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Association between the metabolic syndrome parameters and serum level of uric acid

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ABSTRACT

Introduction: It is well-known that metabolic syndrome is a pathophysiological state with increased risks for diabetes mellitus (DM) and the atherosclerotic cardiovascular disease. Moreover, hyperuricemia can be considered as the main component in metabolic syndrome.

Objectives: The present research aimed at the investigation of the association between serum level of uric acid with metabolic syndrome parameters.

Patients and Methods: The present cross-sectional study population consisted of 200 subjects susceptible to metabolic syndrome. Data related to weight, height, waist circumference, body mass index (BMI), history of the disease, as well as drug consumption were recorded. All patients underwent routine blood tests for C-reactive protein (CRP) as well as uric acid levels. According to the diagnostic criteria for metabolic syndrome, we divided the patients into two groups. The first group was affected by metabolic syndrome(case) and the second was without metabolic syndrome (control). Then, we utilized Pearson's correlation coefficient to investigate the correlation of the serum level of uric acid with the continuous metabolic syndrome parameters. Finally, significant level was $P<0.05$ throughout this survey.

Results: In the case group, the level of uric acid was higher (6.55 ± 1.24 mg/dL) than the control level (4.76 ± 1.24 mg/dL) ($P<0.001$). We found a significant correlation between the uric acid level and hip circumference, waist circumference, fasting blood sugar, and CRP only in obese patients.

Conclusion: As demonstrated, a positive association between the level of serum uric acid and BMI ≥30 kg/m2 in the case group suggests greater role of obesity in metabolic syndrome. Since there is a strong correlation between serum CRP and uric acid levels in the case group with BMI ≥30 kg/m^2. High plasma concentration of uric acid can be an inflammatory marker and risk factor for obesity. Therefore, obese people with metabolic syndrome are recommended to control their hyperuricemia.

Implication for health policy/practice/research/medical education:
With a cross-sectional study on 200 patients(100 suffering from metabolic syndrome and 100 without metabolic syndrome), we found a positive association between serum levels of uric acid and BMI ≥30 kg/m^2. We also found a significant correlation between serum C-reactive protein and uric acid levels in the metabolic syndrome..

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Introduction

Metabolic syndrome is characterized by the cluster of adverse cardiovascular disease risk factors like abdominal obesity, dyslipidemia, hyperglycemia, and high blood pressure (BP) (1,2).

Uric acid is a product of oxidation product of purine nucleotides in the human metabolism, that can cause vascular endothelial cells dysfunction and increase the risk for atherosclerosis by reducing nitric oxide production, smooth vascular muscle proliferation, and insulin resistance escalation (3). The cardiovascular prevention guideline suggests uric acid measurement as a part of routine tests to assess the risk for cardiovascular diseases (4).

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A recent meta-analysis, however, has not verified any connection between hyperuricemia and cardiovascular diseases (5).

Objectives

Investigations focused on a relationship between uric acid level and the metabolic syndrome as a risk factor of metabolic syndrome or a part of its parameters. Therefore, the objective of the present research was to elevate the level of uric acid related to the parameters of the metabolic syndrome.

Patients and Methods

Study design

Our investigation is a descriptive, cross-sectional study on 200 patients prone to metabolic syndrome referred to the endocrine clinic of Loghman-Hakim hospital between 2018-2019. Participants' characteristics including age, gender, medicine intake, and illness were recorded by trained experts. In addition, we measured weight, height, body mass index (BMI), BP, and waist circumference of participants and recorded using standard devices in the research center. After 12-hour fasting, blood samples of all participants were obtained. Then fasting blood sugar test with glucose oxidase (GOD/POD method), using an available commercial kit. Serum triglyceride, high-density lipoprotein (HDL-C) cholesterol, and low-density lipoprotein (LDL-C) cholesterol were measured using standard kits, while serum uric acid was assessed with calorimeter method via standard kits too. The C-reactive protein (CRP) concentration was measured using the turbidimetric laboratory method. The fasting insulin level was measured using the immunoassay method and the homeostatic model assessment (HOMA) was used to measure insulin resistance. Patients were diagnosed with or without metabolic syndrome based on the NCEP ATP-III [National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III)] concept after all the necessary tests were collected (6, 7). In each group, we divided the participants into two sub-groups with BMI ≥30 kg/m^2 and BMI <30 kg/m^2 respectively. Correlation between the serum level of uric acid and continuous metabolic syndrome parameters in each subgroup analyzed. Patients with a history of heart attack or stroke, cardiovascular bypass, malignancy, gout, psoriasis, consumption of diuretic and corticosteroid, acute infection, kidney failure, cigarette smoking, or alcohol consumption were excluded.

Statistical analysis

For qualitative and quantitative variables mean, standard deviation (SD), frequency, and percentage were utilized to explain descriptive analysis. Comparison between basic characteristics in participants with or without metabolic syndrome applied with independent t-test. In addition, we utilized Pearson's correlation coefficient for determining the association between the serum level of uric acid and continuous metabolic syndrome parameters in patients with metabolic syndrome. Also this test was employed to show the association between metabolic syndrome parameters on the basis of BMI ≥30 kg/m^2 or BMI<30 kg/m^2. The significance level was considered <0.05, using the SPSS program for analysis of the data.

