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Original Article

The role of uric acid and hscrp in predicting metabolic syndrome

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Abstract

Aim: Metabolic syndrome is a group of diseases characterized by the coexistence of cardiometabolic risk factors such as abdominal obesity, dyslipidemia, glucose intolerance, and high blood pressure. Metabolic syndrome is a common disease that can lead to high mortality with cardiovascular complications. Many studies are ongoing for laboratory parameters that can be used in the early diagnosis of this syndrome, but for daily clinical use and the diagnostic criteria, any parameter has not been revealed yet. We planned to carry out this study to predict the usability of uric acid and HSCRP in clinical practice, which have been reported to be associated with metabolic syndrome in the literature.
Material and Methods: Patients with metabolic syndrome who applied to Ankara Training and Research Hospital's Internal Medicine department outpatient clinic for any reason within nine months were included in the study group. In the same period, completely healthy cases who applied to the outpatient clinic for any reason were included in the control group. Demographic data, physical examination findings, anthropometric measurement results, biochemical parameters, and HSCRP levels of the cases were recorded. Metabolic syndrome and the control group were analyzed for uric acid and HSCRP values. SPSS 25.0 was used for statistical analysis. The data were evaluated within the 95% confidence interval, and $p<0.05$ was considered significant.
Results: In the study conducted that with a total of 174 patients, including 95 patients with metabolic syndrome and 79 healthy patients, the mean uric acid level of the metabolic syndrome group (5.22±1.39mg/dl) was significantly higher than that of the control group (4.35±1.11mg/dl) ($p<0.01$). With the ROC curve, the uric acid cut-off value for detecting metabolic syndrome incidence was found to be 5.45mg/dl (specificity 89.9%; sensitivity 51.6%). Its positive predictive value was 86%, and its negative predictive value was 60.7%. The mean HSCRP levels of the metabolic syndrome group (4.72±3.54mg/L) were found to be significantly higher than the control group (3.30±3.21mg/L) ($p<0.01$).
Conclusion: Serum uric acid and HSCRP levels in the study group with metabolic syndrome were significantly higher than in the control group. This syndrome, which is very common today, can lead to various outcomes in terms of mortality and morbidity; when the early diagnosis is delayed, it constitutes an important part of health expenditures. We believe that early diagnosis with laboratory parameters that can be very practical in daily practice will prevent metabolic syndrome complications.

Keywords: Metabolic syndrome, obesity, systemic inflammation, uric acid, HSCRP

INTRODUCTION

Metabolic syndrome, which is becoming increasingly common worldwide, is defined as the combination of all metabolic risk factors such as abdominal obesity that starts with insulin resistance, glucose intolerance or diabetes mellitus, dyslipidemia, hypertension, and systemic disorders such as coronary artery disease, and it has high morbidity and mortality rates with cardiometabolic complications (1). Despite significant advances in treatment approaches, atherosclerotic cardiovascular diseases remain the most common cause of death worldwide.

This pioneering status of cardiovascular diseases parallels the increasing epidemic of obesity and type 2 diabetes mellitus, the most common endocrine disease worldwide. The most important etiological factor that brings this trio together is the metabolic syndrome, which now affects so many regions in the world that it can be called a pandemic. This prevalent worldwide syndrome that cannot be diagnosed with a single parameter can lead to critical consequences with high morbidity and mortality when the diagnosis is delayed.

Metabolic syndrome can be mentioned as a result of specific anthropometric measurements, laboratory results, and clinical evaluation, starting with the syndrome being thought of first. In addition to the metabolic syndrome's first defined diagnostic criteria, which was published in 1998, various diagnostic criteria are defined by many organizations worldwide, and new parameters that are thought to be helpful in diagnosis are being studied (2). Most of the parameters investigated in patients with metabolic syndrome remained at the level of scientific studies. They could not take their place among the diagnostic criteria, and they were not used in daily clinical use due to the fact that scientific competence could not be achieved, and they were not financially cost-effective.

Uric acid and high-sensitivity C-reactive protein (HSCRP) are two parameters that have been reported in the literature to be associated with metabolic syndrome and its components such as hypertension, hyperglycemia, obesity, and dyslipidemia.

