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# The prevalence of hyperuricemia and its associated risk factors in patients presenting with joint pain in Karachi

**Muhammad Muzzammil[1]*, Abdul Qadir[2], Ayesha Mughal[3], Jahanzeb Effendi[3], Muhammad Saeed Minhas[4], Syed Jahanzeb[2]**

[1]Department of Orthopaedics, Sindh Govt. Services Hospital, Karachi, Pakistan
[2]Department of Orthopaedics, Civil Hospital, Karachi, Pakistan
[3]Department of Orthopaedics, Jinnah Postgraduate Medical Centre, Karachi, Pakistan
[4]Department of Orthopaedics, United Medical and Dental College, Karachi, Pakistan

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***Correspondence:**
Dr. Muhammad Muzzammil,
E-mail: muzzammil_sangani@hotmail.com



## ABSTRACT

**Background:** To determine the prevalence and association of hyperuricemia with genetic factors, dietary and alcohol consumption, metabolic syndrome, diuretic use and chronic renal disease in patients presenting with joint pain in the outpatient department (OPD) at a tertiary care hospital of Karachi, Pakistan and to establish a significant correlation between concentration of serum creatinine and triglyceride with uric acid concentration statistically.
**Methods:** This study was conducted on 2200 patients. The data included age, gender, occupation, genetic factors (family history), dietary and alcohol consumption, metabolic syndrome, hypertension, obesity, diuretic use and chronic renal disease. Serum uric acid concentration of 2.4-6.0 mg/dl (female) and 3.4-7.0 mg/dl (male) labelled as normal values. All participants' serum uric acid concentration compared with serum creatinine and triglyceride concentration.
**Results:** Overall prevalence of 30.1% (662 patients) hyperuricemia in patients presenting with joint pain. Majority of the patients belonged to age group 30-34 and highest average uric acid value (7.7±2.01) was found to be in the age group of 65 and above. Hyperuricemia was related to increased age (56.25%), genetic factors 159 (24.01%), dietary 370 (55.89%) and alcohol consumption 33 (4.98%), metabolic syndrome (hypertension 146 (22.05%), obesity 121 (18.27%), diuretic use 215 (32.47%) and chronic renal disease 53 (8.00%). On laboratory investigations, hyperuricemia was directly related to serum creatinine and triglyceride.
**Conclusions:** This study emphasized the high prevalence of hyperuricemia in patients presenting with joint pain and it is directly proportional to the age. Increased serum uric acid levels with increasing age might be secondary to impaired renal function, use of diuretics, and hypertension as commonly seen among elderly patients. Early diagnosis, management of risk factors and treatment will prevent adverse effects on health.

**Keywords:** Hyperuricemia, Prevalence, Associations, Increase age, Genetic factor, Metabolic syndrome

## INTRODUCTION

Hyperuricemia is a disease in which defective metabolism of uric acid causes arthritis, especially in the smaller bones of the feet, deposition of chalk-stones, and episodes of acute pain. The common factors causing gout are dietary food, medications, and alcohol. Severe pain, joint swelling and discolouration are the manifestations of acute gout which may sometimes respond well to non-steroidal anti-inflammatory drugs (NSAIDs).

Repeated episodes especially involving same joints may cause degenerative changes and complicate into gouty arthritis.

Hyperuricemia is one of the oldest recognised diseases and was first documented as a painful condition affecting the great toe by Egyptians in 2640 BC. Hippocrates described this 'unwalkable disease' in the 5th century BC, which he referred to as 'podagra'. The term gout was given by de Vielehardouin in the 13th century in 1907.[1] Today, gout remains renowned for its tendency to affect the foot, manifesting clinically with painful episodes of acute arthritis resulting from an inflammatory reaction to monosodium urate (MSU) crystals which deposit in joints and soft tissues in the presence of hyperuricemia.

