



## RESEARCH ARTICLE

### ASSOCIATION OF SERUM URIC ACID WITH SEVERITY OF OSTEOARTHRITIS OF KNEE

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#### ABSTRACT

**Aim:** The objective of the study was to find out association between serum uric acid (UA) levels and severity of pain in different grades of osteoarthritis of knee (KOA) patients.

**Methods:** After obtaining ethical clearance, 160 patients suffering from KOA were enrolled in the study. Informed consent was taken and blood samples along with the radiographs of the knee joints were obtained. On the basis of the radiographic pictures the patients were categorised into four grades according to Kellgren Lawrence (KL) grading method. For each patient serum UA level was estimated and degree of pain was calculated using Visual Analogue Scale (VAS).

**Results:** Both the UA levels and severity of pain were found to be in increasing order in parallel from grade-I to grade- IV patients. The severity of pain was significantly higher in grade IV as while the increase in UA levels was not significant.

**Conclusion:** It may be concluded that the level of UA is raised in parallel with the severity of KOA.

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## INTRODUCTION

Osteoarthritis (OA) is a progressive, immune mediated inflammatory disorder involving the entire joint structure including the synovial membrane, cartilage and sub-chondral 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 (Anandacoomarasamy and March, 2010; Dicesare and Abramson, 2005). The global prevalence of KOA is 3.8% among population between age 50-80 years; incidence being higher in females than in males (Cross *et al.*, 2014; Cushnaghan and Dieppe, 1991). In recent times the incidence of OA is increasing and the disease is observed to be developing in earlier age (Bhatia *et al.*, 2013). Such exponential progression of the disease is mainly due to the risk factors like obesity, changes in lifestyle patterns, diet routine and work environment conditions among the adult population (Esser and Bailey, 2011). If not detected and managed at earlier stage, OA may severely disable the patient; hence, early detection and prevention of progression should be ideal management.

All over the world, the researchers are trying to establish a relationship between certain biomarkers and KOA for its early identification. Among such biomarkers UA has also been studied for its involvement/role in KOA (Schouten *et al.*, 1992; Rahman and Rasool, 2011). UA is an endogenous antioxidant which contributes as much as 2/3rd of total free radical scavengers present in plasma and may serve protective physiological role by preventing lipid peroxidation (Squadrito *et al.*, 2000). Reaction of UA with oxidizing species generates UA radical which is capable of causing biological damage (Baillie *et al.*, 2007). Many workers have tried to establish an association with UA levels and OA; however, the exact picture is still not clear. Thus, we planned to investigate the association pattern of UA in KOA severity.

## MATERIALS AND METHODS

The present study was carried out on the patients who reported in the Out Patients' Department of Orthopaedics in King George's Medical University for KOA. The criteria used for establishing a patient suffering from KOA were according to 'The American College of Rheumatology' and these are:

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- Knee pain
- Osteophytes on X-ray

- Crepitus on knee range of motion
- Morning stiffness of short duration (<30 min).

### Inclusion Criteria

Patients within the age group of 41-80 years of both sexes, who were suffering from primary KOA were included in the study.

### Exclusion Criteria

Patients aged less than 41 years and more than 80 years, pregnant women and those suffering from secondary OA, Rheumatoid arthritis, Diabetes Mellitus, Renal insufficiency, Hepatic disease, Cardiovascular disease, gout or with any other systematic disease were excluded from the study.

The study was approved by the Institutional Ethics Committee (Ref.code:57 E.C.M. IIB/P12), of King George's Medical University, Lucknow (India). After obtaining ethical clearance, 160 patients suffering from KOA were enrolled in the study. Written informed consent was obtained from all patients and severity of pain was also recorded by using VAS (Burekhardt and Jones, 2003). Blood samples along with the radiographs of the knee joints were also taken. Depending upon the radiographic appearance of knee joints, the patients were categorised into four grades according to KL grading system (Kellgren and Lawrence, 1957):

Grade 0- Normal

Grade 1-Doubtful narrowing of the joint space and possible osteophytic lipping

Grade 2-Definite osteophytes and possible narrowing of the joint space

Grade 3-Moderate multiple osteophytes, definite narrowing of the joint space, some sclerosis and possible deformity of the bone contour

Grade 4- Large osteophytes with marked narrowing of the joint space, severe sclerosis and definite deformity of the bone contour

### Laboratory investigations

Blood samples were allowed to clot and then centrifuged at 3000 rpm for 30 minutes to get serum which was stored at -80°C until analysis. UA levels were estimated by Vitros 250 dry chemistry analyzer.

### Statistical analysis

Data obtained was analyzed using Graph Pad prism 6 software. One way analysis of variance (ANOVA) along with Tukey's post hoc comparison tests was used to compare UA and VAS scores among different grades of the disease. The results are presented in Mean  $\pm$  SEM and p value <0.05 was considered to be significant.

