

## Association of High Serum Uric Acid With Risk Factors of Cardiovascular Disease in the Rheumatology Clinic of a Tertiary Care Hospital of Karachi

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### Abstract

**Introduction:** Uric acid is the end product of purine metabolism in humans due to the loss of uricase activity. Elevated uric acid is one of the metabolic abnormalities associated with cardiovascular disease. There are some studies found that hyperuricemia has been linked with cardiovascular diseases. Hyperuricemia predispose to the development of hypertension and is also thought to result in increased oxidative stress and generation of free radicals, which eventually can be the nidus of future cardiovascular disease.

**Objective:** To determine the association of high serum uric acid with risk factors of cardiovascular disease (obesity, hyperuricemia, diabetes or hypertension). This Cross sectional comparative study was carried out in Tertiary Care Unit of Karachi, Pakistan from Feb, 2013 till September, 2013.

**Methods:** A total of 120 subjects of both sexes were taken and divided into two groups. Fasting glucose levels, serum uric acid was done. Those with hyperuricemia were taken as cases and individuals with normal level were taken as controls. Lipid profile was performed in both groups by enzymatic kit. The data feeding and analysis was done on computer package SPSS (Statistical Packages of Social Sciences) version 16.0. The results were given in the mean and Standard Deviation (SD) i.e. age, weight, height, Body Mass Index (BMI), fasting blood sugar, serum cholesterol, serum triglyceride, Low Density Lipoprotein C (LDL-C), High Density Lipoprotein C (HDL-C), Very Low Density Lipoprotein C (VLDL-C) and serum uric acid. T-test was used for comparison between control and hyperuricemic patients group. In statistical analysis ( $p < 0.01$ ) was considered statistically significant.

**Results:** This study showed significantly raised levels of fasting blood glucose, serum cholesterol, LDL-C, triglyceride, systolic and diastolic blood pressure in hyperuricemic patients when compared to healthy control group ( $p < 0.01$ ).

**Conclusion:** The results of the present study suggest that high serum uric acid is associated with risk factors of cardiovascular disease thus hyperuricemia may results in cardiovascular disease.

**Keywords:** Uric Acid, Diabetes Mellitus, dyslipidaemia, cardiovascular disease.  
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### Introduction

Uric acid [UA (2,6,8 trioxypurine-C<sub>5</sub>H<sub>4</sub>N<sub>4</sub>O<sub>3</sub>)] is an organic compound that is endogenously produced by humans as a purine metabolite. It is formed by the liver and mainly excreted by the kid-

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neys (65–75%) and intestines (25–35%). Uric acid is the end product of purine metabolism in humans due to the loss of uricase activity, which led to humans having higher UA levels than other mammals<sup>1</sup>. The hyperuricemia is defined as  $\geq 7$  mg/dL for men and  $\geq 6.0$  mg/dL for women and is found mainly in postmenopausal women, African American, patients with renal disease and alcohol intake<sup>2,3</sup>. Higher serum uric acid results in different diseases, and usually uric acid is involved in the pathogenesis of gouty arthritis<sup>4</sup>. Some studies have suggested that hyperuricemia is a risk factor for cardiovascular disease in the general population<sup>5</sup>. Since hyperuricemia

can be an accompaniment disorder with syndrome X (characterized by abdominal obesity, impaired glucose intolerance, increased low density lipoprotein-cholesterol & decreased high density lipoprotein-cholesterol), its presence is usually an indication for screening and aggressively treating any accompanying obesity, hyperuricemia, diabetes or hypertension<sup>6</sup>. Elevated serum uric acid levels are commonly seen in association with glucose intolerance, hypertension and dyslipidemia, a cluster of metabolic and haemodynamic disorders which characterize the so called metabolic syndrome<sup>7</sup>. Increased serum uric acid (SUA) concentrations have consistently been reported to be associated with the progression of Cardiovascular Disease (CVD), and SUA concentrations have been documented over the past 5 decades to be modestly higher in patients with coronary heart disease (CHD) than in healthy control individuals<sup>8</sup>. Much controversy exists, however, as to whether SUA is an independent risk factor, because a patho-physiological link between hyperuricemia and subsequent cardiovascular complications has yet to be confirmed and because SUA is related to many of the established risk factors, including hypertension, dyslipidemia, obesity, and excessive alcohol consumption<sup>9</sup>. Because of very controversial epidemiologic findings and a lack of consistent evidence, the role of SUA as an independent and causal risk factor for cardiovascular events remains unclear<sup>10</sup>. The association of uric acid with almost all risk factors for CVD has made it very difficult to determine whether uric acid has a causal role in these conditions or whether it is simply a marker for individuals at increased risk.

