# Serum Uric Acid and Radiographic Osteoarthritis

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## Abstract

**Objectives:** To investigate the association between serum uric acid levels and radiographic osteoarthritis (OA).

**Methods:**Two hundred and forty one patients (135 males, 106 females) were enrolled in this study,covering fourteen primary care clinics.Their serum uric acid results and radiograph of knees and hands were obtained prospectively.The presence of radiographic osteoarthritis of the knee and generalised osteoarthritis were analysed in relation to serum uric acid values.

**Results:** Their mean age was 48.9 ± 15.3 (female 46.1 ± 13.9, males 51.3 ± 16.1). Knee OA was present in 120 patients (48.8%), 57 (23.6%) females and 63 (26.1%) males. Generalized OA was seen in 54 (22.4%) patients, 20 (8.2%) females and 34 (14.1%) males. After adjusting for age, sex, BMI, serum cholesterol and triglycerides, there was an association between knee OA, generalized OA and the highest tertile of serum uric acid [adjusted odds ratio (OR) 2.03, 95% CI, l.58-2.71 and 1.81, 95% CI, 1.33-2.57 respectively).

**Conclusion:** It is concluded that knee and generalized OA are associated with hyperuricemia (JPMA 53:187; 2003.

## Introduction

Osteoarthritis (OA) is the most common arthritis worldwide.[1] The association 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 these studies accounted for serum uric acid and found 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 specifically investigated serum uric acid relationship with osteoarthritis and concluded that although uric acid was associated with generalized osteoarthritis in patients undergoing hip replacement, there were no association with knee OA or bilateral hip or knee OA.[8] Others reported an association with OA of multiple joints.[9] Both osteoarthritis and hyperuricemia are common in Saudi Arabia.[10,11] We sought to investigate the relationship between serum uric acid and knee and generalized osteoarthritis in this community.

## Patients and Methods

As part of a study of the prevalence of rheumatic diseases in the northern part of Riyadh, Saudi Arabia, and over a period of seven months extending from September 1998 to March 1999, covering 14 primary care clinics, we interviewed the first two adult patients over the age of 20 years each day.A total of 471 patients attending these clinics for a variety of medical complaints were interviewed, consented and their uric acid level was assayed.

Radiograph of hands and knees [anteroposterior (AP), lateral (L)] were available for 241 patients (135 males, 106 females). Their age, sex, BMI (weight in kg divided by the square of height in meters), serum uric acid, serum cholesterol and triglycerides were recorded. The presence of osteoarthritis was defined as having grade 2 or more of the Kellgren-Lawrence grading system.[12] This system has the following scheme: grade 0 normal, grade 1 minute osteophytes of doubtful significance, grade 2 definite osteophytes, grade 3 moderate narrowing of joint space, grade 4 greatly reduced joint space and subchondral bone sclerosis. Generalized OA was defined as the simultaneous presence of radiographic changes of knee and hand OA.

The serum uric acid values were classified into tertiles, and 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 was calculated for higher two tertiles in reference to the first (lowest). This was then adjusted for age, sex, BMI, serum cholesterol, and serum triglycerides using the Mantel-Haenszel stratified analysis method.

## Results

Two hundred and forty one cases (135 males and 106 females) were available for analysis. The mean age was 48.9 ± 15.3 (female mean age 46.1 ± 13.9, male mean age 51.3 ± 16.1) years.

**Table 1. Knee and generalized OA relative to uric acid.**

| Uric acid tertiles (μmol/L) | | Knee OA (n) | | Generalized OA (n) | |
|---|---|---|---|---|---|
| | | Present | Absent | Present | Absent |
| Whole | 1(<239) | 39 | 40 | 16 | 63 |
| Group (n=241) | 2 (239-308.5) | 41 | 40 | 22 | 59 |
| | 3 (>308.5) | 40 | 41 | 16 | 65 |
| Females (n=106) | 1(<214) | 14 | 19 | 5 | 28 |
| | 2 (214-281) | 22 | 15 | 7 | 30 |
| | 3 (>281) | 21 | 15 | 8 | 28 |
| Males (n=135) | 1(<262) | 22 | 22 | 14 | 30 |
| | 2 (262-321) | 21 | 25 | 11 | 35 |
| | 3 (>321) | 20 | 25 | 9 | 36 |

