=187)	<4 mg/dl	27	21	16
	4.1-7 mg/dl	12	16	18
	>7 mg/dl	21	32	24
Generalized Osteoarthritis (n=54)	<4 mg/dl	9	6	4
	4.1-7 mg/dl	5	4	5
	>7 mg/dl	3	7	11
Total		**77**	**86**	**78**

Table 3 shows this relationship expressed as odd ratio. The crude odd's ratio was above unity in the relationship between generalized osteoarthritis, knee osteoarthritis and the second uric acid tertile [1.05 (95% CI, 0.52-2.07), 1.95 (95% CI, 0.96-2.75)] respectively. After adjusting for all parameters (age, sex, BMI), odd's ratio was most significant for the association between the second tertile and third tertile of uric acid values and both knee and generalized osteoarthritis [odd's ratio- 2.25 (95% Confidence Interval: 1.58-2.95), odd's ratio 3.27 (95% Confidence Interval, 2.85-4.02)] respectively.

Table 3: The relationship between uric acid tertiles and knee and generalized osteoarthritis expressed as odd's ratio and 95% confidence interval

Disease	Uric acid tertiles	Crude odd's ratio (95% confidence interval)	Odd's ratio adjusted for age, sex, BMI (95% confidence interval)
Knee joint osteoarthritis (n=187)	<4 mg/dl	1.00 (reference)	1.00 (reference)
	4.1-7 mg/dl	1.05 (0.52-2.07)	1.27 (0.99-1.67)
	>7 mg/dl	1.00 (0.52-1.87)	2.25 (1.58-2.95)
Generalized osteoarthritis (n=54)	<4 mg/dl	1.00 (reference)	1.00 (reference)
	4.1-7 mg/dl	1.95 (0.96-2.75)	2.27 (1.25-3.15)

	>7 mg/dl	1.00 (0.67-1.76)	3.27 (2.85-4.02)
Rheumatoid arthritis (n=34)	< 4 mg/dl	1.00 (reference)	1.00 (reference)
	4.1-7 mg/dl	0.99 (0.56-1.86)	1.15 (0.86-1.87)
	> 7 mg/dl	0.98 (0.50-1.35)	1.02 (0.75-1.57)

n=number of patients, BMI= body mass index

There is a significant association present between knee osteoarthritis, generalized osteoarthritis and the highest tertile of serum uric acid [adjusted odds ratio - 2.25, 95% confidence interval- l.58-2.95 and adjusted odd's ratio- 3.27, 95% confidence interval- 2.85-4.02 respectively). There is a significant positive association between serum uric acid and progression of the knee joint osteoarthritis (highest tertile versus lowest tertile of serum uric acid odd's ratio- 2.03, 95% confidence interval-1.02-3.76) (table 4).

Table 4: The relationship between serum uric acid tertiles and progression of knee osteoarthritis expressed as odd ratio (OR) with 95% confidence interval

Serum uric acid tertiles (mg/dL)	Patients with grade II knee osteoarthritis	Patients with grade III and grade IV knee osteoarthritis	Crude odd's ratio (95% confidence interval)	Odd's ratio adjusted for age, sex, BMI (95% confidence interval)
< 4 mg/dl	36	47	1.00 (reference)	1.00 (reference)
4.1-7 mg/dl	17	43	0.89 (0.55-1.47)	0.83 (0.50-1.36)
> 7 mg/dl	24	74	2.25 (1.03-3.75)	2.03 (1.02-3.67)

DISCUSSION

This study found an association between hyperuricemia and generalized osteoarthritis as has been reported previously.[8, 9] We also found an association between hyperuricemia and knee osteoarthritis along with progression as previously reported by Hart et al and Al Afraj.[6,7,12] Our study showed the association between serum uric acid and radiographic severity in knee joint osteoarthritis as measured by Kellgren-Lawrence grading system has been previously reported by Ning et al[13]. A recent large prospective study showed that men in the highest quintile of meat intake had 41% higher risk for gout compared with the lowest quintile, and men in the highest quintile of seafood intake had 51% higher risk as compared with the lowest quintile. Correspondingly, in a nationally representative sample of men and women in the United States, higher levels of meat and seafood consumption were associated with the higher serum uric acid levels. In India, costal region has highest consumption of meat compared to other regions.[10] Another reason for the observed association between uric acid level and osteoarthritis in our study may be that we did not excluded patients with diabetes and medications including diuretics which have been shown to be associated with osteoarthritis. This study didn't draw any conclusions about the association between hyperuricemia and osteoarthritis. Possible explanatory mechanism for association between hyperuricemia and osteoarthritis includes genetic predisposition, insulin resistance, and endogenous hormonal environment. The increase in both hyperuricemia and osteoarthritis in women after menopause may point to hormonal mechanisms. In conclusion, our data points to a possible association between hyperuricemia and knee osteoarthritis and generalized osteoarthritis.

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