Original Article

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# Role of Uric Acid in Coronary Artery Disease

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## ABSTRACT

**Background:** It has been seen that free radicals are involved in the pathogenesis of atherosclerosis. Serum uric acid act as aprooxidant particularly at higher concentration and considered to be associated with various cardiovascular risk factors.As it acts as a prooxidant at higher concentration, our aim isto see whether theincreased serum uric acid levels can be used for monitoring CAD.

**Methods:** 300 patients of CAD were included. In addition to a detailed history and physical examination, anthropometric parameters like body mass index, waist circumference, systolic blood pressure, diastolic bloodpressure, fasting serum lipid profile, uric acid and glucose levels were measured. Prevalence of metabolic syndromeusing ATP III criteria was studied.

**Result:** In our study hypertriglyceridemia, BMI and prevalence of metabolic syndrome showed a steady and a significant increase with increasing levels of serum uric acid.

**Conclusion:** In our study there is significant positive relationship of increased serum uric acid with two cardiovascular risk factors i.e. Triglyceride and prevalence of metabolic syndrome.

***Keywords:*** *Uric Acid, Coronary Artery Disease*

## Introduction

Coronary artery disease (CAD) remains the major cause of morbidity and mortality in all the developed countries in the world and in India, it has already climbed the charts from the 14th to 4th place only behind tuberculosis, communicable disease and malnutrition. Lipids and lipoproteins are major risk factors for CAD; however, they do not account for the disease in 30% to 40% of the population with CAD. [1] Other risk factors include smoking, hypertension, diabetes mellitus etc.[2] Major CAD risk factors do not predict subsequent myocardial infarction accurately and do not fully explain social class differences in Indians as Indians have a high incidence of CAD which is not fully explained by conventional risk factors. The search for CAD risk factors that might explain these variations has been stimulated by the evidence that free radicals are involved in the pathogenesis of atherosclerosis and that antioxidants, both dietary and endogenous, may play a role.[3] Uric acid can act as a prooxidant, particularly at increased concentrations and thus may be a marker of oxidative stress. [4,5] Some researches have proposed that hyperuricemia – induced oxidative stress represents a cause of the metabolic syndrome. [6]

## Materials and Methods

Present study was conducted in the department of pathology at Sanjay Gandhi Institute of Medical Sciences Lucknow. A total of 300 CAD patient from the cardiology department were included in the study. The detailed history was taken regarding demographic profile, family history of premature coronary artery disease and smoking. Anthropometric measurements including BMI, height, waist circumference, systolic blood pressure, diastolic blood pressure, fasting glucose levels, lipid profile and serum uric acid were measured. Prevalence of metabolic syndrome was studied in study population. All the assays were carried out in the serum samples of CAD patients after a twelve hour overnight fasting. The serum was separated within 60 minutes of sample of collection. For metabolic syndrome ATPIII criteria were used.

## Results

The present study comprised of 300 CAD patient, out of which 250 were males and 50 were females. The clinical and metabolic characteristics of the 300 CAD patients in the study population are presented in Table 1.

The age of the CAD patients in the study population ranged from 30 to 80 years, with 83.4% males and 16.6% females. In the study population, 35% were smokers, while 19% had a positive CAD family history. Range of fasting levels of serum glucose, total cholesterol, HDL cholesterol, Triglycerides were 65- 394 mg/dL, 72-262 mg/dL, 20-65 mg/dL and 35-315 mg/dL respectively.

Serum uric acid levels were divided into four quartiles. The levels of serum uric acid were 2.3-4.8 mg/dL in I quartile,

4.9-5.6 mg/dL in II Quartile, 5.7- 7.0 mg/dL in III Quartile and 7.1-12.6 mg/dL in IV Quartile respectively (Table 2)

The body mass index (BMI) values in the four different Uric acid quartiles are given in Table 3, for the study population. The median BMI (25.0) was markedly higher in Quartile IV compared to Quartile I median BMI value of 23.9.

The prevalence of metabolic syndrome (ATP III criteria) exhibited an increase with increasing serum uric acid levels and was highest (59.2%) in the fourth quartile compared to the first quartile (32.9%) and was significant.

There was a steady and a significant increase in % hyper triglyceridemia with increasing serum uric acid levels.

**Table 1: Clinical and Metabolic characteristics of the study population (n=300).**

| S. No. | Parameter | Range | |
|---|---|---|---|
| 1 | Age (years) | 30-80 | |
| 2 | Sex (Male) | 250 | 83.4% |
| | (Female) | 50 | 16.6% |
| 3 | Body weight, Kg | 45-94 | |
| 4 | Body mass index (BMI) (kg/m2) | 17.1-40 | |
| 5 | Fasting glucose, mg/dL | 65-394 | |
| 6 | Total cholesterol, mg/dL | 72-262 | |
| 7 | LDL cholesterol, mg/dL | 45-191 | |
| 8 | HDL cholesterol, mg/dL | 20-659 | |
| 9 | Triglyceride, mg/dL | 35-315 | |
| 10 | VLDL cholesterol, mg/dL | 07-63 | |
| 11 | Positive CAD family history | 52/300 | 17.3% |
| 12 | Smoking | 106/300 | 35.33% |
| 13 | Height (cm) | 141-185 | |
| 14 | Waist (cm) | 84-115 | |
| 15 | Systolic Blood Pressure, mm Hg | 100-190 | |
| 16 | Diastolic Blood Pressure, mm Hg | 70-110 | |

