

Metabolic Syndrome: Can Serum Uric Acid Along With Hepatic Enzymes Serve As Potential Marker For Metabolic Syndrome?

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ABSTRACT:

Background: With worldwide prevalence in cases of metabolic syndrome (MetS), is a cluster of clinical conditions characterized by high blood pressure, dyslipidemia, hyperglycemia and central abdominal obesity. **Material and Methods:** We have determined the level of liver enzymes along with serum uric acid (UA) to assess whether hyperuremia with dysfunctional liver enzyme are associated with MetS. Sixty four subjects at least showing one of the symptoms of MetS and sixty four age matched controls were selected from OPD/IPD of S.M.S. Medical College and Hospital, Jaipur for eleven months. **Results:** Participants with MetS had statistically significantly higher values of blood pressure, body mass index, waist circumference, fasting glucose and triglycerides while HDL-c levels are statistically significantly lower when compared with control group. The mean values of ALP, GGT and uric acid were 146.36 U/L, 53.39 U/L and 6.22 mg/dl respectively and were statistically significantly higher in MetS participants when compared with control group. Uric acid showed a statistically significant positive correlations with waist circumference ($r = 0.4997$), Triglycerides ($r = 0.6696$), and fasting glucose levels ($r = 0.4573$). **Conclusion:** GGT and uric acid may play a role in early diagnosis of metabolic syndrome with a high predictive value for both metabolic syndrome and CVD. Regarding the availability and simplicity of these tests in routine clinical practice and their universal standardization, these findings indicate the potential of liver enzymes, especially GGT, to be considered in algorithms for metabolic syndrome.

Key words: Metabolic Syndrome, serum uric acid, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase.

INTRODUCTION:

The relationship between serum uric acid and a variety of cardiovascular conditions have been reported earlier with controversial debate over the direct association between metabolic

syndrome and role of serum uric acid as a predictive marker. Uric acid is a byproduct of cell death, produced when there is cell destruction and nuclear degradation and end

product of purine metabolism (1). Increased activity of liver enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP) are associated with metabolic syndrome, type 2 diabetes, insulin resistance and cardiovascular disorders (2-13). The aim of present study is to determine whether liver enzymes markers along with uric acid can serve as markers and provide further prognostic information in subjects with metabolic syndrome.

MATERIALS AND METHODS

This study was approved by institutional ethical Committee of SMS Medical College, Jaipur, Rajasthan, India and informed consent was obtained from all the participants. The study population was divided into two groups, healthy subjects as control (n = 64) and subjects diagnosed with MetS (n = 64) for the time period of December 2013 to November 2014. MetS was defined according to the IDF criteria (14) having central obesity (waist circumference ≥ 94 cm in males and ≥ 80 cm in females) with at least one of the risk factors following 4 factors: triglyceride levels (TG ≥ 150 mg/dL); HDL-cholesterol (HDL-C ≤ 40 mg/dL in males and ≤ 50 mg/dL in females); high blood pressure (systolic BP ≥ 130 mmHg, diastolic BP ≥ 85 mm Hg or treatment of previously diagnosed hypertension), and fasting plasma glucose level (FPG ≥ 100 mg/dL or treatment of previously diagnosed diabetes). All statistical analyses were performed using Analyze it software version 2.26. Continuous variables are expressed as mean \pm standard deviation (SD) and p value < 0.05 was considered statistically significant. Independent t-test and one way ANOVA were used to identify statistically significant difference between groups with and without MetS.

RESULTS

The characteristics of the participants among overweight or obese people in relation to metabolic syndrome are presented in Table 1. Participants with MetS had statistically significantly higher values of blood pressure, body mass index, waist circumference, fasting glucose and triglycerides while HDL-c levels are statistically significantly lower when compared with control group. The association between the ALT, AST, GGT, ALP, serum uric acid, urea and creatinine with metabolic syndrome are presented in Table 2. The mean values of ALP, GGT and uric acid were 146.36 U/L, 53.39 U/L and 6.22 mg/dl respectively and were statistically significantly higher in MetS participants when compared with control group. Uric acid showed a statistically significant positive correlations with waist circumference ($r = 0.4997$), Triglycerides ($r = 0.6696$), and fasting glucose levels ($r = 0.4573$).