Chronic inflammation is the main factor in the development and progression of atherosclerosis and cardiovascular diseases. Many inflammatory markers have been studied in this regard; the most critical acute phase response marker associated with cardiovascular disease risk in different populations is CRP. Studies in the literature show that a high CRP level is one of the critical risk factors for developing chronic diseases with increasing prevalence, such as diabetes or hypertension (3,4). Upon the demonstration of the effectiveness of CRP in predicting subclinical inflammation, the HSCRP test, which can measure CRP levels at lower concentrations, and which is determined by high-sensitivity methods, was developed (5).

Obesity, the main component of metabolic syndrome, is associated with systemic inflammation originating from adipose tissue. That cytokines such as tumor necrosis factor-alpha and IL-6, which are released in large amounts from adipose tissue, trigger chronic subclinical inflammation by stimulating CRP production from the liver, which is thought to be the underlying mechanism of high HSCRP levels in obese individuals (6).

Elevated uric acid is thought to be an essential risk factor for developing cardiovascular events related to oxidative stress and endothelial dysfunction (7). It has been observed that insulin resistance underlying the metabolic syndrome is inversely related to renal uric acid clearance, and as a result, there is a decrease in renal excretion of uric acid in patients with hyperinsulinemia (8,9).

Although uric acid and HSCRP measurements are strongly associated with metabolic syndrome and its components, they are not included in the diagnostic criteria for metabolic syndrome defined by different organizations and in the recently published review of these definitions. In this study, we aimed to evaluate the usability of measurement of serum uric acid levels and HSCRP values, which can also be studied in our hospital laboratory, in clinical practice, in the prediction of metabolic syndrome, which can lead to serious outcomes in terms of mortality and morbidity when the diagnosis is delayed.

MATERIAL AND METHODS

The study included 95 patients with metabolic syndrome who applied to the Internal Medicine outpatient clinic of SBU Ankara Training and Research Hospital for any reason within nine months after the ethics committee's approval. Ethics committee approval was obtained from Ankara Training and Research Hospital, Education, Planning and Coordination Ethical Board (2012/02).

The diagnosis of metabolic syndrome was made according to the criteria of NCEP ATP III (The National Cholesterol Education Program's Adult Treatment Panel III report), which is the most accepted definition in practice due to its ease of application (10). Patients with known renal insufficiency, hepatic insufficiency, pregnancy, active malignancy, active infection, psoriasis, aspirin, diuretic, cyclosporine, pyrazinamide, ethambutol-containing drug users, alcohol, and cigarette users were excluded from the study. The control group includes 79 completely healthy volunteers who applied during the same period as the study group. Demographic data of the subjects included in the study, physical examination findings, anthropometric measurement results, fasting blood glucose (FBG), urea, creatinine, total cholesterol, HDL-C, LDL-C, TG, uric acid, insulin, biochemical including hemoglobin A1c (HbA1c) parameters and HSCRP levels were recorded.

SPSS 25.0 was used for statistical analysis. Independent sample t-test was used to compare parametric data, one-way analysis of variance (ANOVA) was used to compare more than two independent samples, chi-square test was used to compare categorical values, and correlation test was used to compare values with each other. Data were evaluated at a 95% confidence interval. $p<0.05$ was considered significant.

RESULT

The study was carried out with a total of 174 cases, including 95 patients with metabolic syndrome and 79 healthy patients. Of the patients in the metabolic syndrome group, 58.9% (56) were female, 41.1% (39) were male; 57% (45) of the control group were female, and 43% (34) were male, and the mean age of the study population was 51.25±11.60 years (Table 1). The mean body mass index of all subjects included in the study was 27.79±6.05, and the mean waist circumference was 96.24±16.05. Mean waist circumference and body mass indexes of patients

with metabolic syndrome were statistically significantly higher than the control group (p<0.01). Fasting glucose, triglyceride, LDL, HbA1c, fasting insulin level, and insulin resistance were significantly higher in the metabolic syndrome group compared to the control group (p<0.01). There was no significant difference between serum creatinine levels of both groups (p:0.960). HDL levels of patients with metabolic syndrome were found to be lower than the control group (p<0.01) (Table 2).