The purpose of this study is to investigate the association of hyperuricemia with cardiovascular risk factors in local population, at the rheumatology clinic of a tertiary care hospital of Karachi.

## Patients and Methods

The research protocol was approved by the Basic Medical Sciences Institute (BMSI) research ethics committee. All clinical investigation was conducted according to the principles expressed in the declaration of Helsinki. All the participants were vol-

unteered who were explained the minimal risk research procedure and were asked to complete a verbal and written informed consent.

This is a cross sectional comparative study was carried out in rheumatology clinic of tertiary care unit from February, 2012 to September, 2013. Of the 120 subjects both sexes were included in our study which was divided into two groups. Sample size was calculated by open Epi software. A random sample of 120 individuals was taken which was sufficient, with 95% confidence interval and 5% margin of error. Control group A comprised of normal healthy subjects showing no clinical sign and symptom of any disease. The hyperuricemic group B comprised of subjects having high serum uric levels, and were taken as cases.

Patients with obvious ischaemic heart disease (angina, myocardial infarction) and other vascular diseases and with any concurrent sickness like chronic liver disease, thyroid dysfunction and history of renal disorder. Patients on drugs like thiazide diuretics, antihypertensives, cytotoxic drugs, cyclosporine, antitubercular drugs like ethambutol & pyrazinamide, recent intake of allopurinol & women's on oral contraceptives were excluded from our study.

After consent was taken, venous blood samples were collected after 8-10 hours overnight fasting. The samples were then centrifuged at 80xg (3000 rpm) for 10 minutes and supernatant was separated. Fasting glucose was done by GOD-PAP (Glucose Oxidase-Phenol-Aminophenazone) method (Merck France). Serum uric acid, assayed by uricase method (Merck France). Serum cholesterol was done by CHOD-PAP method. Serum triglyceride was done by GPO-PAP method. LDL-C and VLDL-C was done by Friedewald's Formula.

A descriptive statistical analysis of continuous variable was performed using SPSS (Version 16). Data on continuous variables i.e. biophysical parameters (age,height,weight,BMI, blood pressure) statistically analysis by using chi-square test and biochemical parameter (serum fasting blood glucose, serum uric acid lipid profile) were calculated

as mean  $\pm$  standard deviation(SD) by using a student t-test. In all statistical analysis performed, (p-values<0.01) were considered statistically significant.

## Results

A total 120 subjects participated in this study and were divided into two groups. Group A consist of 60 healthy subjects and group B consist of 60 hyperuricemic subjects. All the subjects were age matched and therefore no significant difference was observed between the groups.

Table 1 showed the comparison of mean of biophysical variables and there was no significant differences in height, weight and BMI, but the mean systolic and diastolic blood pressure were significantly increased in hyperuricemic subjects. Table 2 shows the comparison of biochemical variables among the groups. The result of this table showed that serum uric acid, serum fasting blood sugar, serum cholesterol, serum Low Density Lipoprotein (LDL)-cholesterol, serum triglyceride and serum Very Low Density Lipoprotein (VLDL) cholesterol were significantly higher in hyperuricemic patients group when compared to control group.

**Table 1.** Comparison of Biophysical Variables among -Group A (normal healthy subjects, controls) and Group B (Subjects with hyperuricemia, cases) in the Rheumatology Clinic of a Tertiary Care Hospital of Karachi.

Variables	Group A (Controls) n=60 Mean $\pm$ SD	Group B (Cases) n=60 Mean $\pm$ SD
Age ( years)	42.42 $\pm$ 8.38	43.87 $\pm$ 8.05
Weight (Kg)	69.13 $\pm$ 8.51	66.82 $\pm$ 7.96
Height (meter)	1.6860 $\pm$ 0.06	1.6763 $\pm$ 0.079
BMI (kg/m <sup>2</sup> )	24.2133 $\pm$ 2.04	23.6583 $\pm$ 1.47
Systolic blood pressure	120.00 $\pm$ 0.0	130.59 $\pm$ 13.13*
Diastolic blood pressure	79.08 $\pm$ 2.83	82.05 $\pm$ 11.05*

\*Significantly high as compare to control group p-value< 0.01

**Table 2.** Comparison of Biochemical Variables among -Group A (normal healthy subjects, controls) and Group B (subjects with hyperuricemia, cases) in the Rheumatology Clinic of a Tertiary Care Hospital of Karachi.