Gout is one of the common rheumatic disease. It is affecting millions of people in western countries. The greater numbers are seen in united states.[2] The risk factors for gout include sex, age, environmental factors and genetics. Genetic factors play important role in pathogenesis. Serum uric acid concentration and renal clearance of uric acid by products proven significant heritability.[3,4] This disease is progressing significantly in Western countries recently.[5]

Using nationally representative data, National health and nutrition examination survey (NHANES) from 2007-2008.[6] The prevalence of gout in the United States adults was 3.9% (8.3 million individuals). Among these, men were 5.9% (6.1 million) and women were 2.0% (2.2 million). There is an increment by an estimate of 1.2% over past 2 decades. Black men suffered from gout twice more than white men. The cumulative incidence of gout was 10.9% among black men and 5.8% among white.[7] A Rochester epidemiology project study showed an increase in the incidence of gout from 45.0 per 100,000 in 1977-1978 to 63.3 per 100,000 in 1995-1996. Male to female ratios were 3.3 to 1 at both time periods. Considering primary gout (excluding people with gout on diuretics), the incidence of gout increased from 20.2 to 45.9 per 100,000.8 Family history was found positive among most of the people suffering from gout. Approximately 20 to 80% seen more common in adult men than in women and children, as serum uric acid known to be increase with age and after menopause.[8]

The risk of hyperuricemia increases in overweight population which makes them prone to developing gout. This is because of increase in amount of tissue for turnover and breakdown. Excessive alcohol intake may also lead to hyperuricemia and gout as the alcohol shows interference with the removal of uric acid from the body. Having food rich in purine diet may also cause or aggravate gout. Common cause of gout in older people is the inability of the kidneys to eliminate by products. Other medical problems that contribute to high blood levels of uric acid include: high blood pressure, hypothyroidism (underactive thyroid gland), conditions that cause an excessively rapid turnover of cells, such as psoriasis, haemolytic anemia, or some cancers and the two rare conditions enzymes controlling uric acid levels, found in low quantities or absent. These are Kelley-Seegmiller syndrome or Lesch-Nyhan syndrome. A close relationship between hyperuricemia and hypertension, insulin resistance and cardiovascular disease risk factors (such as obesity and smoking) has been reported in some epidemiologic studies.[9-12] Some of the medications may put people at risk for developing hyperuricemia and gout. These include: diuretics, salicylate-containing drugs, niacin, cyclosporine and levodopa. The signs and symptoms of gout include: hyperuricemia, monosodium urate crystals in synovial fluid, multiple attacks of arthritis that develops in daytime that produces swollen red and warm joint. This attack of arthritis is only in one joint, often toe, ankle or knee. High-purine foods like anchovies, asparagus, beef kidneys, brains, and liver also contribute in developing gout.

## METHODS

This descriptive cross-sectional study was conducted on 2200 patients who presented with a history of joint pain at the orthopaedic surgery outpatient department (OPD) of a tertiary care hospital in Karachi, Pakistan from January 2018 to December 2018.

Patients who came with a history of joint pain were included in the study. A performa was designed and administered after taking consent from the patients. The data included age, gender, occupation, genetic factors (family history), dietary and alcohol consumption, metabolic syndrome, hypertension, obesity, diuretic use and chronic renal disease. Serum uric acid concentration of 2.4-6.0 mg/dl (female) and 3.4-7.0 mg/dl (male) labelled as normal values. All participants with hyperuricemia were subjected to a complete physical examination and their serum uric acid concentration compared with serum creatinine and triglyceride concentration. Standard gauge mercurial sphygmomanometer used to measure arterial blood pressures and the criterion for hypertension was blood pressure of 140/90 mm Hg or higher or patients previously diagnosed with hypertension. Waist circumference was measured by a measuring tape, midway between the superior border of the iliac crest and inferior margin of the ribs. Using seca digital scale, weight was measured (kilograms) with the subject wearing light clothes. Body mass index (BMI) was calculated by the equation: weight in kilograms divided by height in meters squared.

The following tests were carried out in the clinical biochemistry laboratory. All the necessary quality control measures were applied. Measurement of these parameters has been done on semi-autoanalyzer: serum uric acid – by urease/POD method, blood sugar – by GOD – POD method, serum creatinine – by Jaffe's method and serum triglycerides – by glycerol-3-phosphate-oxidase (GPO).

