ORIGINAL RESEARCH PAPER

General Medicine

A STUDY OF ASSOCIATION BETWEEN SERUM URIC ACID LEVELS WITH VARIOUS COMPONENTS OF METABOLIC SYNDROME

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ABSTRACT

Background : The metabolic syndrome is a widely prevalent and multi-factorial disorder that presents in a distinct, heterogeneous phenotype. The clinical relevance of the metabolic syndrome is related to its role in the development of cardiovascular disease. The major features of the Metabolic Syndrome include central obesity, Hyper-triglyceridemia, low high-density lipoprotein (HDL) cholesterol, Hyperglycemia and Hypertension. Mean serum uric acid levels vary with variable components of metabolic syndrome. There is a direct linear relationship between serum uric acid level and number of metabolic syndrome patients. Increased levels of serum uric acid should be considered as an important marker in patients with metabolic syndrome and Hyperuricemia is an associated abnormality that should be considered in those with metabolic syndrome.

Aim & Objective : To evaluate the association between serum uric acid and metabolic syndrome and correlation of uric acid levels with various components of metabolic syndrome.

Material and Method: This study was conducted among 100 patients with metabolic syndrome (cases) admitted in JLN hospital Ajmer and 100 subjects (age and sex matched controls) who do not have any component of metabolic syndrome. The subjects for the study were selected from the patients attending medical outdoor and admitted in various medical wards and MICU from Jan 2018 to Oct 2019. Total of 100 subjects of old and newly diagnosed metabolic syndrome on the basis of NCEP ATP III CRITERIA and Both sex (male and female) greater than 18 years of age who have given consent to participate in the study were included and Patients with severe liver dysfunction, renal failure, known malignant disease, chronic inflammatory disease such as rheumatoid arthritis, gout, tuberculosis and sarcoidosis, history of acute myocardial infarction and history of CVA were excluded.

Result: It is seen when mean serum uric acid of triglycerides, HDL, Fasting plasma glucose, Blood Pressure and WC was compared to mean of uric acid of controls, results was significant.

Conclusion: Hyperuricemia should be considered as a component of metabolic syndrome and risk factor for cardiovascular diseases.

INTRODUCTION

Metabolic syndrome (MetS) is defined by a cluster of risk factors, including obesity, dyslipidemia, hypertension and insulin resistance [1]. When occurring together, they increase the risk of developing cardiovascular disease (CVD) and diabetes [2]. Previous studies have shown that the defined MetS risk factors cannot explain all CVD events observed in these subjects. Therefore, several other risk factors such as inflammatory markers, microalbuminuria, hyperuricemia and disorders of coagulation have been debated to be included in the MetS definition [3–6].

The prevalence reported of MetS in India was 44.6% (35.4% in males and 55.6% in females).[7]

Although several definitions are used for the diagnosis of metabolic syndrome, the most clinically applicable method of diagnosis is to use Adult Treatment Panel (ATP III) definition. According to this definition, the affected person must have at least three of the cardiovascular risk factors simultaneously (Table 1).[8]

TABLE – 1 NCEP ATP III CRITERIA[9]----

1. Waist circumference>90 cm(M)   >80cm(F) in South Asian individuals
2. Triglyceride level >150 mg/dl or specific medication
3. HDL cholesterol <40 mg/dl(M)   <50 mg/dl(F) or specific medication
4. Blood pressure>130mmof hg systolic or >85mm of hg diastolic or specific medication
5. Fasting plasma glucose level >100 mg/dl or specific medication

In addition to the risk factors outlined in the ATP III, some studies have reported an association between metabolic syndrome and some other risk factors such as increased blood uric acid, increased oxidative stress, and low status systemic inflammation[10-11]. Uric acid is generated as a result of purine metabolism; because of its endothelial pro-inflammatory effect, it is associated with metabolic syndrome risk factors such as hypertension, insulin resistance, and elevated triglyceride levels[12]. Several studies have examined the relationship between increased levels of uric acid and metabolic syndrome [13-15]. Although various studies have reported elevated levels of uric acid in patients with metabolic syndrome, its clinical interpretation is still controversial and challenging [16]. And its role as a risk factor for metabolic syndrome and as criteria for predicting the syndrome is under debate [17-19]. In view of that, this study was aimed to investigate the association between serum uric acid levels and the risk factors metabolic syndrome.

MATERIALS AND METHOD

This study was conducted among 100 patients with metabolic syndrome (cases) admitted in JLN hospital Ajmer and 100 subjects (age and sex matched controls) who do not have any component of metabolic syndrome. The subjects for the study were selected from the patients attending medical outdoor and admitted in various medical wards and MICU from Jan 2018 to Oct 2019.

