ORIGINAL ARTICLE

Relationship of Hyperuricemia and Metabolic Syndrome

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Abstract

Background: The metabolic syndrome (MetS) - also called "the deadly quartet" is a constellation of metabolic abnormalities that confer an increased risk of cardiovascular disease and diabetes mellitus. Hyperuricemia is a well-known risk factor for atherosclerotic events like myocardial infarction and stroke, and is associated with other cardiovascular risk factors like hypertension and dyslipidemia. ***Purpose:*** To study the association of serum uric acid in the causation of metabolic syndrome. ***Material and Methods:*** An observational case control study was conducted in the medicine department in a tertiary care hospital in North India. Cases were selected with age 18 and above with metabolic syndrome IDF criteria. Controls were taken from other persons matched on the basis of age and sex. Hyperuricemia was defined as serum uric acid (UA) concentration >7.0 mg/dL in men or >6.0 mg/dL in women. Data was entered and analysed using SPSS version 25 for windows and Microsoft Excel applications. ***Results:*** The mean age in the cases was 53.53 ± 12.14 years and in controls was 50.12 ± 10.24 years. Majority of patients in metabolic syndrome group were males (65%) vs females (35%) and in the control group were also males (57%) and females (43%). The mean uric acid was 7.07 ± 1.31 mg% in the metabolic syndrome group whereas in the controls was 4.4 ± 1.14 mg%. In our study the overall prevalence of hyperuricemia was 64% in the metabolic syndrome group whereas in the control group, hyperuricemia was seen in only 20% of the individuals (p<0.05). ***Conclusion:*** Substantial high prevalence of hyperuricemia was seen among patients with metabolic syndrome. Serum uric acid level can also be considered as a part of regular follow up of patients with any of the metabolic syndrome components.

Key Words

Metabolic syndrome, uric acid, hyperuricemia

Introduction

The metabolic syndrome (MetS) - also called Syndrome X, Reaven's syndrome, "the deadly quartet" and insulin resistance syndrome - was originally described in 1988 and refers to the commonly occurring disorder comprising central obesity, systemic hypertension, insulin resistance and atherogenic dyslipidemia (1). The underlying cause of the metabolic syndrome continues to challenge the experts but both insulin resistance and central obesity are considered signiûcant factors. Genetics, physical inactivity, ageing, a pro-inûammatory state and hormonal changes may also have a causal effect, but the role of these may vary depending on ethnic group.

MetS is a modern epidemic that is strongly associated with the development of cardiovascular disease and diabetes mellitus (2). It is a constellation of metabolic abnormalities that confer an increased risk of cardiovascular disease and diabetes mellitus (3). The International Diabetes Federation (IDF) estimates that 25% of the world's population has MetS (4) although this estimate varies widely due to the age, ethnicity, and gender

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of the population studied (5). The prevalence across urban south India documented ranging from 22.1% to 41% (6). A prevalence study of urban community in northern India reported a prevalence of 22.37% for metabolic syndrome (7). On the contrary, a lower prevalence of 19.52% was reported in an urban population in western India (8).

Uric acid is an endogenously produced terminal degradation product of purine catabolism, formed by the liver and excreted by the kidneys primarily and intestines secondarily. Hyperuricemia is a well-known risk factor for atherosclerotic events like myocardial infarction and stroke, and is associated with other cardiovascular risk factors like hypertension and dyslipidemia (9).

In this context it becomes very interesting to study the causative role of serum uric acid in the causation of metabolic syndrome. Therefore, in an attempt to determine the association of serum uric acid in metabolic syndrome, we conducted an observational case control study to reinforce the already available vast evidence interlinking the two variables in our study.

Material and Methods

An observational case control study was conducted from November 2018 to October 2019 in the Department of Medicine, Government Medical College and associated hospital, Jammu after getting valid, informed consent from the patients and after getting permission from the institutional ethics committee vide number: IEC/GMC/2019/795. All principles of bioethics were followed in this study. Cases were selected from the patients presenting to the OPD and IPD of Department of Medicine, GMC Jammu. Controls were taken from other persons matched on the basis of age and sex.

Inclusion criteria: Age group: 18 and above with metabolic syndrome, IDF criteria.

Exclusion criteria: 1) Renal disorders; 2) Alcoholics**;** 3) Smokers; 4) Thyroid disorders; 5) Hepatic disorders**;** 6) Drugs which causes increased or decreased uric acid levels; and 8) Myocardial infarction.

Total of 200 patients were studied and were divided into two groups- Cases comprising of 100 patients with metabolic syndrome and Controls comprising of 100 patients without metabolic syndrome.

There is no universally-accepted definition for hyperuricemia based only on serum UA levels. We defined participants as having hyperuricemia if their serum UA concentration was >7.0 mg/dL in men or >6.0 mg/dL in women (10).

The socioeconomic, demographic, clinical and metabolic profile of patients with metabolic syndrome was analysed in comparison to hyperuricemia. Each patient was subjected to detailed history regarding the illness. Examination was conducted in detail and routine laboratory parameters were tested.