DISCUSSION

In this study, uric acid, ALP and GGT were compared within the participants with MetS with those of age and sex match controls in the study population. The clustering of cardiovascular disease (CVD) risk factors that typifies the metabolic syndrome is now considered to be the driving force for a new CVD epidemic. A membrane bound enzyme GGT, has unique role of glutathione resynthesis and serve as a marker of oxidative stress (15). The predictive ability of increased uric acid along with GGT levels to diagnose MetS were higher than hypertriglyceridemia, increased waist circumference, increased systolic blood pressure. Higher levels of GGT are associated with cardiovascular disease, metabolic syndrome via nonalcoholic fatty liver disease which is considered as one of the feature of MetS (16).

Table 1: Characteristics of Participants Among Overweight/Obese People

	Metabolic Syndrome	Non metabolic Syndrome	P
N	64	64	
Fasting glucose (mg/dl)	103.94 ± 9.01	86.34 ± 10.92	0.0001
Triglycerides (mg/dl)	160.42 ± 23.17	146.44 ± 14.29	0.0001
HDL-cholesterol (mg/dl)	36.78 ± 4.56	44.88 ± 7.03	0.0001
Waist circumference (cm)	98.67 ± 5.97	91.69 ± 6.08	0.0001
Body mass index (kg/m ²)	34.70 ± 2.94	31.94 ± 3.05	0.0001
Systolic blood pressure (mmHg)	143.75 ± 7.06	126.88 ± 7.52	0.0001
Diastolic blood pressure (mmHg)	88.94 ± 2.81	81.59 ± 3.54	0.0001

* indicates statistically significant values, $p < 0.05$

Table 2: Hepatic and Renal Biomarkers Levels Among Overweight/Obese People

	Metabolic Syndrome	Non metabolic Syndrome	P
Aspartate aminotransferase (U/L)	29.87 ± 7.16	28.88 ± 8.02	0.464
Alanine aminotransferase (U/L)	37.99 ± 7.67	36.52 ± 7.78	0.286
Gamma glutamyltransferase (U/L)	53.39 ± 19.12	32.78 ± 10.71	0.0001
Alkaline phosphatase (U/L)	146.36 ± 25.70	112.53 ± 18.22	0.0001
Uric acid (mg/dl)	6.22 ± 1.10	4.87 ± 0.83	0.0001
Urea (mg/dl)	40.63 ± 9.81	38.14 ± 8.03	0.119
Creatinine (mg/dl)	0.96 ± 0.28	0.95 ± 0.23	0.927

* indicates statistically significant values, $p < 0.05$

ALP is also associated with MetS by nonalcoholic fatty liver disorders (16, 17). Uric acid is also a marker of cardiovascular disease (18, 19) and higher levels of uric acid are often associated with MetS Patients (17; 20; 21).

In this study, GGT showed significant difference between the participants with MetS on comparing with the control groups. GGT of participants with MetS and control group were found to be 53.39 ± 19.12 IU/L and $32.78 \pm$

10.71 IU/L respectively with significant value of 0.0001. Although value of GGT falls within the normal limits, they were higher than the control group. Similar studies by B. Kasapoglu et al in 2010 and Nannipieri M et al in 2005 showed increase in GGT is positively correlated with increased prevalence of metabolic syndrome and CVD (16, 22). Uric acid showed a strong correlation with a number of MetS features like waist circumference, triglycerides and fasting glucose. Studies by Evangelo poulos et al in

2010 and Joo JK et al in 2014 also reported a strong association between MetS and uric acid levels (17, 20).

GGT plays a central role in glutathione homeostasis and important in antioxidant defense for the cell (23, 24). Moreover uric acid is also associated with oxidative stress. (25). In this study, correlation of uric acid along with GGT are strong predictive indicator of MetS. Higher levels of uric acid and GGT possibly could predict increased risk of cardiovascular disease in patients and also serve as a potential biomarker for prognosis of the disease. Although in this study, adequate statistical power was achieved (80%) at $P < 0.05$ but had a limitation of relatively small sample size.

CONCLUSION

Metabolic syndrome is a rising disease entity characterized by a clustering of metabolic conditions. The present study gives us an idea that the derangement in levels of uric acid and hepatic enzymes are associated with metabolic abnormalities. GGT and uric acid may plays a role in early diagnosis of metabolic syndrome with a high predictive value for both metabolic syndrome and CVD. Regarding the availability and simplicity of these tests in routine clinical practice and their universal standardization, these findings indicate the potential of liver enzymes, especially GGT, to be considered in algorithms for metabolic syndrome.

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