# **RESEARCH ARTICLE**

# A study on association of hyperuricemia among patients of metabolic syndrome attending outpatient department of North Bengal Medical College and Hospital

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## ABSTRACTS

Background: Metabolic syndrome (MS) refers to a group of modifiable risk factors consisting of insulin resistance, glucose intolerance, increased triglyceride and decreased high-density lipoprotein (HDL) cholesterol levels, and arterial hypertension, occurring in some individuals and associated with an increased risk of developing cardiovascular disease and type 2 diabetes mellitus. The raised serum uric acid level as a marker for generalized metabolic derangement is on the rise. An independent effect of elevated serum uric acid on atherosclerosis, as measured by such a surrogate marker, has been suggested for the influence of MS and other factors. Asymptomatic hyperuricemia is also found to have an independent association with a cardiovascular disorder. Metabolic disturbances such as visceral obesity, dyslipidemia, hyperglycemia, and hypertension are risk factors for cardiovascular disease. Aims and Objectives: The study was conducted to find out any association between MS and hyperuricemia which would be relevant as a biomarker to diagnose the fatal but avoidable cardiovascular complication and to treat them at the earliest. Materials and Methods: Height, weight, blood pressure, waist circumference, body mass index (BMI), blood uric acid levels, fasting blood sugar levels, serum triglyceride, and serum HDL cholesterol measured among a group of 298 subjects (198 cases and 100 controls) attending outpatient department of North Bengal Medical College and Hospital. Results: Hyperuricemia significantly increases with an increase in age and BMI. Subjects of MS (Cases) significantly have more systolic and diastolic blood pressure, fasting plasma glucose, raised serum triglyceride, uric acid, and low HDL than their healthy counterparts (control). Hyperuricemia is significantly associated with MS cases irrespective of sex after menopause of females, but males are more affected than females when the age group is not considered. Conclusion: An association was found between MS and uric acid level that may help the medical community to include the uric acid level measurement to be a routine diabetic, hypertensive care level, and decrease the burden of cerebrovascular disorder arising out of complication due to hyperuricemia. Association of serum uric acid level with MS and its relevance as a biomarker as cardiovascular risk outcome will have significant clinical importance.

**KEY WORDS:** Metabolic Syndrome; Hyperuricemia; Oxidative Stress; Atherosclerosis; Cardiovascular and Cerebrovascular Risk

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#### **INTRODUCTION**

Metabolic syndrome (MS) is defined by abdominal obesity in combination with any two of the following four factors: High triglyceride, low high-density lipoprotein (HDL) cholesterol, raised blood pressure, and raised fasting plasma glucose (FPG). Insulin resistance and obesity are regarded as the

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most important risk factors. Hyperuricemia was found to be associated with MS.<sup>[1]</sup>

Plasma uric acid is a circulating marker of oxidative damage in a variety of pathological conditions such as ischemic liver injury, hyperlipidemia, chronic heart disease, atherosclerosis, ischemic reperfusion injury, and diabetes.<sup>[2-6]</sup> The serum uric level depends on gender, lifestyle, meals, and previous use of diuretics.<sup>[7]</sup> Very less information is available concerning the prevalence of hyperuricemia in MS.

# Objectives

We conducted the study to find out any association between MS and hyperuricemia and its relevance as a biomarker whose early detection would help to diagnose the fatal but avoidable cerebrovascular (CV) complication or to treat them at an earliest.

## MATERIALS AND METHODS

After getting approval from IEC, this study was conducted in the Department of Physiology of North Bengal Medical College and Hospital. Patients attending the Medicine Outpatient Department of North Bengal Medical College and Hospital were taken as the study population. It was a crosssectional study with double-blinding to prevent any selection or interview bias. Cases and controls are matched accordingly.

#### **Study Variables**

This study was height, weight, blood pressure, waist circumference, body mass index (BMI), blood uric acid levels, fasting blood sugar levels, serum triglyceride, and serum HDL cholesterol.

#### **Inclusion Criteria**

Subjects of both sexes having features of MS as per IDF criteria within the age group of 20–70 years were taken.

#### **Exclusion** Criteria

Subjects receiving drugs modifying uric acid levels in blood, addiction, malignancy, myopathy, muscle injury, and severely ill and moribund patient.

#### Sample Size

A total of 298 male and female subjects comprising 198 cases and 100 controls were taken in the study.