Inclusion criteria

1. Total of 100 subjects of old and newly diagnosed metabolic syndrome on the basis of NCEP ATP III CRITERIA
2. Both sex (male and female) greater than 18 years of age who have given consent to participate in the study

Exclusion criteria

1. Patients with severe liver dysfunction (viral hepatitis or liver cirrhosis)
2. Patients with renal failure

3. Patients with known malignant disease
4. Patients with chronic inflammatory disease such as rheumatoid arthritis, gout, tuberculosis and sarcoidosis.
5. Patients with history of acute myocardial infarction
6. Patients with history of CVA

The patients attending the OPD were screened for the disease and a detailed and relevant present, past, personal, family and medical history was taken. Special emphasis was given on the obesity and co-morbid conditions associated with it, followed by baseline laboratory investigations to assess the metabolic status of the patient. After a 12 hour fasting period, venous samples were collected from all cases and control. Serum was used for analysis of uric acid and lipids. Patients fulfilling all inclusion and exclusion criterion were enrolled in the study.

Statistical analysis
All the data was analyzed by SPSS statically software and basic parameter was compared using ANOVA test and chi square and p value was calculated.

RESULTS AND OBSERVATION
A Case Control Study with 100 subjects as cases and 100 subjects as control, which studied as role of serum uric acid with each component of metabolic syndrome, undertaken at Department of General Medicine, JLN Medical College and attached hospitals, Ajmer, Rajasthan.

Table – 2 Various Clinical Parameters

Parameter	Cases (n=100)	Controls (n=100)	P value
Age (years)	47.8±8.4	43.1±7.5	0.07(NS)
Bmi (kg/m2)	29.7±2.3	23.0±1.6	0.001(S)
Waist Circumference (cm)	94.6±3.1	82.0±5.2	0.001 (S)
Fasting Sugar Level (mg/dL)	105.7±13.2	91.4±5.5	0.001(S)
SBP (mmHg)	135.5±7.9	119.5±8.9	0.001(S)
DBP (mmHg)	80.7±2.0	79.3±3.7	0.001(S)
HDL Level (mg/dL)	29.6±5.3	50.2±5.0	0.001(S)
Triglycerides (mg/dL)	176.5±20.6	122.3±10.8	0.001(S)
Serum Uric Acid (mg/dL)	6.3±0.6	5.4±0.5	0.001(S)

S- Statically significant (p value <0.05) and NS- Statically not significant (p value >0.05)

Table – 3 Serum Uric Acid Level In Cases And Controls

Serum Uric Acid	Groups (n=100)		Total (n=200)
	Case	Control	
4.1-5.0	3(3%)	28(28%)	31(15.5%)
5.1-6	17(17%)	52(52%)	69(34.5%)
6.1-7	76(76%)	20(20%)	96(48%)
>7.1	4(4%)	0(0%)	4(2%)
Total	100(100%)	100(100%)	200(100%)

Table – 4 Comparison Of Serum Uric Acid With Various Component Of Metabolic Syndrome

Variables	Case (n=100)	Control (n=100)	P value
	mean±SD	mean±SD	
TGD>150	6.39 ±0.52	5.46±0.58	0.01 (S)
HDL, M<40, F<50	6.38±0.62	5.46±0.58	0.01 (S)
BP>130/85	6.33±0.61	5.46±0.58	0.01 (S)
FBS >100 mg/dL	6.34±0.47	5.46±0.58	0.01 (S)
WC, M>90, F>80	6.38±0.62	5.46±0.58	0.01 (S)

Table – 5 Serum Uric Acid And Smokers In Cases

	N	Mean±S.D.	P value
Yes	24	6.79±0.77	0.01 (S)
No	76	6.26±0.50	
Total	100	6.39±0.622	

DISCUSSION
In our study, 200 subjects were recruited comprising 100 cases of metabolic syndrome and 100 age and sex matched controls. The mean age of the cases was 47.83 ± 8.43 years, whereas the mean age of the controls was 43.14 ± 7.58 years. The difference between the two groups was not statistically significant [P=0.07(NS)]. There were 61% males and 39% females in the study group whereas 63% males and 37% females in the control group.

In a similar study done by B Kasapgoluet al,[20] the mean age was 51.3±3.2 and the gender distribution showed 62% females and 38% males in the study group. This difference may suggest a higher incidence of metabolic syndrome in males in the Indian sub-continent.

The constellation of metabolic abnormalities including centrally distributed obesity, decreased high-density lipoprotein cholesterol (HDLC), elevated triglycerides, elevated blood pressure (BP), and hyperglycaemia is known as the metabolic syndrome. This study has been conducted on the basis of newly approved and widely used definition of metabolic syndrome ie NCEPATPIII criteria.

Our study revealed a significant increase in serum uric acid levels in cases (6.38± 0.62) as compared to controls (5.46±0.58), (p=0.001) which corroborates with **Ishizaka N et al,**[21] who concluded that the prevalence of metabolic syndrome showed a graded increase along with increasing serum uric acid levels in both sexes (p<0.05).