All data was analyzed through statistical package for social sciences (SPSS) version 20. Cross-tabulations were performed to get relations between study variables. Chi square test was used to observe the significant relationships between categorical variables. Statistically significant p value $<0.05$ was considered.

## RESULTS

A total of 2200 patients were included, age range from 12-85 years, mean 28.5±51.61 standard deviation (SD). Females were 1232 (56%) and male were 968 (44%). We report an overall prevalence of 30.1% (662 patients) hyperuricemia in this population of patients presenting with joint pain in our OPD, of which 19.2% were male and 10.9% were females.

Out of the total hyperuricemic patients, 422 (63.7%) were males and 240 (36.3%) were female. Majority of the patients belonged to age group 30-34 and 40-44 (33.45%). Proportion of patients in the 60-64 group was 21.95% and age 65 were 11.15%. Highest average uric acid value (7.7±2.01) was found to be in the age group of 65 and above. Average uric acid level in male was 6.7±1.08 and for the female was 5.9±1.03. The prevalence of hyperuricemia was highest in 65 years and above group (56.25%). Hyperuricemia was related to increased age, genetic factors 159 (24.01%), dietary 370 (55.89%) and alcohol consumption 33 (4.98%), metabolic syndrome (hypertension 146 (22.05%), obesity 121 (18.27%), diuretic use 215 (32.47%) and chronic renal disease 53 (8.00%). On laboratory investigations, hyperuricemia was directly related to serum creatinine and triglyceride and was not seen to be related to blood sugar level.

**Table 1: Patient demographics.**

| | Patient demographics |
|---|---|
| **No. of patients** | 2200 |
| **Average age (years)** | 12-85, 28.5±51.61 SD |
| **Gender** | |
| Male (%) | 968 (44.00) |
| Female (%) | 1232 (56.00) |

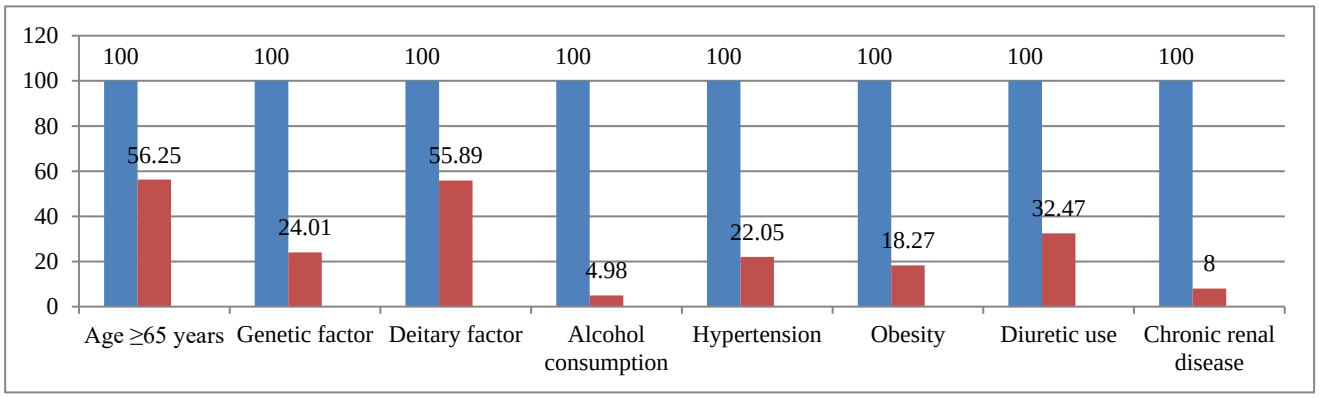


**Figure 1: Study outcomes.**

## DISCUSSION

The aim of our study is to determine the prevalence of hyperuricemia among patients with joint pain and identify important risk factors associated with elevated serum uric acid levels. On our literature review, we did not find a previous study on hyperuricemia among this population of patients in Karachi, Pakistan. Broadly, the main observations of our study are that the prevalence of the hyperuricemia was higher in males with joint pain compared to women, higher in the older age group and that serum uric acid level is influenced by the triglycerides and the creatinine levels.

