

## ASSOCIATION OF SERUM URIC ACID LEVELS AND THE COMPONENTS OF METABOLIC SYNDROME- A COMPARATIVE STUDY

Jaya Jose<sup>1</sup>, Sajeevan K. C<sup>2</sup>, Pushpalatha M<sup>3</sup>, Sujina C. M<sup>4</sup>, Anupa Lucas<sup>5</sup>

<sup>1</sup>Assistant Insurance Medical Officer, ESI Hospital, Thrissur.

<sup>2</sup>Associate Professor, Department of Biochemistry, Government Medical College, Thrissur.

<sup>3</sup>Professor, Department of Biochemistry, Government Medical College, Thrissur.

<sup>4</sup>Assistant Professor, Department of Community Medicine, Government Medical College, Manjeri.

<sup>5</sup>Assistant Professor, Department of Community Medicine, Government Medical College, Thrissur.

### ABSTRACT

#### BACKGROUND

Metabolic syndrome is an emerging threat in our population. Metabolic syndrome is characterised by central obesity, hypertriglyceridaemia, low HDL cholesterol, hyperglycaemia and hypertension. Serum uric acid level has been reported to be associated with various cardiovascular complications of metabolic syndrome. However, its direct relationship with metabolic syndrome remains controversial. Thus, we planned this study to find the association of serum uric acid with all the components of metabolic syndrome.

#### MATERIALS AND METHODS

The study was a comparative study conducted among patients attending obesity clinic in Thrissur from March 2014 to March 2015. 56 subjects with metabolic syndrome and 54 subjects without metabolic syndrome between the age group 25-65yrs. with BMI  $\geq 25\text{kg/m}^2$  were included in the study. Fasting blood glucose, lipid profile and uric acid estimation were done by analysers in the Central Laboratory, Government Medical College, Thrissur. Data analysis was done using SPSS software. The tests were statistically significant, if 'p' value  $< 0.05$ .

#### RESULTS

Metabolic syndrome was observed in 50.9% of obese patients in our study. The mean serum uric acid levels were  $6.07 \pm 1.61$  and  $4.62 \pm 1.33$  in metabolic and non-metabolic syndrome respectively and were found to be statistically significant. The association of mean uric acid levels with BMI, FBS and triglycerides were statistically significant.

#### CONCLUSION

A significant positive association of uric acid with body mass index, waist circumference, triglycerides and fasting blood glucose. The association of uric acid with various components of metabolic syndrome support that it might be taken as a marker for metabolic syndrome.

#### KEYWORDS

High-Density Cholesterol (HDL), Low-Density Cholesterol (LDL), Triglycerides (TG), Fasting Blood Sugar (FBS), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP).

**HOW TO CITE THIS ARTICLE:** Jose J, Sajeevan KC, Pushpalatha M, et al. Association of serum uric acid levels and the components of metabolic syndrome- A comparative study. J. Evid. Based Med. Healthc. 2017; 4(74), 4382-4386. DOI: 10.18410/jebmh/2017/872

#### BACKGROUND

The metabolic syndrome refers to a clustering of metabolic factors including central obesity, glucose intolerance, hyperinsulinaemia, low HDL, high triglycerides and hypertension.<sup>1</sup> For the past two decades, the prevalence of metabolic syndrome has increased worldwide including developing countries like India due to the changing

lifestyle.<sup>2</sup> Recent studies show the prevalence of metabolic syndrome is 25.8% among Asian and 53.2% among obese persons.<sup>3,4,5,6</sup> The prevalence rate of metabolic syndrome was 33.5% in a community study conducted among urban eastern civilians in India.<sup>3</sup> Old age, female gender and general obesity significantly contributed the risk of metabolic syndrome in their study.

Uric acid is the final breakdown product of catabolism of the purine nucleotides. Uric acid is a non-protein nitrogenous compound, which is cleared from the body by the kidney.<sup>7</sup> Purines formed from the catabolism of dietary nucleic acid are directly converted to uric acid. The bulk of uric acid arises from the degradation of nucleic acids. Uric acid is primarily produced in the liver and small intestine. Serum urate levels vary with rates of purine biosynthesis and their excretion. The normal uric acid level is 3-7mg/dL.

Financial or Other, Competing Interest: None.

Submission 23-08-2017, Peer Review 28-08-2017,

Acceptance 11-09-2017, Published 13-09-2017.