In our study there were 96 cases in whom triglycerides level >150mg/dL in these patients mean serum uric acid was (6.39±0.52) when compared to mean serum uric acid of controls (5.46 ± 0.58), (p=0.01) it shows positive correlation, in concordance with **ZhenZhen Cai, Xiaofeng Xu et al**[22] which showed significant relation of uric acid with serum triglycerides (p<0.05). According to **Clausen JO et al.**[23] there is a greater demand for NADPH during synthesis of triglyceride. The synthesis of fatty acids is associated with de novo synthesis of purines, therefore increasing the production of uric acid.

In our study there were 100 patients in whom HDL level was decreased (Male<40, Female<50) in these patients mean serum uric acid was (6.38 ± 0.62) compared to mean serum uric acid of controls (5.46±0.58), There was a positive relation with HDL levels (p=0.01), similar to study of **Ahoud F.Al Meshaweh et al,.**[24] showing similar results (p<0.05).

In our study out of 100 cases 76 patients had BP >130/85, a positive relation was shown , when serum uric acid was compared with blood pressure, the mean of uric acid for cases (6.33 ± 0.60) and mean of controls (5.46 ± 0.58), which resulted as significant (p=0.01). **Lin., S.D, et al**[13] which showed increase levels of uric acids with blood pressure (P<0.001).

In our study there were 68 cases in whom FBS was >100 mg/dL. There is also a co-relation of levels of serum uric acid with glycemia, in our study the mean of serum uric acid (6.34 ± 0.47) was compared with mean of uric acid for controls (5.46±0.58) which resulted in significant results (P=0.01), which matched the results of a study conducted by **Qin Li et al**[25] showing a positive relation between hyperglycemia and uric acid (P<0.001).

Waist circumference, had a significant relation with uric acid. In our study out of 100 cases, 100 had increased waist circumference (Male >90, Female >80cm) the mean value of S. uric acid in these patients was 6.38 ± 0.62 as compared to mean value of uric acids in control (5.46 ± 0.58) this showed a significant result (P =0.01), similar **S.D Lin et al**[13] showing significant increase in uric acid when compared to obesity or

waist circumference (P<0.001).

Strasak et al[26] observed a positive significant correlation between serum uric acid and smoking (r = 0.11, P < 0.001**). Mozos et al**[27] **also** found that serum uric acid level were significantly higher in smoker as compare to non smoker (5.7 ± 1.3 mg/dl Vs 5.0 ± 1.1 mg/dl; P< 0.05). **In our study** mean SUA level in smoker was 6.79±0.77 mg/ dl and in non smoker was 6.26 ± 0.50 mg/dl and **P value was 0.01(S)**. Thus a significant association was found between serum uric acid and smoking which supports above studies. **Bonora et al**[28] observed no significant association between smoking and uric acid level. **Tripathi VD et al**[29] observed statistically insignificant (P>0.05) association between serum uric acid level and smoking.

Hyperuricemia is a risk marker for coronary artery disease, Similar to study conducted by **Kim SY,**[30] *et al*, that hyperuricemic patients (in which uric acid is above desirable range) are at risk of coronary artery disease.

Therefore the study has shown a significant relation between serum uric acid and components of metabolic syndrome.

CONCLUSION
There is a positive association between uric acid and metabolic syndrome and positive correlation between individual components of metabolic syndrome with Uric acid. Hyperuricemia should be considered as a component of metabolic syndrome and risk factor for cardiovascular diseases.