Results

In this research 200 individuals including 100 suffering from metabolic syndrome (case) as well as 100 without the metabolic syndrome(control), were participated. Table 1 reveals substantial differences between two groups concerning waist and hip circumference, systolic blood pressure (SBP) and diastolic blood pressure (DBP), total cholesterol, LDL-C, fasting blood sugar (FBS), HDL-C, insulin and HOMA-IR with a P value <0.05.

The levels of serum uric acid were higher in the metabolic syndrome group (6.55 ± 1.24 mg/dL) versus (4.76 ± 1.24 mg/dL) (P<0.001; Figure 1). Therefore, we investigated association of the level of uric acid with the metabolic syndrome parameters in both groups. An obvious correlation was observed in case group between the levels of serum uric acid with waist circumference (r=0.493; P<0.001), hip circumference (r=0.457; P<0.001), BMI (r=0.438; P<0.001), SBP (r=0.328; P=0.001), DBP (r=0.425; P<0.001), CRP (r = 0.346; P=0.05), fasting blood sugar (r=0.259; P=0.027), and HOMA-IR (r=0.328; P=0.032); whereas, an inverse association of serum uric acid with levels of HDL-C (r=-0.30; P=0.002) was detected. Additionally the association of serum uric acid with diastolic BP was observed in the case group was detected (r=0.26; P=0.047; Table 2).

Table 3 shows the correlation of serum uric acid with the parameters of metabolic syndrome based on BMI such as hip circumference (r = 0.465; P=0.01), fasting blood sugar (r = 0.298; P=0.01), CRP levels (r=0.34; P=0.05), and waist circumference (r = 0.399; P=0.01) only in patients with BMI ≥ 30 kg/m^2.

Discussion

This study assessed the relationship between hyperuricemia and metabolic syndrome parameters among people with and without this syndrome. The observations from our study showed higher uric acid level in metabolic syndrome, that is compatible with other research outputs (8-12).

Uric acid measurement may, therefore, be considered as the main component in metabolic syndrome, or even as its predictor.

Although the exact mechanism of the correlation of

Table 1. Characteristics of case and control group participants

Variables		With metabolic syndrome 100 (50%)	Without metabolic syndrome 100 (50%)	*P* value
Gender	Female	67(67%)	73(73%)	**0.42**
	Male	33(33%)	27(27%)	**0.56**
BMI (kg/m^2)		36.23 ± 6.36	30.30 ± 6.98	<0.001*
Waist circumference (cm)		111.50 ± 9.93	99.05 ± 13.77	<0.001*
Hip circumference (cm)		129.99 ± 11.65	111.00 ± 13.59	<0.001*
Blood pressure (systolic)		125.9 ± 14.67	115.04 ± 10.78	<0.001*
Blood pressure (diastolic)		78.5 ± 10.06	73.35 ± 8.07	<0.001*
Fasting blood sugar (mg/dL)		112.12 ± 13.75	91.95 ± 10.53	<0.001*
Total cholesterol (mg/dL)		194.91 ± 43.93	177.14 ± 43.04	**0.004** *
LDL-C (mg/dL)		125.61 ± 38.93	111.84 ± 33.79	**0.007** *
HDL-C (mg/dL)		41.77 ± 9.70	49.62 ± 11.48	<0.001*
Triglyceride (mg/dL)		213.00 ± 97.69	108.55 ± 47.38	<0.001*
Uric acid (mg/dL)		6.55 ± 1.24	4.76 ± 1.24	<0.001*
Insulin level (mlU/mL)		19.60 ± 12.27	10.09 ± 5.26	<0.001*
Creatinine (mg/dL)		0.96 ± 0.16	0.98 ± 0.58	**0.684***
CRP (mg/dL)		5.41 ± 11.77	2.52 ± 2.78	**0.018***
HOMA-IR		5.42 ± 3.61	2.28 ± 1.21	<0.001*

* $P < 0.05$.

serum uric acid with metabolic syndrome continues to remain uncertain, however reduced production of nitric oxide production by endothelial cells can justify it. Moreover, a high insulin level in people with this syndrome can reduce uric acid secretion from proximal tubule in the kidney which, in turn, can cause hyperuricemia (12).

In this analysis, a significant relationship of serum uric acid with waist circumference, hip circumference, and BMI was seen. Likewise, the significant correlation of serum uric acid with waist circumference, BMI, and hip circumference in the study conducted by Tanaka et al was found (13).

Figure 1. Mean level of uric acid in case and control participants

Table 2. Association of the levels of uric acid with the continuous variables in the case and control groups

Adjustment for age and gender	Without metabolic syndrome	With metabolic syndrome
	Pearson's coefficients	Pearson's coefficients
BMI (kg/m^2)	0.03	0.438*
Waist circumference (cm)	0.10	0.493*
Hip circumference (cm)	0.15	0.457*
Blood pressure (systolic)	0.18	0.328*
Blood pressure (diastolic)	0.266*	0.425*
FBS (mg/dL)	0.02	0.259*
HDL-C (mg/dL)	-0.10	-0.30*
Triglyceride (mg/dl)	0.00	0.10
CRP (mg/dL)	0.03	0.34*
HOMA-IR	0.02	0.328*

* $P < 0.05$.