All data was entered and analysed using SPSS version 25 for windows and Microsoft Excel applications. Data was presented as Mean ± SD for quantitative variable and as N (%) for qualitative variable. The suitable statistical comparison was applied accordingly and $p<0.05$ was considered significant.

Results

In this study out of 100 individuals with metabolic syndrome, 65% were males and 35% were females whereas in controls 57% were males and 43% were females. The mean weight in the study population was 71.21 ± 10.19 kg and 65.72 ± 11.64 kg in cases and controls respectively. The abdominal circumference was 100.78 ± 5.7 cms and 79.57 ± 5.8 cms in cases and controls respectively (p=0.00) (*Table 1*).

The mean systolic blood pressure was 140 ± 15 and 117 ± 10 mm of Hg in cases and controls respectively. The mean diastolic blood pressure was 86 ± 8 and 74 ± 7 mm of Hg in the cases and control population respectively (*Table 1*). In our study 90 patients in the metabolic syndrome group had impaired blood sugar levels and rest 10 were normal. However, in the control group the prevalence of impaired blood sugar level was in 12 patients as compared to 88 with normal.

Table 1: Clinical Profile of Study Population

Parameter	Cases	Controls	*p* value
Age (yrs.)	53.53±12.14	50.12±10.24	0.56
Weight (kg)	71.21±10.19	65.72±11.64	0.00
Abdominal Circumference (cms)	100.78±5.7	79.57±5.8	0.00
Systolic BP (mm Hg)	140±15	117±10	0.00
Diastolic BP (mm Hg)	86±8	74±7	0.00

In our study, out of 100 cases of metabolic syndrome, 64 (64%) had hyperuricemia and 36 (36%) had normal uric acid levels whereas out of 100 controls from normal population 20 (20%) had hyperuricemia and 80 (80%) had normal uric acid levels. p value for this distribution was 0.000 which was statistically significant relating the positive association of higher uric acid levels with metabolic syndrome (*Table 2*). Biochemical profile of the study population is shown in *Table 3*.

Table 2: Prevalence of Hyperuricemia in our Study Population

	Cases	Controls	*p* value
Hyperuricemia	64	20	0.000
Normal uric acid	36	80	
Total	100	100	

Table 3: Biochemical Profile of the Study Population

	Cases	Controls	*p* value
Uric acid (mg %)	7.07±1.31	4.4±1.7	0.00
BSF (mg/dL)	152±46	90±21	0.00
S. Urea (mg/dL)	30±9	24±7	0.00
S. Creat. (mg/dL)	0.9±0.2	0.8±0.2	0.02
S. Bil. (mg/dL)	0.8±0.4	0.7±0.2	0.65
SGOT (IU/L)	38±15	41±25	0.95
SGPT (IU/L)	41±17	43±23	0.88
ALP (IU/L)	102±29	93±29	0.02
S. Prot. (g/dL)	7.6±0.8	7.8±0.7	0.21
S. Alb. (g/dL)	3.7±0.4	3.9±0.4	0.08
S. Chol. (mg%)	148±39	119±33	0.00
S. TG's (mg%)	182±39	136±21	0.00
S. HDL (mg%)	40±7	50±6	0.00

Discussion

This study was conducted among 200 patients who attended OPD as well as IPD of Government Medical College, Jammu during the year 2018-2019. All of them had at least one of the five components of metabolic syndrome and the presence of other components were actively searched. The mean age in the cases was 53.53 ± 12.14 years and in controls was 50.12 ± 10.24 years. Majority of the patients were in age group of 50-70 years and 30-50 years in controls (p=0.568).

The mean uric acid was 7.07 ± 1.31 mg% in the metabolic syndrome group whereas in the control group it was 4.4 ± 1.14 mg%. Soans *et al.* (11) recruited 200 subjects and found that in cases mean uric acid was 7.43 ± 0.90 and in the control group it was 4.43 ± 1.00. Ismail *et al.* (12) in their study found mean uric acid levels of 6.0 ± 1.7 mg/dL.

In our study the overall prevalence of hyperuricemia was 64% in the metabolic syndrome group whereas in the control group, hyperuricemia was seen in only 20% of the individuals. Ismail *et al.* (12) in a descriptive cross-sectional study showed a prevalence of hyperuricemia among metabolic syndrome group of 60% (p<0.01). Nejatimini *et al.* (13) in a case control study of 101 subjects which included 41 in metabolic syndrome group and 60 in control group concluded that uric acid was significantly higher in cases than in control group (OR: 2.11, (95% CI: 1.30-3.41). Vayá *et al.* (14) investigated the association between serum uric acid and metabolic syndrome in a case control study of 71 patients with 122 healthy control and showed a higher risk of hyperuricemia than those without metabolic syndrome (OR: 2.87; 95% CI: 1.48-5.55; p=0.002). Ishizaka *et al.* (15) investigated the relationship between uric acid and metabolic syndrome and found that uric acid increases with the number of components of the condition, and is an indicator of worse cardiovascular risk profile.