We report an overall prevalence of 30.1% hyperuricemia in this population of patients presenting with joint pain of which 19.2% were male and 10.9% were females. When compared to a study on Thai adults who presented for annual health exams, our prevalence was much higher (30.1% versus 10.6%), however the male to female ratio was comparable (our study: 19.2% versus 10.9%; Thai 18.4% versus 7.8%). Our higher overall prevalence can be attributed to our study sample who sought consultation for joint pain.

When prevalence is compared in the elderly population, our figures of 21.0% in elderly men and 15.1% in elderly women are consistent with data from a study on the Thai population reported as 35.2% in men and 21.0% in women.[13] A study on elderly population in Taiwan reported an overall prevalence of 36% (46% for males and 26% for females). This study also noted that females of 75-79 years had significantly higher serum urate levels (376 µm) than that of the 65-69 and ≥80 age groups.[14] Gordon et al explained that serum uric acid level increased after the menopause in females which could be attributed to the effect of sex hormones.[15]

In our study there were significant associations and positive relationship between age and uric acid. Increasing age leads to increase in uric acid could be explained by age related changes in renal function as the kidneys are unable to excrete out uric acid adequately from the body.[16]

In our study we found that patients with raised BMI and waist circumference are at increasing risk of having hyperuricemia, which was reported in several other studies.[17-19] This can be explained by the presence of insulin resistance. Obesity is one of the components of metabolic syndrome and this gives rise to insulin

resistance, even in individuals with normal glucose tolerance test. The association between insulin resistance syndrome, hyperuricemia, and hypertriglyceridemia are complicated. This can be explained by the fact that uric acid production is linked to glycolysis and that glycolysis is controlled by insulin. Phosphoribosylpyrophosphate (PPRP) is an important metabolite and its availability is dependent on ribose-5-phosphate (R-5-P), the production of which is regulated by glycolytic flux. Diversion of glycolytic intermediates toward R-5-P, PPRP, and uric acid will occur if there is diminished activity of glyceraldehyde-3-phosphate dehydrogenase (GA3PDH), which in turn is regulated by insulin. Serum triglyceride concentrations may also increase, as might can result from accumulation of glycerol-3-phosphate. Therefore, intrinsic defects in GA3PDH and a loss of its responsiveness to insulin, by causing accumulation of glycolytic intermediates, may explain the association between insulin resistance, hyperuricemia, and hypertriglyceridemia.[20]

Insulin resistance is known to be inversely related to 24 hours urinary clearance of uric acid.[21-23] Previous studies as well as this study reported that serum uric acid is more closely related to impaired fasting glucose.[24-27]

Hyperuricemia is significantly associated with raised systolic as well as diastolic blood pressure. Though, it has been shown previously that the association between hyperuricemia and hypertension was partly mediated by obesity.[28]

Our study reported serum uric acid being significantly associated with high-density lipoprotein (HDL) and triglycerides (TG) which is consistent with previous studies.[29-32] Furthermore, our results also showed that serum uric acid level was directly proportional to the serum creatinine. A previous study reports similar results showing significant association between serum uric acid and renal function.[33]

Many prospective studies as well as this study reported a significant association between hyperuricemia and ischemic heart disease (IHD). The possible explanation to this could be the atherosclerotic effect of uric acid; as elevated uric acid may cause vascular endothelial cell damage and facilitates the proliferation of smooth muscle cells. These data have been documented in several reviews and meta-analysis studies.[34,35] Not only this (association between hyperuricemia and IHD) but it may also be secondary to the association between hyperuricemia and the other cardio vascular risk factors.

## CONCLUSION

This study emphasized the high prevalence of hyperuricemia in patients presenting with joint pain and it is directly proportional to the age. Increased serum uric acid levels with increasing age might be secondary to impaired renal function, use of diuretics, and hypertension as commonly seen among elderly patients. Early diagnosis, management of risk factors and treatment will prevent adverse effects on health.

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