## RESULTS

Demographic characteristics of the patients are shown in Table-1. Out of 160 patients, the highest number (79) were reported in age group of 41 to 50 years and it was followed by the age group of 51 to 60 years; 66 patients. The number of female patients suffering from KOA was more than the men. As shown in Table-2 and Fig.-2, VAS score of KL grade-III and grade-IV patients were significantly higher ( $p < 0.05$ ) than KL grade-I and grade-II patients, respectively. The levels of serum UA were also found to be increased in KL grade-III and grade-IV patients as compared to KL grade-I and grade-II patients, but this increase was not significant. Correlation coefficient ( $r$ ) was found to be positively correlated for VAS and UA as shown in Table-3 and Fig.3. This shows that the rise in both the parameters was in parallel with the progression of the disease.

**Table 1. Demographic data of patients**

Age in years	Number of patients		Total
	Male	Female	
41-50	21	58	79
51-60	26	40	66
61-70	7	4	11
71-80	3	1	4
Total	57	103	160



**Figure 1. KL grading of KOA on the basis of radiographic appearance**

**Table 2. Association of UA level and VAS score with different grades of the disease**

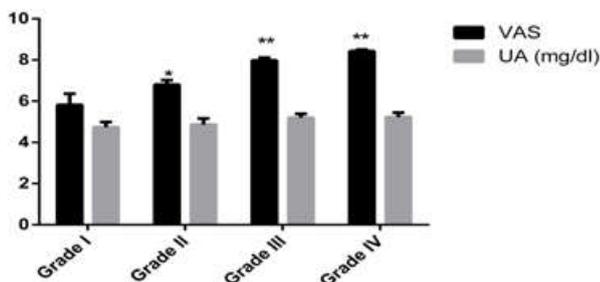
KL-grade	VAS	UA (mg/dl)
I	5.82±0.54	4.74±0.25
II	6.80±0.22*	4.86±0.30
III	7.98±0.13**	5.20±0.19
IV	8.43±0.07**	5.23±0.22
p-value	0.0001	0.57

\*Significant (p<0.05) as compared to grade I  
 \*\*Significant (p<0.05) as compared to grade I & II

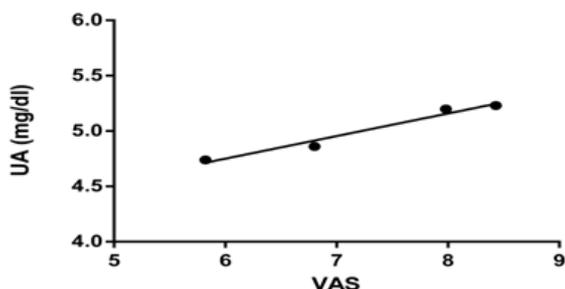
**Table 3. Correlation between VAS and UA**

	Correlation coefficient	VAS
UA (mg/dl)	r	0.98
	p-value	0.016*

\*Correlation is significant (p<0.05)



**Figure 2. Graphical presentation of VAS and UA levels according to KL-grading**



**Figure 3. Correlation between VAS and UA levels in different grades of the disease**

**DISCUSSION**

OA is a progressive, inflammatory disorder in which one or more joints are affected. However, the knee joint is affected most (Anandacoomarasamy and March, 2010); hence, the patients of KOA were included in our study. Out of 160 patients 145 were in the age group of 41 to 60 years, a finding which is in concurrence with the global data: maximum numbers of reported patients are around 55 years of age (Cross *et al.*, 2014; Bannuru *et al.*, 2015). It was observed that the number of females was almost 2/3<sup>rd</sup> (64.4%) of the total number of patients. Although, there are few isolated reports that KOA is found more in males as compared to females (Afraj, 2003; Supradeeptha *et al.*, 2013); however, majority of studies have reported that the prevalence of KOA is more in females (Afraj, 2003; Denoble *et al.*, 2011). We observed that the severity of pain was parallel to the KL grade of the disease.

As expected, the severity of pain was much more in patients with higher grades of disease. Among many inflammatory biochemical substances, possible association of UA with OA has been studied by many workers (Erden *et al.*, 2012; Murakiy *et al.*, 2011). In the studies of late 20<sup>th</sup> century an association between raised UA levels and OA could not be established (Anderson and Felson, 1988; Felson *et al.*, 1988; Schouten *et al.*, 1992). However, recent studies have shown correlation between higher UA levels and generalized OA / KOA (Sun *et al.*, 2000; Ding *et al.*, 2016). In the present study, although the rise in UA levels in all grades was not significant i.e. there was no hyperuricemia, but a strong correlation has been observed. The level of serum UA was found to be in increasing order, parallel to the grades of the disease. A probable mechanism of such UA related OA may be that the higher level of UA might lead to the formation of microcrystals in the joint space which is responsible for the commencement of inflammatory chain reaction leading to OA. Thus, it may be concluded that higher plasma UA levels have strong association with KOA.

**Conflict of interest**

The authors declare no conflict of interest regarding the publication of this paper.

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