REFERENCES

1. Grundy SM, Brewer Jr HB, Cleeman JI, Smith Jr SC, Lenfant C. National heart, lung, and blood institute; american heart association. Definition of metabolic syndrome: report of the national heart, lung, and blood institute/ american heart association conference on scientific issues related to definition. Circulation. 2004;109:433–8.
2. Wilson PW, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation. 2005;112:3066–72.
3. Ramakrishna V, Jailkhani R. Oxidative stress in noninsulin-dependent diabetes mellitus (NIDDM) patients. Acta Diabetol. 2008;45:41–6.
4. Fu CC, Wu DA, Wang JH, Yang WC, Tseng CH. Association of C-reactive protein and hyperuricemia with diabetic nephropathy in Chinese type 2 diabetic patients. Acta Diabetol. 2009;46:127–34.
5. Guo L, Cheng Y, Wang X, Pan Q, Li H, Zhang L, et al. Association between microalbuminuria and cardiovascular disease in type 2 diabetes mellitus of the Beijing Han nationality. Acta Diabetol. 2012;49 Suppl 1:S65–71.
6. Meigs JB, Mittleman MA, Nathan DM, Tofler GH, Singer DE, Murphy-Sheehy PM, et al. Hyperinsulinemia, hyperglycemia, and impaired hemostasis: The Framingham Offspring Study. JAMA. 2000;283:221–8.
7. Banerjee R, Dasgupta A, Naskar NN, Kundu PK, Pan T, Burman J. A study on the prevalence of metabolic syndrome and its components among adults aged 18–49 years in an urban area of West Bengal. Indian journal of community medicine: official publication of Indian Association of Preventive & Social Medicine. 2019 Jul;44(3):261.
8. Genuth SAK, Bennett P, Buse J, Defronzo R, Kahn R, Zimmet P, et al. Expert committee on the diagnosis and classification of diabetes mellitus. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003;26:3160–7.
9. https://www.labce.com/spg362891_ncep_atp_iii_diagnostic_criteria_for_metabolic_syn.aspx.
10. Ford ES, Li C, Cook S, Choi HK. Serum concentrations of uric acid and the metabolic syndrome among US children and adolescents. Circulation 2007;115(19):2526–32.
11. Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y, et al. Increased oxidative stress in obesity and its impact on metabolic syndrome. J Clin Investig 2004;114(12):1752.
12. Yang T, Chu C-H, Bai C-H, You S-L, Chou Y-C, Hwang L-C, et al. Uric acid concentration as a risk marker for blood pressure progression and incident hypertension: a Chinese cohort study. Metabolism 2012;61(12): 1747–1755.
13. Lin S-D, Tsai D-H, Hsu S-R. Association between serum uric acid level and components of the metabolic syndrome. J Chin Med Assoc 2006;69(11): 512–516.
14. Reimann M, Schutte AE, Malan L, Huisman HW, Malan NT. Hyperuricaemia is an independent factor for the metabolic syndrome in a sub-Saharan African population: a factor analysis. Atherosclerosis 2008;197(2):638–45.
15. Liu P-W, Chang T-Y, Chen J-D. Serum uric acid and metabolic syndrome in Taiwanese adults. Metabolism 2010;59(6):802–7.
16. Borges RLRA, Zanella MT. Uric acid as a factor in the metabolic syndrome. Curr Hypertens Rep 2012;12:113–9.
17. Lim JH, Kim Y-K, Kim Y-S, Na S-H, Rhee M-Y, Lee M-M. Relationship between serum uric acid levels, metabolic syndrome, and arterial stiffness in Korean. Korean Circ J 2010;40(7):314–20.
18. Liou TLLM, Hsiao LC, et al. Is hyperuricemia another facet of the metabolic syndrome? J Chin Med Assoc 2006;69:104–9.
19. Ferrara LA, Wang H, Umans JG, Franceschini N, Jolly S, Lee ET, et al. Serum uric acid does not predict incident metabolic syndrome in a population with high prevalence of obesity. Nutr Metab Cardiovasc Dis 2014;24(12):1360–4.
20. B.kasapgolu, C.turkay, Y.bayram et al. Role of GGT in diagnosis of metabolic syndrome: A clinic-based cross-sectional survey. Indian J Med Res 2010; 132: 56-61
21. Ishizaka N, Ishizaka Y, Toda El et al, Association between serum.Uric acid, metabolic syndrome and carotid atherosclerosis,1P:122;17;2011.
22. Zhenzhen Cai; Xiaofeng Xu; Hyperuricaemia and metabolic syndrome in Hangzhou; Asia pacific journal 2009; Vol 18; 81-87.
23. Clausen JO et al, Analysis of the relationship between serum uric acid and insulin sensitivity index in a population based study
24. Ahoud F.Al-Meshaweh, Yaqoub Jafar, Mohammad Asem (2011): determinants of blood uric acid levels in a dyslipidemic Arab Population
25. Qin Li, Zeng Yang: elevated levels of uric acid concentrations in those group of people who have increased risk for metabolic syndrome.
26. Strasak A, Ruttmann E, Brant L, Kelleher C, Klenk J, Concin H, Diem G, et al. Serum uric acid and risk of cardiovascular mortality: a prospective long-term study of 83,683 Austrian men. Clin Chem. 2008;54(2):273-284.
27. Mozos I, Chiulana C, Goruna C, Costeab S. Serum uric acid in stroke. Annals of West University of Timisoara, Series of Chemistry 16 (2) (2007) 227 - 236.
28. Bonora E, Targher G, Zenere MB, et al. Relationship of uric acid concentration to cardiovascular risk factors in young men, Role of obesity and central fat distribution, The Verona Young Men Atherosclerosis Risk Factors Study. Int J Obes Relat Metab Disord. 1996;20(11):975–80.
29. Tripathi VD, Hussain Z. A study to find out relationship in between serum uric acid level and stroke .Int J Adv Med. 2017 Oct;4(5):1255-1259.
30. Kim SY; Guevera JP; Kim KM; Hyperuricemia and coronary heart disease: A systemic review and metanalysis; feb 2010;170-80.