Variables	Group A (Controls) n=60	Group B (Cases) n=60
Serum Uric Acid(mg/dl)	4.505 $\pm$ 0.69	8.61 $\pm$ 0.86*
FBS (mg/dl)	92.62 $\pm$ 7.98	155.33 $\pm$ 17.46*
Serum Cholesterol(mg/dl)	140.45 $\pm$ 16.47	245.03 $\pm$ 20.00*
LDL-C (mg/dl)	65.18 $\pm$ 13.10	146.23 $\pm$ 15.78*
HDL-C(mg/dl)	48.80 $\pm$ 5.64	48.10 $\pm$ 0.10
TG(mg/dl)	132.47 $\pm$ 16.68	253.92 $\pm$ 77.77*
VLDL-C (mg/dl)	26.670 $\pm$ 3.28	50.783 $\pm$ 15.55*

\*Significantly high as compare to control group p- value< 0.01

FBG=fasting blood sugar, serum LDL-C= Low Density Lipoprotein-cholesterol, serum TG=triglyceride and serum VLDL-C= Very Low Density Lipoprotein (VLDL) cholesterol

Fig.1 shows that the serum uric acid of hyperuricemic group was significantly higher when compared to control subjects. Fig. 2 shows that the fasting blood sugar was significantly higher in

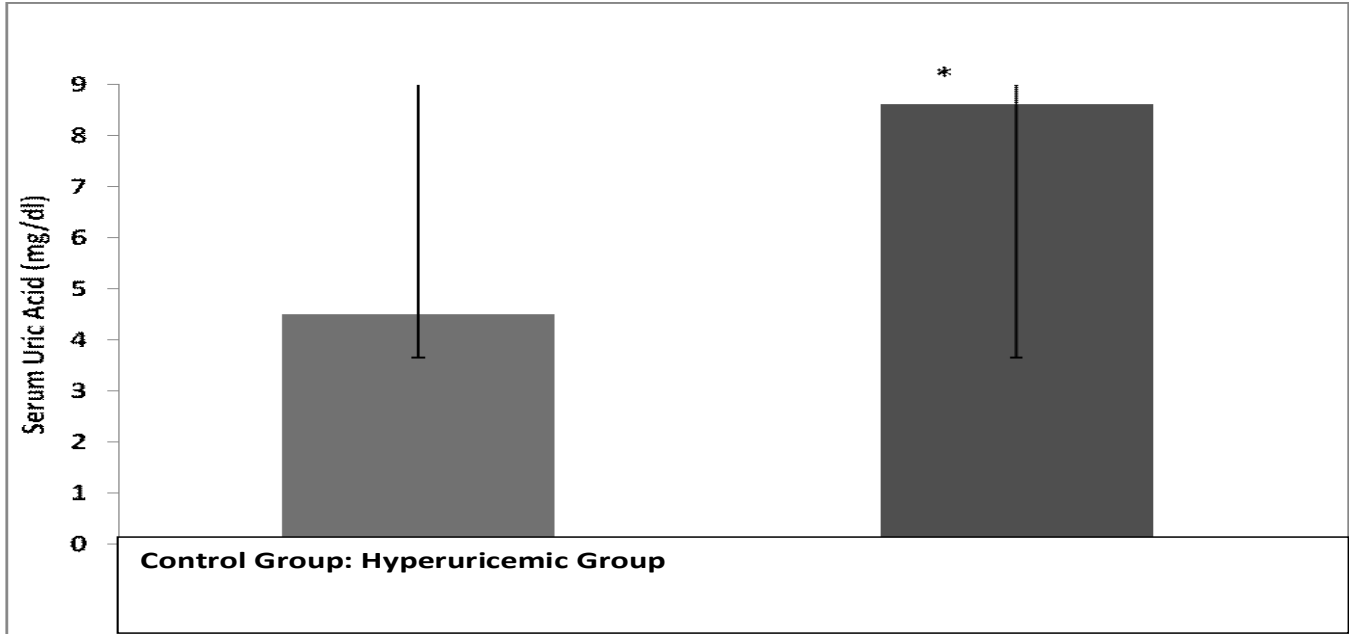
## Discussion

Hyperuricemia is a metabolic consequence originating with a wide range of aetiology concerned with increase production or decrease excretion of uric acid and also as a combination of both<sup>11</sup>. There is enough evidence that hyperuricemia has been linked with cardiovascular diseases. Hyperuricemia predispose to the development of hypertension and is also thought to result in increased oxidative stress and generation of free radicals, which eventually can be the nidus of future cardiovascular disease<sup>12</sup>.