### Methods

To measure waist circumference, locate top of the right iliac crest and place a measuring tape in a horizontal plane around the abdomen at the level of iliac crest. Measurement is made at the end of a normal expiration.<sup>[8]</sup> Blood pressure was measured using a sphygmomanometer after the subjects had rested for more than 5 min. Blood pressure was measured on two occasions after resting, and average values were then taken.<sup>[9]</sup>

Laboratory analysis – After overnight fasting, blood samples were collected to determine lipid profile, blood glucose level, and serum uric acid concentration.

# **Statistical Analysis**

Total data of total 298 subjects (198 cases and 100 controls) and statistically analyzed using IBM SPSS V20.

# RESULTS

Table 1 shows that the mean values and the SD of FPG and triglycerides (TG), HDL, and uric acid are varying widely in control and cases. Hence, this signifies that the wide variation in the values of the above parameters affects both sexes of MS patients equally. Table 2 depicts that hyperuricemia is significantly associated with BMI (Sig-0.032). It is inferred from the result that, with an increase in BMI, there will be an elevation of serum uric acid level. Table 3 shows the relationship between MS and hyperuricemia in cases and controls. It is observed that MS positively and significantly associated with hyperuricemia (Sig- 0.033). From the above findings, we may infer that hyperuricemia is significantly associated with MS cases irrespective of sex. Although hyperuricemia is a prevalent finding in patients of MS, its clinical meaning is still controversial and often underestimated. There is recent evidence related to the clinical significance of hyperuricemia in both sexes and the potential benefits of lowering serum uric acid levels.<sup>[10]</sup>

| Table 1: The mean and standard deviation of different parameters among the control and cases |   |        |   |       |                                   |        |                          |        |  |       |                      |        |
|--|---|--------|---|-------|-----------------------------------|--------|--------------------------|--------|--|-------|----------------------|--------|
| Parameters   | meters Systolic blood<br>pressure<br>(mm of Hg) |        | Diastolic blood<br>pressure<br>(mm of Hg) |       | Fasting plasma<br>glucose (mg/dl) |        | Triglycerides<br>(mg/dl) |        | High-density<br>lipoprotein<br>(mg/dl) |       | Uric acid<br>(mg/dl) |        |
|  | Mean  | SD     | Mean                                      | SD    | Mean                              | SD     | Mean                     | SD     | Mean                                   | SD    | Mean                 | SD     |
| Control (n=100)  | 120.86  | 7.260  | 79.18                                     | 3.888 | 88.37                             | 7.019  | 130.90                   | 14.424 | 49.95                                  | 5.328 | 5.148                | 1.7924 |
| Case ( <i>n</i> =198)  | 133.26  | 12.598 | 84.52                                     | 6.899 | 112.39                            | 45.367 | 163.93                   | 76.152 | 43.03                                  | 9.443 | 5.886                | 1.5802 |

SD: Standard deviation

| Table 2: Relation of hyperuricemia with body mass index among cases and control |             |            |       |                  |  |  |  |
|---|-------------|------------|-------|------------------|--|--|--|
| Variables   | Hyperu      | ricemia    | Total | Chi-square value |  |  |  |
|   | No          | Yes        |       |                  |  |  |  |
| Body mass index   |             |            |       |                  |  |  |  |
| 18.5–24.99  | 45(62.50%)  | 27(37.50%) | 72    | 8.831            |  |  |  |
| 25-29.99  | 156(74.64%) | 53(25.36%) | 209   | df=3             |  |  |  |
| 30-34.99  | 11(73.33%)  | 4(26.67%)  | 15    | Sig-0.032        |  |  |  |
| ≥35   | 0(0.00%)    | 2(100.00%) | 2     |                  |  |  |  |
| Total   | 212         | 86         | 298   |                  |  |  |  |

| Table 3: Relationship between metabolic syndrome and<br>hyperuricemia in cases and controls |             |             |       |            |  |  |  |
|---|-------------|-------------|-------|------------|--|--|--|
| Variables   | Metabolic s | yndrome (%) | Total | Chi-square |  |  |  |
|   | Control     | Case        | -     | value      |  |  |  |
| Hyperuricem   | ia          |             | 4.528 |            |  |  |  |
| No  | 79 (37.26)  | 133 (62.74) | 212   | df=1       |  |  |  |
| Yes   | 21 (24.42)  | 65 (75.58)  | 86    | Sig-0.033  |  |  |  |
| Total   | 100         | 198         | 298   |            |  |  |  |

# DISCUSSION

According to our study, with an increase in age and BMI uric acid level significantly increases. MS subjects (cases) significantly have more BMI, SBP, DBP, FPG, TG, uric acid, and low HDL than their healthy counterparts (control). With advancing, age hyperuricemia is significantly associated with MS cases irrespective of sex [Table 2]. Our study also shows that MS cases had elevated levels of serum uric acid level than their normal counterpart [Table 3, sig.-0.033].