**Table 2: Serum Uric Acid Levels in the four different Quartiles in the Study Population (n=300).**

| S. No. | Quartile | Uric acid level (mg/dL) | Number of cases |
|---|---|---|---|
| 1. | I Quartile | 2.3-4.8 | 79 |
| 2. | II Quartile | 4.9-5.6 | 73 |
| 3. | III Quartile | 5.7-7.0 | 77 |
| 4. | IV Quartile | 7.1-12.6 | 71 |

**Table 3: Body Mass Index (BMI) values of the CAD patients in the four different Uric Acid Quartiles.**

| S.NO | Uric acid Quartile | Body Mass Index (kg/m2) | | |
|---|---|---|---|---|
| | | Range | Mean | Median |
| 1 | I Quartile (2.3-4.8 mg/dL) (n=79) | 17.3-33.3 | 24.3 | 23.9 |
| 2 | II Quartile (4.9-5.6 mg/dL) (n=73) | 19.3-33.6 | 25.2 | 24.2 |
| 3 | III Quartile (5.7-7.0 mg/dL) (n=77) | 17.1-40.0 | 24.4 | 25.4 |
| 4 | IV Quartile (7.1-12.6 mg/dL) (n=71) | 18.3-40.0 | 25.4 | 25.0 |

**Table 4: Prevalence of metabolic syndrome by ATP III Criteria in the different Uric acid Quartiles in the study population.**

| S. No | Uric acid Quartile | Prevalence of Metabolic syndrome | |
|---|---|---|---|
| | | Number | % |
| 1 | I Quartile (2.3-4.8 mg/dL) (n=79) | 26 | 32.9 |
| 2 | II Quartile (4.9-5.6 mg/dL) (n=73) | 28 | 38.4 |
| 3 | III Quartile (5.7-7.0 mg/dL) (n=77) | 34 | 44.2 |
| 4 | IV Quartile (7.1-12.6 mg/dL) (n=71) | 42 | 59.2 |

**Table 5: Hypertriglyceridemia in the different Uric acid Quartiles in the study population.**

| S. No | Uric acid Quartile | Hypertriglyceridemia (>150mg/dl) | |
|---|---|---|---|
| | | number | % |
| 1 | I Quartile (2.3-4.8 mg/dL) (n=79) | 15 | 18.99 |
| 2 | II Quartile (4.9-5.6 mg/dL) (n=73) | 14 | 19.18 |
| 3 | III Quartile (5.7-7.0 mg/dL) (n=77) | 26 | 33.77 |
| 4 | IV Quartile (7.1-12.6 mg/dL) (n=71) | 28 | 39.44 |

## Discussion

The mechanism by which uric acid may cause CAD has been explored using cell culture and animal models. It appears that uric acid must enter the endothelial and vascular smooth muscle cells via a specific organic anion exchanger, where it activates a variety of intracellular signaling molecules involved in inflammation and proliferation. In the endothelial cells, there is a decrease in nitric oxide levels and an inhibition of endothelial proliferation, whereas in vascular smooth muscle cells, there is activation of proliferative and inflammatory pathways.[7,8] Local activation of the nitric oxide also have a central role in the induction of insulin resistance, as insulin requires nitric oxide for its action (by stimulating blood flow to the skeletal muscle). New studies also have suggested that hyperuricemia may have a pathogenetic role in obesity-related metabolic syndrome. Thus, an elevated uric acid level predicted the development of obesity and hyperinsulinemia in normal subjects [9,10] and an elevated uric acid level is universally present in patients with metabolic syndrome. In recent studies, in which rats were fed fructose to induce metabolic syndrome found that lowering uric acid levels with allopurinol could significantly prevent hypertension, hyperinsulinemia, hypertriglyceridemia and obesity. [11]