Though it was out of preview of this study, the possible mechanism for hyperuricemia in metabolic syndrome patients may be due to overproduction of uric acid caused by increased consumption of carbohydrate as it represents 60-70% % of average daily calories. This high intake of fructose and sucrose may explain the rise in obesity. The high prevalence of obesity may be explained by the accelerated urbanization that has been accompanied by nutrition transition, resulting in lower levels of physical activity, and the exchange of traditional foods high in complex carbohydrates for new foods high in refined carbohydrates. Hyperuricemia may be partially responsible for inflammatory imbalances in adipose tissues that lead to low-grade inflammation and insulin resistance. Also, metabolic syndrome may cause nucleic acid metabolism abnormalities, which stimulate adenosine monophosphate (AMP) deaminase that produce uric acid which promotes fat storage and insulin resistance.

Uric acid is considered as one of the major factors that raises blood pressure by stimulating intracellular oxidative stress and activation of NADPH oxidase in the cytosol and mitochondria. Hyperuricemia may induce insulin resistance causing vasodilatation and increase blood flow that interfere with the action of nitric oxide, which facilitates glucose absorption. Other results suggest that hyperuricemia is caused by hyperinsulinemia acting on the renal tubules to facilitate the reabsorption of uric acid.

Limitations: Small sample size and an observational nature of study. Since it was a hospital-based study, the sample studied might not be truly representative of the population in totality. The study design was not meant to comment on the biological plausibility of the correlation.

Conclusion

Substantial high prevalence of hyperuricemia was seen among patients with metabolic syndrome. Serum uric acid

level can also be considered as a part of regular follow up of patients with any of the metabolic syndrome components and patients with hyperuricemia to be carefully monitored for the development of cardiovascular complications.

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Conflicts of Interest
There are no conflicts of interest.

References

1. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome - a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabet Med* 2006;23(5):469-80.
2. Tsouli SG, Liberopoulos EN, Mikhailidis DP, Athyros VG, Elisaf MS. Elevated serum uric acid levels in metabolic syndrome: an active component or an innocent bystander? *Metabolism* 2006;55(10):1293-301.
3. Patni R, Mahajan A**.** The metabolic syndrome and menopause. *J Midlife Health* 2018;9(3):111-12.
4. O'Neill S, O'Driscoll L**.** Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev* 2015;16(1):1-12.
5. Kaur J**.** A comprehensive review on metabolic syndrome. *Cardiol Res Pract* 2014; 2014:943162.
6. Ramachandran A, Snehalatha C, Satyavani K, Sivasankari S, Vijay V. Metabolic syndrome in urban Asian Indian adults - a population study using modified ATP III criteria. *Diabetes Res Clin Pract* 2003;60(3):199-204.
7. Ravikiran M, Bhansali A, Ravikumar P, Bhansali S, Dutta P, Thakur JS *et al.* Prevalence and risk factors of metabolic syndrome among Asian Indians: a community survey. *Diabetes Res Clin Pract* 2010;89(2):181-88.
8. Sawant AM, Shetty D, Mankeshwar R, Ashavaid TF. Prevalence of dyslipidemia in young adult Indian population. *J Assoc Physicians India* 2008;56: 99-102.
9. Silva HA, Carraro JC, Bressan J, Hermsdorff HH. Relation between uric acid and metabolic syndrome in subjects with cardiometabolic risk. *Einstein (Sao Paulo)* 2015;13(2):202-08.
10. Nagahama K, Iseki K, Inoue T, Touma T, Ikemiya Y, Takishita S. Hyperuricemia and cardiovascular risk factor clustering in a screened cohort in Okinawa, Japan. *Hypertens Res* 2004;27(4):227-33.
11. Soans G, Murgod R. Evaluation of role of hyperuricemia as an active component of metabolic syndrome. *Int J Anal Pharm Biomed Sci* 2012;1(3):1-8.
12. Ismail EM, Elbadawi N, Hassan D. Uric acid as a biomarker of metabolic syndrome in Sudanese adults. *Int J Biochem Physiol* 2018;3(4):000137.
13. Nejatinamini S, Ataie-Jafari A, Qorbani M, Nikoohemat S, Kelishadi R, Asayesh H, *et al.* Association between serum uric acid level and metabolic syndrome components. J *Diabetes Metab Disord* 2015;14:70.
14. Vayá A, Rivera L, Hernández-Mijares A, Bautista D, Solá E, Romagnoli M, *et al.* Association of metabolic syndrome and its components with hyperuricemia in a Mediterranean population. *Clin Hemorheol Microcirc* 2015;60(3):327-34.
15. Ishizaka N, Ishizaka Y, Toda E, Nagai R, Yamakado M. Association between serum uric acid, metabolic syndrome, and carotid atherosclerosis in Japanese individuals. *Arterioscler Thromb Vasc Biol* 2005;25(5):1038-44.