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Original Research Article

Relationship between Serum Uric Acid Levels and Components of Metabolic Syndrome

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Abstract:

Background: A number of risk factors, including central obesity, high blood pressure, raised blood sugar, high triglycerides, and low levels of high-density lipoprotein (HDL) cholesterol, are associated with metabolic syndrome (MetS). MetS has been linked to an increased risk of death, cardiovascular disease (CVD), and type 2 diabetes. Several population-based studies have demonstrated that people with MetS are more likely to develop cardiovascular disease (CVD) than people without the syndrome. MetS has also been associated with non-traditional risk factors, such as microalbuminuria, inflammatory indicators, and elevated uric acid levels. Studies have shown a link between obesity and elevated uric acid levels, which makes obesity and MetS a substantial risk factor for CVD. MetS is becoming more and more common in both developed and developing countries. Adults from Bangladesh are especially prone to MetS, and its prevalence has significantly increased in recent years. According to a recent assessment, 32% of women and 25% of men in Bangladesh have MetS, which has a high prevalence (30%).

Material and Method: The Department of General Medicine was the site of this cross-sectional investigation. Those between the ages of 30 and 49 who had no prior history of gout, diabetes, cancer, heart attack, stroke, or renal illness met the eligibility requirements. Three people with kidney and heart failure were eliminated from the group that was chosen, leaving 30 people in the MetS group and another 30 in the control group. Additionally excluded were subjects on lipid-lowering, antihypertensive, or anti-diabetic drugs, as well as hypouricemic agents. Before the test, participants were told to eat only vegetables for three days. Before participating in the study, each subject gave written, informed consent.

Results: Serum uric acid levels in the MetS group were considerably greater than those in the non-MetS group, even after controlling for confounding variables. In comparison to the non-MetS group, the MetS group participants showed lower levels of high-density lipoprotein (HDL) and higher levels of triglycerides (TG), total cholesterol (TC), waist circumference (WC), lean body mass (LBM), body fat mass (BFM), trunk fat mass, insulin levels, HOMA index, fasting plasma glucose (FPG), and systolic and diastolic blood pressure (DBP). Even after controlling for age, sex, and BMI in this investigation, the mean serum uric acid level in the MetS group remained considerably higher. After correcting for gender and age, the odds ratios (ORs) rose. The regression model results indicated that in model III (adjusted for age, sex, and BMI), each 1 mg/dl increase in serum uric acid level approximately doubled the odds of developing metabolic syndrome.

Conclusion: Serum uric acid almost increased the chance of developing MetS and showed an independent correlation with its components. Future studies should examine the function of uric acid in the pathophysiology of MetS and the clinical significance of these findings, given the high prevalence of obesity and MetS and the possible link between hyperuricemia and CVD. According to this study, there is a high correlation between serum uric acid and the metabolic syndrome and its constituents, including serum triglycerides and waist circumference.

Keywords: Uric acid, Metabolic syndrome, Insulin resistance and Body composition.

Introduction

Obesity, dyslipidemia, hypertension, and insulin resistance are among the risk factors that make up metabolic syndrome (MetS), which raises the risk of both diabetes and cardiovascular disease (CVD). Previous studies have shown that not all CVD events identified in patients with MetS can be fully explained by these specified MetS risk factors. As a result, other risk factors that have been suggested

for incorporation into the MetS criteria include coagulation disorders, microalbuminuria, hyperuricemia, and inflammatory indicators. Globally and in Asian nations alike, the prevalence of MetS is increasing; in Iran, it has been reported to be as high as 30.1%.[1]

MetS has become a major public health concern and a worldwide epidemic. According to data from the National Health and Nutrition Examination Survey (NHANES), between 2011–2012 and 2015–2016, the total crude prevalence of MetS in the USA increased from 32.5% to 36.9%. With a fast-increasing frequency of MetS, the Asia Pacific region is likewise undergoing a serious epidemic. In 2009, the age-standardized prevalence in China was approximately 20%. According to a 2018 analysis, there are around one billion MetS sufferers globally. Furthermore, a large body of research has demonstrated that MetS raises the risk of cancer, heart disease, type 2 diabetes, and overall mortality.[2,3]