Corresponding Author:

Dr. Sajeevan K. C,

Associate Professor, Department of Biochemistry,  
Government Medical College, Thrissur.

E-mail: drsajeevankc@gmail.com

DOI: 10.18410/jebmh/2017/872



The daily excretion of uric acid is 500-600mg. Serum urate varies with age, sex, height, body weight, blood pressure, renal function and alcohol intake. Exercise, alcohol, obesity and purine diet are the common causes of increased urate production in humans.

The increased mortality and morbidity in metabolic syndrome is due to the atherosclerotic cardiovascular diseases, hypertension and diabetes mellitus.<sup>7,8,9,10,11</sup> Elevated serum uric acid levels are significantly associated with insulin resistance of metabolic syndrome<sup>12</sup> and its components.<sup>13</sup> Decreased renal uric acid clearance due to hyperinsulinaemia is the reason for elevated uric acid levels in metabolic syndrome.<sup>14</sup> Hyperuricaemia along with other components of metabolic syndrome may act synergistically increasing the cardiometabolic risk.<sup>13</sup> Recently, serum uric acid has been proposed as a marker of oxidative stress, which is considered to be one of the major mechanism for the development of metabolic syndrome and cardiovascular diseases.<sup>15</sup> The positive association of serum uric acid with the components of metabolic syndrome remains controversial. So, we investigated the association of serum uric acid with all the components of metabolic syndrome in obese patients in our population.

**Aim-** To study the association between serum uric acid levels and the components of metabolic syndrome.

## MATERIALS AND METHODS

This study was conducted among 110 patients from March 2014 to March 2015 at the obesity clinic, Thrissur, Kerala, India. 56 subjects with metabolic syndrome and 54 subjects without metabolic syndrome were taken. Sample size was calculated using the following formula taking 80% power and error fixed at 5%.

$$\text{Sample size} = \frac{(Z_{\alpha} + Z_{\beta})^2 \cdot 2SD^2}{d^2}$$

The institutional ethical committee approved the study and informed consent was taken. All patients in the age group 25-65 years with BMI  $\geq 25$  kg/m<sup>2</sup> were included in the study. Diagnosis of the metabolic syndrome was made by the IDF (International Diabetes Federation) criteria.

**Central Obesity-** (defined as waist circumference  $\geq 90$ cm for Indian men and  $\geq 80$ cm for Indian women).

### Plus any of the following features

**Raised Triglycerides Level-**  $\geq 150$ mg/dL (1.7mmol/L) or specific treatment for this abnormality.

**a. Reduced HDL Cholesterol-**  $< 40$ mg/dL (1.03mmol/L) in males and  $< 50$ mg/dL (1.29mmol/L) in females or specific treatment for this lipid abnormality.

**b. Raised Blood Pressure-** Systolic BP  $\geq 130$  or diastolic BP  $\geq 85$ mm of Hg or treatment of previously-diagnosed hypertension.

**c. Raised Fasting Plasma Glucose (FPG)-**  $\geq 100$ mg/dL (5.6mmol/L) or previously-diagnosed type 2 diabetes mellitus.

### The following patients were excluded from the study-

1. Patients with a history of hypothyroidism, hyperparathyroidism, diabetes insipidus and glucose-6-phosphate dehydrogenase deficiency, liver diseases, renal diseases and alcoholism.
2. Patients taking medications like salicylates, diuretics or uricosuric drugs.
3. Pregnant and lactating mothers.

Those patients taking antihypertensive, antidiabetic or antilipidemic drugs were considered to have hypertension, hypercholesterolaemia, hypertriglyceridaemia and diabetes mellitus.

### Anthropometric and Blood Pressure Measurement-

Weight was measured in kilograms using a weighing machine. Height was taken in centimetre. Body Mass Index (BMI) was calculated from the formula BMI = body weight in kg/height in m<sup>2</sup>. Waist circumference was measured at the midpoint between the lowest part of costal margin and superior border of the iliac crest. Blood pressure was recorded on the right arm of patients seated at rest using a sphygmomanometer.