Moreover, Modino et al (10), Cardoso et al (14), Khichar et al (9), and Popescu et al (12) reported the significant correlation of serum uric acid with abdominal obesity and BMI.

In this study, we found an association between the uric acid level with SBP (r = 0.328, $P = 0.001$) and with DPB (r = 0.425 $P < 0.001$) after adjust of age, gender and BMI in the case group. In addition, a significant relationship was existed between serum uric acid and DBP (r = 0.266 $P = 0.047$) in the control group. These findings also reported by Yokokawa et al (15). Studies have shown that uric acid level escalation causes micro-vascular and inflammatory damages to kidneys. It may also stimulate arteries smooth muscle proliferation and inflammatory alterations in kidneys, which can justify the relationship of a high level of uric acid and BP in our study. This study indicated the relationship of serum uric acid with insulin resistance index (r = 0.328; $P = 0.032$) in the case group, which is consistent with other studies (10,16,17). In the case group, a substantial association between the CRP and the levels of uric acid (r=0.346; $P = 0.05$) was seen. This can be attributed to CRP as one of the hazardous factors for cardiovascular disease. Therefore, a high level of serum uric acid can be regarded as a cardiovascular risk factor (9,14). In our study, participants were categorized into two groups based on their BMI status, while in obese participants with higher BMI, the level of serum uric acid was related to the most metabolic syndrome parameters (hip and waist circumferences, FBS, HDL-C, LDL-C,

Table 3. Association of serum uric acid value with continuous variables in the case and control groups based on BMI (≥ 30 or < 30 kg/m²)

Adjustment for age and gender	With metabolic syndrome		Without metabolic syndrome	
	Srum uric acid		Srum uric acid	
	BMI < 30	BMI ≥ 30	BMI < 30	BMI ≥ 30
Number of persons	16 (16%)	84 (84%)	54 (54%)	46 (46%)
Waist circumference (cm)	0.15	0.39**	0.05	0.23
Hip Circumference (cm)	0.09	0.46**	0.07	0.23
SBP	0.13	0.17	0.23	0.40
DBP	0.11	0.28**	0.04	0.27
Fasting blood sugar (mg/dL)	0.03	0.29*	0.04	0.19
HDL (mg/dL)	-0.11	-0.29*	-0.16	-0.16
Triglyceride (mg/dL)	0.13	0.03	0.01	0.06
CRP (mg/dL)	0.31	0.34*	0.03	0.23
HOMA-IR	0.26	0.02	0.12	0.29

**$P<0.001$, *$P<0.05$.

and DBP); whereas, there was not such a relationship among the participants with lower BMI. In general, our outputs showed patients suffering from metabolic syndrome have a higher serum level of uric acid; whereas, the uric acid level was lower in the patients without the metabolic syndrome. In metabolic syndrome group, obese participants had a higher uric acid level which indicates a considerable role of obesity in this syndrome.

Conclusion

Our findings indicated that obesity has a pivotal role in association with a uric acid level in metabolic syndrome. Depending on the significant association between the level of CRP and uric acid in obese people with metabolic syndrome, CRP acts as one of the risk factor for the CVD. Accordingly, high levels of uric acid may be seen as an inflammatory marker and risk factor for obesity. Therefore, obese people with metabolic syndrome are recommended to control hyperuricemia. This study provided a context for doing further research in this field. It is recommended to perform this research with a larger sample size of different races and in diversified medical settings, to obtain more generalizable results for prevention and treatment of such disorders. More studies are required to establish which metabolic syndrome parameters are highly correlated with uric acid level, and therefore to take them as a part of metabolic syndrome or use them as a prognostic factor in highly susceptible individuals.

Limitations of the Study

This study was associated with some limitations. Patients with diabetes mellitus and hypertension were not assessed separately. As the sample size was not sufficiently large, it was not possible to equally distribute patients with metabolic syndrome based on BMI.

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Authors' contribution

ZD, MM, SHM, and MS conducted the research. ZD and MM finalized the manuscript. All authors read and signed the final manuscript.

Conflicts of interest

Hereby, it is declared that we do not have any conflicts of interests.

Ethical issues

We received an approval of the research proposal through the research committee of the internal medicine department of the Loghman-Hakim hospital affiliated to the Shahid Beheshti University of Medical science, Tehran (Iran). At each research stage, we followed the considerations by the Declaration of Helsinki and the Ethics Committee of Ministry of Health. Each participant signed the informed written consent form. This project was also confirmed by the Ethics Committee of the Shahid Beheshti University of Medical Sciences (#IR.SBMU.MSP.REC.1396.364). This study was extracted from the Mojgan Motevally Bashi residential thesis in the department of internal medicine. Moreover, ethical considerations, such as data collection, plagiarism, and double publications, were thoroughly taken into account.

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