Total 120 subjects were enrolled in this study, which were divided into two groups that are control group A (60), Hyperuricemic group B (60).

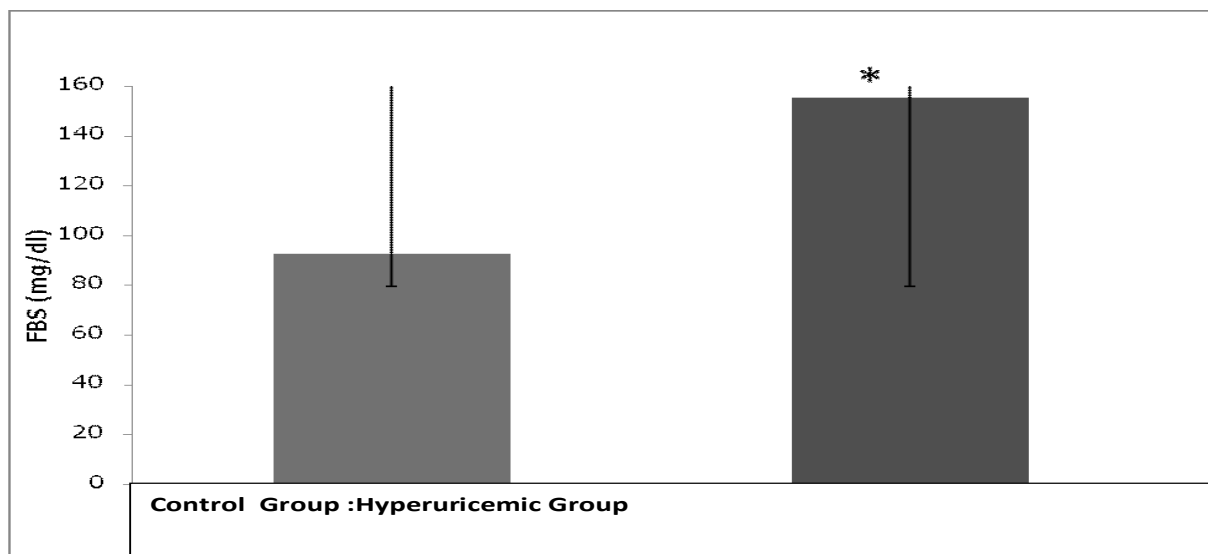
Our study showed significantly higher mean values of systolic and diastolic blood pressure in hyperuricemic group when compared to control group. These finding are matched with study of Kashemet al.<sup>13</sup>. Diabetes mellitus is a worldwide

**Fig 1.** Comparison of Serum Uric Acid among Group A (normal healthy subjects, controls) and Group B (subjects with hyperuricemia, cases), in the Rheumatology Clinic of a Tertiary Care Hospital of Karachi.



\*Significantly higher when compared to control p value < 0.01

**Fig 2.** Comparison of Serum Fasting Blood Sugar among Group A (normal healthy subjects, controls) and Group B (subjects with hyperuricemia, cases), in the Rheumatology Clinic of a Tertiary Care Hospital of Karachi.



\*Significantly higher when compared to control p value < 0.01

problem that affects 200 million people around the world<sup>14</sup>. Our study showed that fasting blood sugar was significantly higher in hyperuricemic group. Safi AJ et al. also observed the strong association between hyperuricemia and diabetes mellitus. Safi AJ et al. have explained that the compensatory hyperinsulinaemia seen in diabetes results in decreased renal excretion of sodium and uric acid which in turns results in high level of serum uric acid in serum<sup>15</sup>. On the other hand Ishihara et al. found negative association in hyperuricemia and diabetes mellitus<sup>16</sup>.

In our study significantly higher mean values of serum cholesterol, LDL-C, Triglyceride, VLDL-C, were found in hyperuricemic patient group. According to the latest ATP-III guidelines the optimal level of serum cholesterol, triglyceride-HDL, LDL-C are <200 mg/dl, <152mg/dl, >40 mg/dl and <100 mg/dl respectively (National Cholesterol Education Program, 2001)<sup>17</sup>. Considering the ATP III guidelines the hyperuricemic patient group was associated with dyslipidemia. These findings are also in agreement with Sarmah et al.<sup>18</sup>.

## Conclusion

Hyperuricemia is associated with diabetes mellitus, hypertension and dyslipidemia. All these risk factors along with high serum uric acid are responsible for cardiovascular disease.

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