Table 1. Demographic and Clinical Characteristics of the Patients

Date		Metabolic Syndrome (n=95) Mean ±SD	Control Group (n=79) Mean ±SD	
Age (year)		53.87±10.43	50.10±12.20	[a]0.961
BMI (kg/m²)		31.56±5.44	23.25±2.69	[a]0.001**
Waist Circumference		106.12±13.55	84.35±9.38	[a]0.001**
Gender		n (%)	n (%)	
	Female	56 (%58.9)	45 (%57.0)	0.792
	Male	39 (%41.1)	34 (%43.0)	

[a]Student-t Test, **p<0.01,
BMI: Body Mass Index

Table 2. Evaluation of Laboratory Results According to Metabolic Syndrome

	Metabolic Syndrome (n=95) Mean ±SD	Control Group (n=79) Mean ±SD	
Fasting Glucose	128.84±56.15	89.01±7.52	[a]0.001**
Creatinine	0.90±0.18	0.90±0.18	[a]0.960
HDL	48.09±10.60	55.78±10.37	[a]0.001**
LDL	133.56±35.93	114.69±29.56	[a]0.001**
Triglyceride	184.21±85.90	105.89±30.14	[a]0.001**
HbA1c	6.98±1.98	5.60±0.53	[a]0.001**
HSCRP	4.73±3.54 (3.70)	3.20±3.21 (1.90)	[b]0.001**
Fasting Insulin	10.24±6.83 (8.90)	7.40±5.33 (6.00)	[b]0.001**
Uric Acid	5.22±1.39	4.35±1.11	[b]0.001**
IR	3.34±3.72 (2.51)	1.67±1.26 (1.30)	[b]0.001**

[a]Student-t Test, [b]Mann-Whitney U Test, **p<0,01, HDL: High Density Lipoprotein,
HSCRP: High-Sensitivity C-Reactive Protein, LDL: Low Density Lipoprotein, IR: Insulin Resistance

The mean uric acid value (5.22±1.39 mg/dl) of the metabolic syndrome group was statistically significantly higher than the uric acid mean value (4.35±1.11 mg/dl) of the control group (p<0.01). With the ROC curve, the cut-off value for uric acid in detecting the incidence of metabolic syndrome was found to be 5.45 mg/dl (specificity 89.9%; sensitivity 51.6%) (Figure 1). Its positive predictive value was 86%, and its negative predictive value was 60.7%. In addition, a statistically significant relationship was found between uric acid levels and metabolic syndrome components such as hyperglycemia, hypertension, dyslipidemia, and abdominal obesity.