**Laboratory Measurements-** The venous blood sample was collected in the morning after 8-12 hours fasting. Fasting blood glucose levels were estimated by glucose oxidase-peroxidase method. Total serum cholesterol was measured by cholesterol oxidase endpoint enzymatic method. Glycerol phosphate oxidase method (Trinder method) was used to determine serum triglycerides. HDL cholesterol was measured by modified polyvinyl sulfonic acid and polyethylene glycol methyl ether coupled classic precipitation method. LDL cholesterol was calculated from the values of total cholesterol, HDL cholesterol and triglycerides using Friedewald's formulae. Serum uric acid was determined by uricase peroxidase method. All biochemical parameters were determined in Transasia fully automated analyser, Central Laboratory, Government Medical College, Thrissur.

### Data Analysis

The Statistical Package for the Social Sciences 18.0 (SPSS) for windows software was used for statistical calculations. Continuous variables were expressed as mean  $\pm$  SD. Qualitative variables were expressed as a percentage. Comparison of group means of the different variables was done using Student's t-test. Chi-square test was done to find out the association between different components in subjects with and without metabolic syndrome and also to detect the association between hyperuricaemia and metabolic syndrome. The tests were statistically significant, if 'p' value  $< 0.05$ .

## RESULTS

The mean age of the study populations was  $40.52 \pm 10.42$  years and 55% of the subjects were females. The mean age of metabolic syndrome patients was  $42.22 \pm 9.85$  and the mean age of non-metabolic syndrome was  $36.86 \pm 10.76$  and this difference was found to be statistically significant ( $p=0.01$ ).

78.2% and 21.8% of study populations were having BMI  $\geq 30$  and BMI  $< 30$ , respectively. Metabolic syndrome was diagnosed in 50.9% ( $n=56$ ) of obese patients in our study. A nonsignificant increase of metabolic syndrome was observed among females. 74.4% of patients with metabolic syndrome have a BMI  $> 30$ .

The anthropometric parameters of all the patients were shown in the Table 1. Table 2 shows that the BMI of patients with metabolic syndrome and non-metabolic syndrome were  $38.20 \pm 7.92$  and  $34.71 \pm 7.01$  respectively and was statistically significant ( $p < 0.02$ ). Height, weight and waist circumference of patients with metabolic syndrome and non-metabolic syndrome were not statistically significant.

Table 3 shows the biochemical parameters and blood pressure of all the study subjects. Serum total cholesterol, HDL cholesterol and LDL cholesterol levels in patients with metabolic and non-metabolic syndrome were statistically not significant ( $p > 0.05$ ). Systolic and diastolic blood

pressure, serum fasting blood sugar and triglyceride levels in patients with metabolic and non-metabolic syndrome were statistically significant ( $p < 0.05$ ).

Table 5 shows the mean serum uric acid levels of male and female in both groups. The mean uric acid level in subjects with metabolic syndrome was  $6.07 \pm 1.61$  and that in patients without metabolic syndrome subjects was  $4.62 \pm 1.33$ . The difference was found to be statistically significant ( $p < 0.001$ ). The difference was statistically significant in both groups.

Table 6 shows the association of mean uric acid levels with different components of metabolic syndrome. The association of mean uric acid levels with BMI, FBS and triglycerides was statistically significant. The association of mean uric acid levels with HDL cholesterol and hypertension was not statistically significant.

| Parameter                | Total (n=110) (Mean $\pm$ S.D.) |
|--------------------------|---------------------------------|
| Weight (kg)              | $96 \pm 24.80$                  |
| Height (meter)           | $1.60 \pm 0.08$                 |
| BMI                      | $37.08 \pm 7.70$                |
| Waist circumference (cm) | $106.48 \pm 11.98$              |

**Table 1. Anthropometric Parameters of Study Subjects**

n = number of subjects.

|                          | Metabolic Syndrome | Non-Metabolic Syndrome | p value |
|--------------------------|--------------------|------------------------|---------|
| Parameter                | (Mean $\pm$ SD)    | (Mean $\pm$ SD)        |         |
| Weight (kg)              | $98.7 \pm 26.62$   | $90.20 \pm 19.70$      | 0.09    |
| Height (meter)           | $1.59 \pm 0.08$    | $1.61 \pm 0.07$        | 0.41    |
| BMI                      | $38.2 \pm 7.91$    | $34.70 \pm 7.0$        | 0.02*   |
| Waist circumference (cm) | $107.73 \pm 11.9$  | $103.92 \pm 11.70$     | 0.12    |

**Table 2. Anthropometric Measurements among Subjects with and without Metabolic Syndrome**

(\* $p = < 0.05$  significant).