The final byproduct of purine metabolism is serum uric acid (SUA). An imbalance in the production and excretion of SUA leads to abnormal SUA levels. Elevated SUA levels are closely associated with conditions that are major contributors to the development and progression of MetS, such as diabetes, hypertension, obesity, deterioration in renal function, and cardiovascular disease.[4] The state of having elevated SUA levels, or hyperuricemia, is linked to a number of cardiovascular disorders and may have a similar etiology to MetS. The connection between MetS and uric acid is still unclear and needs more research.[5]

When comparing the highest SUA level group to the lowest, a meta-analysis of 11 cohort studies revealed that the combined relative risk (RR) of MetS was 1.72 (1.45, 2.03). According to dose-response analysis, for every 1 mg/dL increase in SUA, the probability of getting MetS increased by 1.30 (1.22, 1.38) times. The majority of earlier research used cross-sectional or cohort designs with SUA levels tested just once at baseline, despite the fact that numerous studies have found a link between greater SUA levels and an increased risk of MetS.[6] It remains unclear if temporal changes in SUA levels independently predict MetS, especially for those with baseline SUA levels within the normal range.

Both industrialized and developing nations have seen an increase in the prevalence of hyperuricemia in recent years as their economies have grown. MetS has been linked to hyperuricemia, and numerous investigations have discovered a link between the two. MetS is becoming far more common in both developed and developing countries, which is concerning. In several populations, recent epidemiological studies have shown a correlation between serum uric acid (SUA) and MetS and its constituents. Elevated SUA levels have also been found in other studies to be independent predictors of MetS components, including hyperglycemia and high blood pressure. Our study assessed the relationship between serum uric acid levels and MetS components in light of the increased prevalence of MetS.[7,8]

Material and Methods

This cross-sectional study was conducted in the Department of General Medicine. Participants were eligible if they were aged 30–49 years and had no history of cardiovascular disease, diabetes, cancer, stroke, kidney disease, or gout. Out of the selected individuals, 3 who had heart failure and kidney disease were excluded. The final study population included 30 individuals with Metabolic Syndrome (MetS) and 30 controls. Those taking antihypertensive, antidiabetic, lipid-lowering, or hypouricemic medications were excluded. Participants were instructed to follow a vegetable-based diet for three days prior to the examination. All participants provided written informed consent before being included in the study. The study was conducted in accordance with relevant guidelines and regulations.

The inclusion criteria were: both genders, aged above 25 years, free from severe chronic illness, and willing to participate.

Exclusion Criteria were: pregnant women, lactating mothers, and participants with a history of hepatotoxic drug intake, kidney disease, alcohol intake, and self-reported evidence of acute or chronic hepatitis.

Measurement Methods

To measure waist circumference, first identify the top of the right iliac crest. Place a measuring tape horizontally around the abdomen at the level of the iliac crest. Ensure the tape is snug but does not compress the skin and is parallel to the floor before taking the measurement. Record the measurement at the end of a normal expiration.Blood pressure was measured with a sphygmomanometer after the subjects had rested for more than 5 minutes. For participants with a systolic blood pressure of ≥140 mmHg or a diastolic blood pressure of ≥90 mmHg, blood pressure readings were taken on two additional occasions after further resting, and the average of these readings was used.

Blood Sample Collection

Venous blood samples were collected from each subject after an overnight fast. The samples were centrifuged, and the isolated serum was stored at −20°C until laboratory analysis. HDL-C levels were measured following precipitation with

magnesium phosphotungstate. LDL-cholesterol was calculated using Friedewald's formula. Fasting plasma glucose (FPG) was determined using the glucose oxidase method, and immunoreactive insulin (IRI) was measured via radioimmunoassay.

Laboratory Analyses

Participants provided venous blood samples after an overnight fast. Serum samples were analyzed using an automatic analyzer to determine lipid profiles and fasting blood glucose levels. Serum triglyceride concentrations were measured using standardized enzymatic procedures with a glycerol phosphate oxidase assay.