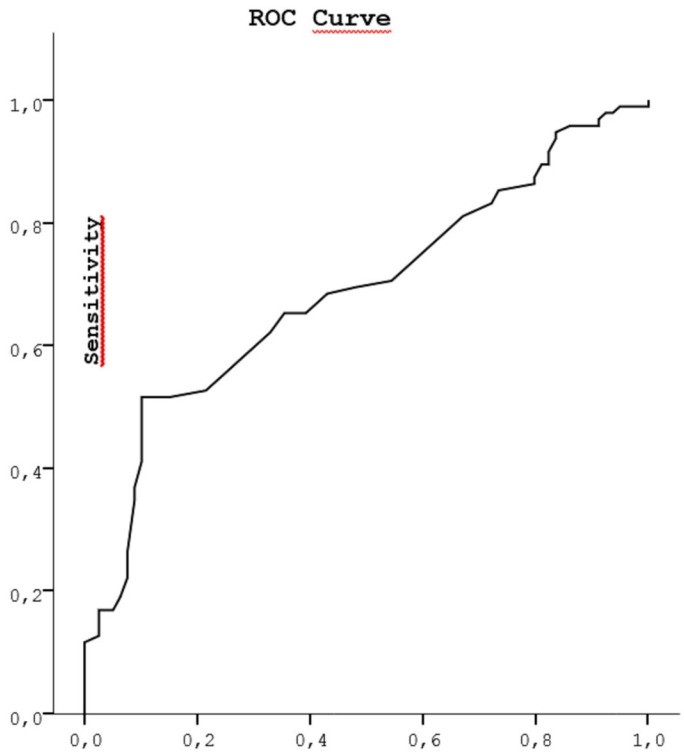

Figure 1. Uric Acid ROC Curve

The area under the curve (AUC) is 0.688

The mean HSCRP levels of the metabolic syndrome group (4.72±3.54 mg/L) were higher than the control group (3.30±3.21 mg/L) ($p<0.01$). While there was a significant relationship between HSCRP levels and hypertension, dyslipidemia, and abdominal obesity; contrary to the data in the literature, no significant relationship was found between hyperglycemia and HSCRP levels.

DISCUSSION

Although uric acid and HSCRP measurements are associated with metabolic syndrome and its components, it is still not among the diagnostic criteria for metabolic syndrome defined by different organizations. In our study, where we aimed to evaluate the usability of serum uric acid and HSCRP measurement, which can be studied in most hospital laboratories, in clinical practice, and in the diagnosis of metabolic syndrome, which can lead to severely poor outcomes when the diagnosis is delayed, we found a significant relationship between these laboratory tests and metabolic syndrome parameters.

In the literature, studies are reporting that the incidence of metabolic syndrome increases as serum uric acid levels increase (11). Gagliardi et al., in their work; was reported that each standard deviation increase in uric acid levels after excluding age, smoking and alcohol consumption increased the development of metabolic syndrome by 35% (12).

In a large-series study with 7399 cases, the relationship between hyperuricemia in patients with metabolic syndrome was investigated, and it was reported that the ROC curve for serum uric acid value in the prediction of metabolic syndrome was found to be 6.3 mg/dl in men and 4.9 mg/dl in women (13). In most laboratories, 7 mg/dl is taken as the upper limit of uric acid. In our study results, that similar to Zhang et al. study, the uric acid cut-off value was determined as 5.45 mg/dl in the prediction of metabolic syndrome, which shows that in association with serum uric acid levels and metabolic syndrome, in addition to overt hyperuricemia, uric acid levels at the upper limit of normal may also be significant.

HSCRP is an acute phase reactant, which has been supported by studies in which high levels are associated with an increased risk of cardiovascular disease and that it is found at higher levels in patients with metabolic syndrome compared to healthy adults (14). In a large series study comparing 3285 patients with metabolic syndrome with 3999 healthy individuals, it was reported that the increase in HSCRP level is an independent risk factor in showing the risk of cardiovascular diseases such as coronary artery disease and ischemic stroke. As the number of metabolic syndrome components increases, HSCRP levels increase in correlation with the number of components (15).

Zuliani et al., in the metabolic syndrome study performed by 1044 cases, it was reported that the rate of HSCRP elevation was found to be significantly higher in the metabolic syndrome group (54.5%) compared to healthy subjects (41.3%) ($p < 0.001$). It has also been reported that there is a positive correlation between the increase in waist circumference and HSCRP levels and that HSCRP values increase as the waist circumference increases, independent of confounding factors such as age, gender, and comorbidity (16).

In our study, according to the correlation analysis between waist circumference measurements and body mass index and HSCRP values, it was determined that there was a positive correlation between body mass index and waist circumference measurements and HSCRP levels.

CONCLUSION

In conclusion; in our study to evaluate the relationship of uric acid and HSCRP levels with the metabolic syndrome and its components, and its usability in predicting metabolic syndrome in daily practice, serum uric acid and HSCRP levels were found to be significantly higher in the metabolic syndrome patient group compared to the control group. In this study, we demonstrated that this syndrome, which is very common today, can lead to various outcomes in terms of mortality and morbidity; when the early diagnosis is delayed, it constitutes an important part of health expenditures. We believe that predicting it with laboratory parameters that can be easily used in daily practice will prevent complications that may develop.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
Ethics committee approval was obtained from Ankara Training and Research Hospital, Education, Planning and Coordination Ethical Board (2012/02).

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