| Parameter (Normal Range)               | Total (n=110) (Mean $\pm$ S.D.) |
|----------------------------------------|---------------------------------|
| Fasting blood sugar (70-110 mg/dL)     | $122.85 \pm 48.32$              |
| Systolic blood pressure (130 mmHg)     | $133.95 \pm 12.08$              |
| Diastolic blood pressure (90 mmHg)     | $85.43 \pm 8.03$                |
| Total cholesterol (150-200 mg/dL)      | $198.91 \pm 32.62$              |
| Triglycerides (50-150 mg/dL)           | $135.93 \pm 44.61$              |
| High-density lipoprotein (30-75 mg/dL) | $38.24 \pm 7.31$                |
| Low-density lipoprotein (60-150 mg/dL) | $135.95 \pm 30.54$              |

**Table 3. Biochemical Parameters of Study Subjects**

N= number of subjects.

| Parameter                           | Metabolic Syndrome (Mean $\pm$ SD) | Non-Metabolic Syndrome (Mean $\pm$ SD) | p value |
|-------------------------------------|------------------------------------|----------------------------------------|---------|
| Fasting blood sugar (mg/dL)         | $131 \pm 48.06$                    | $106 \pm 44.92$                        | 0.01*   |
| Systolic blood pressure (mm of Hg)  | $138.7 \pm 10.21$                  | $124.17 \pm 9.52$                      | 0.001*  |
| Diastolic blood pressure (mm of Hg) | $87.95 \pm 7.82$                   | $80.25 \pm 5.72$                       | 0.001*  |
| Triglycerides (mg/dL)               | $146.01 \pm 48.91$                 | $115 \pm 23.51$                        | 0.001*  |
| High-density lipoprotein (mg/dL)    | $37.5 \pm 6.12$                    | $39.6 \pm 9.091$                       | 0.15    |
| Total cholesterol (mg/dL)           | $198.9 \pm 36.51$                  | $198.41 \pm 23.21$                     | 0.925   |
| Low-density lipoprotein (mg/dL)     | $133 \pm 33.81$                    | $141 \pm 21.72$                        | 0.19    |

**Table 4. Biochemical Parameters of Study Subjects**

P value  $< 0.05$  significant.

| Gender       | Metabolic Syndrome Mean± SD | Non-Metabolic Syndrome Mean± SD | p Value      |
|--------------|-----------------------------|---------------------------------|--------------|
| Male         | 6.38 ± 1.59                 | 5.09 ± 1.37                     | 0.007        |
| Female       | 5.82 ± 1.62                 | 4.29 ± 1.18                     | 0.001        |
| <b>Total</b> | <b>6.07± 1.61</b>           | <b>4.62± 1.33</b>               | <b>0.001</b> |

**Table 5. Uric Acid Levels in Males and Females with Metabolic Syndrome and Non-Metabolic Syndrome**

(\*p= <0.05, significant).

| Variables | Groups  | n  | Mean ± SD   | p value |
|-----------|---------|----|-------------|---------|
| BMI       | <30     | 86 | 5.87 ± 1.62 | 0.002*  |
|           | >30     | 24 | 4.71 ± 1.52 |         |
| FBS       | ≥100    | 78 | 5.95 ± 1.72 | 0.001*  |
|           | <100    | 32 | 4.79 ± 1.44 |         |
| BP        | ≥130/85 | 61 | 5.87 ± 1.72 | 0.06    |
|           | <130/85 | 49 | 5.29 ± 1.66 |         |
| HDL       | Low     | 87 | 5.62 ± 1.71 | 0.823   |
|           | High    | 23 | 5.52 ± 1.71 |         |
| TG        | >150    | 37 | 6.15 ± 1.91 | 0.013*  |
|           | <150    | 73 | 5.31 ± 1.51 |         |

**Table 6. Association of Mean Uric Acid Levels with BMI, Blood Pressure, Fasting Blood Sugar, High-Density Lipoprotein and Triglycerides**

(\*p= <0.05, significant).

|            | Metabolic Syndrome | Non-Metabolic Syndrome |       |            |
|------------|--------------------|------------------------|-------|------------|
| Uric Acid  | (%)                | (%)                    | p     | Odds Ratio |
| >6.8 mg/dL | 35                 | 11                     | 0.001 | 6.51       |
| <6.8 mg/dL | 21                 | 43                     |       |            |
|            | 56                 | 54                     |       |            |

**Table 7. Association of Metabolic and Non-Metabolic Syndrome with Hyperuricaemia**

(\*p= <0.05 significant).