High-density lipoprotein-cholesterol (HDL-C) levels were assessed using a chemical precipitation technique with dextran sulfate. Fasting plasma glucose was measured via the hexokinase method. Serum uric acid concentrations were determined using the uricase EMST method. Metabolic Syndrome was defined as having at least three of the following components: high serum triglyceride levels (≥150 mg/dl and/or use of lipid-lowering medication); low serum HDL-cholesterol levels; and waist circumference ≥ 89 cm in men or > 91 cm in women, based on the guidelines from the First Nationwide Study of the Prevalence of Metabolic Syndrome.[6]

Diagnosis Criteria

1. Hyperuricemia is defined as serum uric acid level ≥7 mg/dl (in men) or ≥6.0 mg/dl (in women).
2. We evaluated metabolic syndrome based on AHA/NHLBI criteria. Metabolic syndrome was defined as having at least three of the following five criteria: (1) waist circumference ≥90 cm for males or ≥80 cm for females; (2) serum triglyceride levels ≥150 mg/dl or treatment with medication for elevated triglycerides; (3) serum HDL-C levels <40 mg/dl for males or <50 mg/dl for females, or treatment with medication for low HDL-C; (4) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, or use of antihypertensive medication for those with a history of hypertension; (5) fasting blood glucose ≥110 mg/dl or treatment with medication for elevated glucose levels.[1]

Statistical Analysis

The findings are presented in the form of mean ± SD. Utilizing the Kolmogorov-Smirnov test, the normality of the relevant variables was investigated. Using the T-test, continuous variables were compared. Pearson's correlation coefficients were used to evaluate the association between the level of uric acid and other variables, such as MetS components. To investigate the connection between the diagnosis of MetS and serum uric acid, a logistic regression analysis was carried out.

Result

The average age of the study population was 36.3 ± 5.0 years. The clinical and metabolic characteristics of the study participants are summarized in Table 1.

Table 1: Characteristics of the participants with or without metabolic syndrome

Variables	MetS group(n=30)	Non-MetS group(n=30)
Age, years	36.3 ± 5.0	37 ± 5.57
Body mass index, kg/m2	23.62 ± 2.63	22.69 ± 2.60
Waist circumference, cm	89.7 ± 13.14	85.60 ± 6.52
Fat-free mass, kg	53.48 ± 10.12	48.25 ± 8.23
Fat mass, kg	22.82 ± 6.5	17.22 ± 5.44
Trunk fat mass, kg	11.33 ± 2.84	8.39 ± 2.21
Systolic blood pressure, mmHg	111.5 ± 10.1	108.4 ± 11.3
Diastolic blood pressure, mmHg	80.4 ± 8.2	75.2 ± 10.23
Fasting glucose, mg/dl	98.6 ± 11.1	93.4 ± 5.7
Fasting insulin, µU/ml	11.4 ± 4.57	7.8 ± 3.26
HOMA-IR	2.24 ± 1.39	2.06 ± 1.04
Triglyceride, mg/dl	196.1 ± 120.1	99.2 ± 52.2
Total cholesterol, mg/dl	198.8 ± 40.7	175.4 ± 25.3
LDL-C, mg/dl	113.5 ± 28.4	104.1 ± 20.1
HDL-C, mg/dl	32.5 ± 5.2	43 ± 9.6
Uric Acid, mg/dl	4.77 ± 1.42	2.75 ± 1.21

Compared to those in the non-MetS group, the subjects in the MetS group had lower levels of HDL and greater levels of BMI, WC, lean body mass (LBM), body fat mass (BFM), trunk fat mass, SBP, DBP, FPG, insulin, HOMA index, TG, TC, LDL, and insulin-like substances. Even after adjusting for age, sex, and BMI, the mean serum uric acid in the MetS group in this study was considerably greater than that in the non-MetS group.