In our study, we have seen that the subjects of MS are having raised FPG and serum uric acid levels. Another study found the common association of MS with an increased risk for CVD and T2DM in both sexes.<sup>[11]</sup> In an Indian study, it was found that MS is a major health problem in this region and proper emphasis should be given on its prevention and control.<sup>[12]</sup> We have found in our study that MS subjects were having elevated levels of serum uric acid, which is coexistent with the above study. In another study, serum uric acid was found to be positively associated with MS, which supports our study.<sup>[13]</sup> Hyperuricemia is significantly associated with MS irrespective of sexes when age advances, especially after menopause. Considering the growing incidence of obesity and MS worldwide and the potential link between hyperuricemia and cardiovascular complications, more emphasis should be put on the evolving prevalence of hyperuricemia in developing countries.<sup>[14]</sup> Results of one study suggest that increased serum uric acid concentration is associated with an increased prevalence of metabolic disorders such as obesity, dyslipidemia, and hypertension in the Hangzhou population.<sup>[15]</sup> Our studies also comply with the above study. Fructose raises uric acid, and the latter inhibits

nitric oxide bioavailability. Uric acid may be a cause of the MS, possibly due to its ability to inhibit endothelial function and fructose may have a major role in the epidemic of MS and obesity due to its role of increasing uric acid.<sup>[1]</sup> Chen and Zhu in a study in a population of 2374 subjects concluded that hyperuricemia is prevalent among the Chinese population and serum uric acid is positively associated with MS.<sup>[16]</sup> We found similar results Wei and Shan studied differences in the morbidity of MS between the case group and the control group and found statistically significant (P < 0.05). They concluded that the history of hyperuricemia is associated with the occurrence of MS and may be an important risk factor of MS.<sup>[17]</sup> Ebrahimpour et al. concluded that an independent relationship exists between hyperuricemia and hypertriglyceridemia, hypertension, and visceral obesity<sup>[18]</sup> which is consistent with our study. Nejatinamini et al. and others in a study observed a higher association of MS with uric acid and they concluded that such association may indicate that uric acid might be an additional component of MS.<sup>[19]</sup> Our findings are at par with the same study and we also found that MS patients are more prone to have hyperuricemia. Bano et al. found that SUA level was positively correlated with blood pressure and obesity indices in young adults and WHR was independently correlated with uric acid. These findings are consistent with our study.<sup>[20]</sup> Srivastava and Dixit in their study found moderate sensitivity and specificity of serum UA and NO in the diagnosis of Type 2 diabetes.<sup>[21]</sup> Their findings also support the findings of our study.

#### Strength and Limitation of the Study

We were true and honest in all aspects to the present study, but in spite of that, there were some limitations we encountered. Duration, as well as the sample size of the control, was small for the study. We did not know how much age distribution affects the uric acid level in the MS subjects. The catchment area was also small in relation to the population of MS patients worldwide. Multicentre cohort studies with a larger population can eliminate the above-mentioned limitations. Further, wide-spectrum research works can validate our observations to apply it in clinical medicine. Double blinding was done at the beginning of the study. We did not know whether the subjects would come in test or control. However, after obtaining the blood reports, we could deduce where to place but that made us vulnerable to examiners' bias. We could find the age distribution is significantly related to hyperuricemia. It is observed that most of the MS cases are older in age. Hence, age distributions become a confounding factor in this case.

#### CONCLUSION

MS is growing to be a worldwide pandemic in the very near future. Aberrations from the traditional diet, adaptation of high sodium-rich, and low fiber western diet along with sedentary life habits all are adding up to cause it. Recent interest in the relationship of uric acid and MS has caused vigil among clinicians. Hyperuricemia is a known and approved risk factor for not only gout but also for multiple renal as well as cardiovascular disorders. It is well known that MS is associated with an increased risk of cardiovascular as well as renal morbidity and mortalities. Early detection of hyperuricemia as a single hand biomarker in cases of MS may be an indicator of impending cardiovascular and CV disease and will have diagnostic and therapeutic importance to clinical medicine. Hence, if an association with MS and uric acid is found, it will be much easier for clinicians to be cautious in advance to prevent it, as a uric acid level measurement is an easy task as well as controlling it with drug management.

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