## DISCUSSION

Older age, females over the age of 45, general obesity, hypertension, glucose intolerance and hypertriglyceridaemia were significantly associated with metabolic syndrome in our study. Older age, female gender, general obesity, hypercholesterolaemia, glucose intolerance and hypertriglyceridaemia significantly contributed to increased risk of metabolic syndrome.<sup>3</sup> Metabolic syndrome was diagnosed in 50.9% of the study population in our study.

The prevalence rate of metabolic syndrome was 53.2% in the CURES study.<sup>16</sup> The significant difference in the mean age group of subjects with and without metabolic syndrome (p<0.01) showed that the prevalence of metabolic syndrome was higher among older age groups. CURES study also observed that the prevalence of metabolic syndrome was higher among older age groups.

Obese individuals were five times more likely to have metabolic syndrome compared with those having normal weight.<sup>17</sup> There was significant difference between the mean BMI of subjects with and without metabolic syndrome in our study (p <0.02). 78.2% of our studied patients have a BMI of more than 30. As the degree of obesity increases, obesity related diseases like cardiovascular diseases, type2 diabetes mellitus and metabolic syndrome becomes greater.<sup>17</sup>

The mean values of FBS in subjects with and without metabolic syndrome were 131 ± 48.06 and 106 ± 44.9 and

this difference was statistically significant (p<0.01). Glucose intolerance was found to be associated significantly with metabolic syndrome and has a very high risk of developing the syndrome. There was a significant difference in the mean blood pressure in subjects with and without metabolic syndrome. The mean HDL value was not statistically significant among subjects with metabolic syndrome and non-metabolic syndrome. There was no significant association seen between total cholesterol and LDL among our study groups. Similar results were observed by Shi-Dou-Lin et al in their study in Taiwan.<sup>13</sup>

We observed that the serum uric acid was significantly higher in patients with metabolic syndrome than with non-metabolic syndrome in our study. We studied the association between uric acid and different components of the metabolic syndrome. Elevated serum uric acid level was significantly associated with BMI, hypertriglyceridaemia and diabetes in our study. Previously, some authors also studied the association of uric acid and components of metabolic syndrome. Elevated serum uric acid level was higher in subjects with abnormal triglycerides, waist circumference, low HDL cholesterol, blood sugar and blood pressure than in patients with normal levels.<sup>13</sup> The most significant association was seen between uric acid and hypertriglyceridaemia in their study.

Individuals with metabolic syndrome had significantly higher fasting plasma glucose, blood pressure, triglycerides, waist circumference, low HDL cholesterol than those without metabolic syndrome (p <0.001).<sup>18</sup> Multiple logistic regression analysis revealed that hyperuricaemia

was an important risk factor of metabolic syndrome in their study. The association of serum uric acid with low HDL cholesterol was not statistically significant in our study.

Higher waist circumference and BMI were associated with higher insulin resistance and reduced renal uric acid clearance leading to hyperuricaemia.<sup>14</sup> HDL cholesterol was negatively associated with insulin resistance in their study.

Uric acid was significantly and positively associated with fasting blood glucose levels in both sexes and the associations remained after adjusting the confounding factors like BMI, waist circumference, total cholesterol, triglycerides, HDL cholesterol and LDL cholesterol.<sup>18</sup> The uric acid level has shown a significant positive correlation with all components of metabolic syndrome except low HDL cholesterol and diastolic BP in our study.

The serum uric acid concentration can be considered as an important predictive factor for metabolic syndrome.<sup>14</sup> The risk of metabolic syndrome has been increased with elevated serum uric acid concentrations in their study.

Significant higher uric acid value was observed in subjects with metabolic syndrome in comparison with subject to non-metabolic syndrome.<sup>19</sup> The same study proved a significant positive correlation of uric acid with blood glucose level. LDL cholesterol and total cholesterol did not show any significant correlation with serum uric acid levels in their study. The findings of our study also consistent with the above studies.

## CONCLUSION

- The study showed that patients with metabolic syndrome have higher uric acid levels.
- A significant positive association of uric acid with body mass index, waist circumference, triglycerides and fasting blood glucose.
- The association of uric acid with various components of metabolic syndrome support that it might be considered as a marker for metabolic syndrome.

**Limitations of the Study-** We have not included control groups in our study. We used standard reference values for comparison.

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