Table 2: Association between uric acid level (mg/dl) and metabolic syndrome in logistic regression models

Serum uric acid	OR(95%CI)
ModelI	1.60(1.23-2.33
ModelII	1.25(1.49-3.81)
ModelIII	1.09(1.30-3.41)

In the logistic regression analysis, Table 2 displays the relationship between the diagnosis of MetS and serum uric acid level. Once age and gender were taken into account, there were increases in ORs. According to the regression model's findings, the odds ratio for developing metabolic syndrome increased by around twofold in model III (age, sex, and BMI corrected) for every 1 mg/dl increase in blood uric acid levels.

Discussion

In this study, we examined the associations between serum uric acid levels and MetS components in individuals with and without MetS. After adjusting for covariates such as gender, age, and BMI, serum uric acid levels were significantly higher in the MetS group compared to healthy individuals. This finding is consistent with several other studies. While hyperuricemia is well-known as a risk factor for atherosclerotic diseases like myocardial infarction and stroke, its independent association with cardiometabolic risk factors remains debated. Hyperuricemia is an increasingly common medical issue, not only in advanced countries but also in developing nations. It has been reported that hyperuricemia is associated with components of metabolic syndrome, including obesity, dyslipidemia, hyperglycemia, and hypertension.[9]

Higher serum uric acid levels, even within normal ranges, were associated with an increased odds ratio for MetS and remained significant after adjusting for confounding factors. This study suggests that serum uric acid is a determinant of MetS. With each one-unit increase in serum uric acid, the odds of developing MetS approximately doubled. Similar findings have indicated that individuals with high uric acid levels have 1.6 times higher odds of developing MetS. However, the precise biological mechanisms underlying the association between serum uric acid and the development of MetS remain unclear. It is speculated that the reduction in endothelial nitric oxide bioavailability by uric acid plays a role. Nitric oxide is thought to be crucial in the development of insulin resistance, and its deficiency is believed to reduce blood flow to insulin-sensitive tissues such as skeletal muscle, liver, and adipose tissue, thereby inhibiting insulin action.[10]

Conen et al.[11] and Schachter et al.[12] found similar results. Hyperuricemia and hypertriglyceridemia are suggested to be linked with insulin resistance syndrome, and many researchers are investigating the mechanisms behind this syndrome. The relationship between insulin resistance syndrome, hyperuricemia, and hypertriglyceridemia is complex. A study by Krishnan et al. [13] found that men with hyperuricemia had a higher risk of developing hypertension. Each unit increase in serum uric acid was associated with a 9% increase in the risk of hypertension. Although the mechanism by which uric acid contributes to hypertension is unclear, hyperuricemia is known to have harmful effects on endothelial function, platelet adhesion, aggregation, and oxidative metabolism.

The results indicated that body fat mass, especially trunk fat mass, might be related to serum uric acid levels. Some studies have reported a relationship between body fat mass and serum uric acid. Hikita et al. [14] found significant correlations between serum uric acid and both visceral fat and total fat mass, with a stronger relationship to visceral fat. It is suggested that insulin resistance caused by the accumulation of visceral fat is the underlying mechanism.

Yoo et al. [15] and Becker and Jolly [16] reported that hyperglycemia is a significant risk factor for hyperuricemia. A study of 3,681 Japanese adults found that higher serum uric acid concentrations in males increased the risk of type 2 diabetes, concluding that hyperuricemia is positively associated with hyperglycemia. Insulin resistance may link these conditions, but no statistical significance was found between elevated fasting glucose and uric acid concentration. A statistically significant positive correlation was observed between serum uric acid concentration and log-transformed fasting plasma glucose only in women.