**Table 2. The relationship between uric acid tertiles and knee and generalized OA expressed as odd ratio (OR)and 95% confidence interval(CI).**

| Disease | Uric Acid Tertiles (μmol) | Crude OR | OR Adjusted for age only (95% CI) | OR adjusted* (95% CI) |
|---|---|---|---|---|
| Knee OA | 1 | 1.00 | 1.00 | 1.00 |
| (n=120) | (<239) | (Reference) | (Reference) | (Reference) |
| | 2 | 1.05 | 1.57 | 1.42 |
| | (239-308.5) | (0.54-2.06) | (0.99-2.53) | (1.09-1.86) |
| | 3 | 1.00 | 2.21 | 2.03 |
| | (>308.5) | (0.51-1.95) | (1.42-3.68) | (1.58-2.71) |
| Generalized OA | 1 | 1.00 | 1.00 | 1.00 |
| (n=54) | (<239) | (Reference) | (Reference) | (Reference) |
| | 2 | 1.92 | 2.50 | 1.40 |
| | (239-308.5) | (0.98-3.74) | (1.30-4.88) | (1.00-1.97) |
| | 3 | 0.98 | 3.29 | 1.81 |
| | (>308.5) | (0.48-1.98) | (1.93-6.85) | (1.33-2.57) |

*Adjusted for sex, age, cholesterol, triglycerides, BMI

Knee osteoarthritis was present in 120 (49.8%) patients, 57 (23.7%) females and 63 (26.1%) males. Generalized OA was seen in 54 (22.4%) patients, 20 (8.2%) females and 34 (14.1%) males. Their distribution among the different serum uric acid tertiles is outlined in Table 1. Table 2 shows this relationship expressed as odd ratio. The crude OR was above unity in the relationship between generalized OA, knee OA and the second uric acid tertile [1.05 (95% CI, 0.54-2.06), 1.92 (95% CI, 0.98-3.74)] respectively.

After adjusting for age only, the most significant association with knee and generalized OA were seen in the third tertile group [2.21 (95% CI, 1.42-3.68), 3.29 (95% CI, 1.93-6.85)] respectively. In the 2nd tertile group, after controlling for age, the association was with generalized OA only, OR 2.50 (95% CI, 1.30-4.88). When we adjusted for all parameters (age, sex, BMI, serum cholesterol and triglycerides), OR was most significant for the association between the third

tertile of uric acid values and both knee and generalized OA [OR 2.03 (95% CI, 1.58-2.71), OR 1.81 (95% CI, 1.33-2.57)] respectively. The odds ratio adjusted for age only, showed clear upward change from its crude value suggesting confounding by age in all groups. Some of this known effect of age on OA was dampened after adjusting for other paramaters, resulting in OR of 2.03 and 1.81 between the third uric acid tertile and knee and generalized OA respectively. However, the higher OR for knee OA compared to generalized OA for the third triglyceride tertile (data not shown) which was not seen when the age only was controlled, would suggest confounding by BMI.

## Discussion

This report found an association between hyperuricemia and generalized OA as has been reported previously.[8,9] We also found an association between hyperuricemia and knee OA. A possible association between hyperuricemia and knee OA was previously reported by Hart et al.[7] Others reported no association between OA and hyperuricemia.[3,13,14] Confounding by age and BMI may have contributed to our positive results in relation to knee OA, which is usually age and weight dependent. This phenomenon was also noted by Sun et al.[8] Another reason for the observed association between uric acid level and OA in our study may be that we did not control for glucose level, hypertension and medications including diuretics which have been shown to be associated with OA.[7]

This is a cross-sectional study and no conclusions are drawn about the direction of the association between hyperuricemia and OA. Possible explanatory mechanism for the association between hyperuricemia and OA includes genetic predisposition, insulin resistance and endogenous hormonal environment.[15-17] Relatives of OA patients with increased uric acid levels were also found to have hyperuricemia.[16] The increase in both hyperuricemia and OA in women after menopause may point to hormonal mechanisms.[15]

In conclusion, our data points to a possible association between hyperuricemia and knee and generalized OA.

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