J. Hjortnaeset al. [12] in 2004 in their nested case-cohort study of 434 patients with 220 cases with a new vascular event during follow-up, showed that elevated serum uric acid levels are strongly associated with the metabolic syndrome, they also showed that in patients without a metabolic syndrome, elevated serum uric acid levels are associated with increased risk for vascular disease. In our study also, there was a steady and a significant increase in the prevalence of metabolic syndrome (ATP III criteria) with increasing serum uric acid levels i.e. 32.5% in Quartile I to 59.2% in Quartile IV. They also showed in their study that serum uric acid concentration increased with the number of individual metabolic syndrome components. In our study, there was a steady and a significant increase in hypertriglyceridemia from 18.92% in Quartile I to 39.22% in Quartile IV, with increasing serum uric acid levels and J. Hjortnaeset al. [12] also got similar findings. Metabolic syndrome was present in 50% of the patients in their study and serum uric acid levels were higher in patients with metabolic syndrome than in patients without metabolic syndrome. S. Car et al. in 2009 [13] showed that higher serum uric acid determined on admission (within 48 hours since the symptom onset) in a cohort of 621 patients from Croatia, was independently associated with higher short-term mortality and poorer long-term survival after AMI. They have claimed that their findings are in agreement with a previous carried out Japanese study [14] and also have documented the relevance of on-admission serum uric acid for risk stratification in AMI patients. The present study brings out the relevance of serum uric acid levels in Indian CAD patients in terms of MI risk. Bickel et al. in 2002 [15] in their study on 1017 CAD patients showed that compared with in lowest quartile of uric acid, the highest quartile was associated with a significant increase in body mass index as well as Triglyceride level (p=0.013). In our study also, there was a steady and a significant increase in both the modifiable risk factors from Quartile I to Quartile IV i.e. BMI (24.3 to 25.4 kg/m2) and Triglyceride (110.6 to 138.7 mg/dl). Thus, the question raised is whether uric acid is only one of the manifestations of metabolic syndrome, in terms of increased BMI and Hypertriglyceridemia. Similar findings were obtained by Brodovet al. [16] in their study on 2966 patients with CAD. Our study could not establish any relationship for other modifiable risk factor i.e. Total cholesterol, LDL cholesterol, VLDL cholesterol, smoking etc. with increasing serum uric acid levels, although previous studies have shown a relationship for HDL cholesterol and diabetes mellitus incidence. In contrast, non-HDL cholesterol showed a steady and a significant increase in the present study.

## Conclusion

Serum uric acid level was first reported to be a risk factor for CAD almost half a century ago. Most epidemiological studies have suggested that there is an association between serum uric acid and CAD. In our study there is significant positive relationship with two cardiovascular risk factors i.e. Triglyceride and prevalence of metabolic syndrome.

## References:


1. Stringer MD, Goros PG, Freeman A, Kakkar VV. Lipid peroxides and atherosclerosis. Br MedJ, 1989; 298: 281-4.
2. Poulter N, Sever P, Thorn S, et al. Cardiovascular diseases: Risk factors and interventions. Oxford: Radcliffe Medical Press, 1993; 351pp.
3. Hennekens CH, Gaziano JM. Antioxidants and heart diseases: epidemiology and clinical evidence. ClinCardiol, 1993; 16(Suppl. 1): 1710-13.
4. Becker BF. Towards the physiological function of uric acid. Free RadicBiol Med,1993; 14: 615-31.
5. Strazzullo P, Puig JG. Uric acid and oxidative stress: relative impact on cardiovascular risk? NutrMetabCardiovasc Dis, 2007; 17: 409-14.
6. Hayden MR, Tyagi SC. Uric acid: a new look at an old risk marker for cardiovascular disease, metabolic syndrome and type 2 diabetes mellitus: the urate redox shuttle.
7. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. N Eng J Med, 2008; 359: 1811-21.
8. Kang DH, Park SK, Lee IK, Johnson RJ. Uric acid induced C-reactive protein expression: Implication on cell proliferation and nitric oxide production of human vascular cells. J Am SocNephrol, 2005; 16: 3553-62.
9. Nakanishi N, Okamoto M, Yoshida H, Matsuo Y, Suzuki K, Tatara K.Serum uric acid and risk of development of hypertension and impaired fasting glucose or Type II diabetes in Japanese male office workers. Eur J Epidemiol, 2003; 18: 523-30.
10. Fachini F, Chen YD, Hollenbeck CB, Reaven GM. Relationship betweenresistance to insulin mediated glucose uptake, urinary uric acid clearance and plasma uric acid concentration. JAMA, 1991; 266: 3008-3011.
11. NakagaweT, Hu H, Zharikor S et al. A causal role for uric acid in fructose –induced metabolic syndrome. Am J Renal Physiol, 2006; 290: F625-F631.
12. Hjortnaes J, Algra A, Olijhoek J, Huisman M, Jacobs J, Graaf Y, Visseren F. Serum Uric acid levels and risk of vascular diseases in patients with metabolic syndrome. Journal of Rheumatology, 2007; 349: 1882-87.
13. Car S, Trkuja V. Higher Sreum uric acid on admission is associated with higher short term mortality and poorer long term survival after myocardial infarction: Retrospective Prognostic Study. Clinical Science, 2009; 50: 559-566.
14. Kojima S, Sakamoto J, Ishihara M, Kimura K, Miyazaki S, Yamagishi M et al. Prognostic usefulness of Serum uric acid after acute myocardial infarction (the Japanese Acute Coronary Syndrome Study). Am J Cardiol, 2005; 96: 489-95.
15. Bickel C, Rupprecht HJ, Blankenberg S, Rippin G, Hafner G, Daunhauer A, Hofman KP, Meyer J. Serum uric acid as an independent predictor of mortality in patients with angiographically proven coronary aretery disease. American Journal of Cardiology, 2002; 89: 12-17.
16. Brodov Y, Behar S, Goldenberg I, Boyko V, Chouraqui P. Usefulness of combining uric acid and C- reactive protein for risk stratification of patients with coronary artery disease. Am J Cardiol, 2009;104:194-198.



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