The study also found that the longitudinal increase of serum uric acid (SUA) was positively associated with the incidence of metabolic syndrome (MetS), independent of the baseline SUA levels. Our observations aligned closely with previous findings on baseline SUA. Similarly, in a population-based study of 6083 Norwegian adults, the risk of developing MetS increased by 1.28 times for every 59 μmol/L increase in longitudinal SUA. Another retrospective cohort study among 407 Japanese community-dwelling women showed that the risk of MetS was 2.49 times higher when comparing the third tertile to the first tertile of longitudinal SUA increase.[17,18]

Conclusion

Serum uric acid (SUA) was independently associated with the components of metabolic syndrome (MetS) and increased the risk of MetS by nearly twofold. Our findings suggest that uric acid could be considered a component of MetS. Given the high prevalence of obesity and MetS, along with the potential link between hyperuricemia and cardiovascular disease (CVD), future studies are needed to elucidate the role of uric acid in the pathogenesis of MetS and the clinical significance of our findings. This study demonstrates that SUA is significantly associated with MetS and its components, particularly serum triglycerides and waist circumference. Considering the global rise in obesity and MetS and the potential link to hyperuricemia, there should be increased focus on the growing prevalence of hyperuricemia in our country.

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. 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.
5. Nestel P, Lyu R, Low LP, Sheu WH, Nitiyanant W, Saito I, et al. Metabolic syndrome: recent prevalence in East and Southeast Asian populations. Asia Pac J Clin Nutr. 2007;16:362–7.
6. Delavari A, Forouzanfar MH, Alikhani S, Sharifian A, Kelishadi R. First nationwide study of the prevalence of the metabolic syndrome and optimal cut-off points of waist circumference in the middle east: the national survey of risk factors for non-communicable diseases of Iran. Diabetes Care. 2009;32:1092–7.
7. Ranasinghe P, Mathangasinghe Y, Jayawardena R, Hills AP, Misra A. Prevalence and trends of metabolic syndrome among adults in the Asia-Pacifc region: a systematic review. BMC Public Health. 2017;17(1):101. 4. Xi B, He D, Hu Y, Zhou D. Prevalence of metabolic syndrome and it is influencing factors among the Chinese adults: the China Health and Nutrition Survey in 2009. Prev Med. 2013;57(6):867–71.
8. Saklayen MG. The global epidemic of metabolic syndrome. Curr Hypertense Rep. 2018;20(2):12.
9. Lehto S, Niskanen L, Ronnemaa T, Laakso M. Serum uric acid is a strong predictor of stroke in patients with non-insulin-dependent diabetes mellitus. Stroke. 1998;29:635–39.
10. Gersch C, Palii SP, Kim M, Angerhofer A, Johnson RJ, Henderson GN. Inactivation of nitric oxide by uric acid. Nucleosides Nucleotides Nucleic Acids. 2008;27:967–78.
11. Conen, D., Wietlisbach, V., Bovet, P., Shamlaye, C., Riesen, W., Paccaud, F., Burnier, M. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. BMC Public Health,2004;4(1):9.
12. Schachter, M. Uric acid and hypertension. Curr. Pharm. Des., 2005;11(32):4139-4143.
13. Krishnan, E., Kwoh, C.K., Schumacher, H.R., Kuller, L. Hyperuricemia and incidence of hypertension among men without metabolic syndrome. Hypertension, 2007;49(2): 298-303.
14. Hikita M, Ohno I, Mori Y, Ichida K, Yokose T, Hosoya T. Relationship between hyperuricemia and body fat distribution. Intern Med. 2007;46:1353–8.
15. Yoo, T.W., Sung, K.C., Shin, H.S., Kim, B.J., Kim, B.S., Kang, J.H., Lee, M.H., Park, J.R., Kim, H., Rhee, E.J., et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. Circ. J., 2005;69(8):928-933.
16. Becker, M.A., Jolly, M. Hyperuricemia and associated disease. Rheum. Dis. Clin. North Am., 2006;32(2):275-287.
17. Norvik JV, Storhaug HM, Ytrehus K, Jenssen TG, Zykova SN, Eriksen BO, et al. Overweight modifies the longitudinal association between uric acid and some components of the metabolic syndrome: the Tromso Study. BMC Cardiovasc Disord. 2016;16:85.
18. Kawamoto R, Ninomiya D, Kasai Y, Senzaki K, Kusunoki T, Ohtsuka N, et al. Baseline and changes in serum uric acid independently predict 11-year incidence of metabolic syndrome among community-dwelling women. J Endocrinol Invest. 2018;41(8):959–68.