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The role of uric acid in metabolic syndrome in patients with psoriasis

Metabolik sendromlu psoriazis hastalarında ürik asitin rolü

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Abstract

Background and Design: Psoriasis patients have increased risk of obesity, metabolic syndrome and cardiovascular disease. Uric acid is a metabolic marker associated with metabolic syndrome and cardiovascular diseases. Uric acid levels increase in psoriasis as well. The aim of this study was to investigate the role of uric acid in metabolic syndrome in patients with psoriasis.
Materials and Methods: Chronic plaque psoriasis patients who presented to the dermatology outpatient clinics in a university-affiliated training and research hospital and age- and gender-matched healthy individuals were included in the study. Waist circumference, height and weight measurements in both groups were recorded, and body mass index was calculated. Serum uric acid, urea, creatinine, C-reactive protein, fasting blood glucose, high-density lipoprotein cholesterol, total cholesterol, triglyceride and insulin levels were determined. Metabolic syndrome and insulin resistance status were evaluated. The findings were compared statistically.
Results: Seventy patients with chronic plaque psoriasis (37 females, 33 males) and 60 healthy individuals (31 females, 29 males) were included in the study. The prevalence of metabolic syndrome and uric acid levels were found to be higher in the psoriasis group than in control group (p=0.003 and p=0.008, respectively). Serum uric acid levels and Psoriasis Area and Severity Index scores were higher in psoriasis patients with metabolic syndrome than in those without metabolic syndrome when psoriasis patients were evaluated separately (p=0.041 and p=0.024, respectively). A positive correlation was observed between abdominal circumference and serum uric acid levels in psoriasis patients (p=0.003, r=0.350).
Conclusion: The results of this study show that uric acid levels are elevated in psoriasis patients with metabolic syndrome. The prevalence of metabolic syndrome was also significantly higher. Hence, patients should be followed up for development of uric acid-related disorders.
Keywords: Metabolic syndrome, uric acid, psoriasis

Öz

Amaç: Enflamatuvar bir hastalık olan psoriaziste son yıllarda obezite, metabolik sendrom ve kardiyovasküler hastalık riskinin arttığı gösterilmiştir. Ürik asit metabolik sendrom ve kardiyovasküler hastalıklarla ilişkili ve aynı zamanda psoriaziste arttığı bilinen metabolik bir belirteçtir. Psoriazis hastalarındaki artmış metabolik sendrom riskinde ürik asitin rol oynayıp oynamadığını araştırmayı amaçladık.
Gereç ve Yöntem: Üniversite afiliye eğitim ve araştırma hastanesi dermatoloji polikliniğinde görülmüş olan kronik plak psoriazisli hastalar ile yaş ve cinsiyet uyumlu sağlıklı kontrol grubu çalışmaya alındı. Hasta ve kontrol grubunun bel çevresi, boy ve kilo ölçümü kaydedildi. Vücut kitle indeksleri hesaplandı. Serum ürik asit, üre, kreatinin, C-reaktif protein açlık glukoz, yüksek yoğunluklu lipoprotein kolesterol, total kolesterol, trigliserid ve insülin değerleri ölçümleri kaydedildi. Hasta ve kontrol grubunda metabolik sendrom varlığı ve insülin direnci değerlendirildi. Sonuçlar istatistiksel olarak karşılaştırıldı.
Bulgular: Kronik plak psoriazisli 70 hasta (37 kadın, 33 erkek) ile 60 sağlıklı kontrol (31 kadın, 29 erkek) çalışmaya alındı. Psoriazis hastalarında metabolik sendrom sıklığının kontrol grubuna göre daha sık ve ürik asit düzeyinin daha yüksek olduğunu saptadık (p=0,003, p=0,008, sırasıyla). Ayrıca, psoriazis hastaları kendi içlerinde değerlendirildiğinde metabolik sendromu olanlarda, olmayanlara göre serum ürik asit düzeyleri ve Psoriazis Alan Şiddet İndeks skorları daha yüksekti (p=0,041, p=0,024, sırasıyla). Ayrıca, psoriazis hastalarında bel çevresi ile serum ürik asit düzeyleri arasında korelasyon gözledik (p=0,003, r=350).

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Sonuç: Çalışmamızın sonuçları metabolik sendromu olan psoriazis hastalarında ürik asit düzeylerinin artmış olduğunu göstermektedir. Ayrıca, psoriazis hastalarında metabolik sendrom prevalansı istatistiksel olarak anlamlı olarak yüksek bulunmuştur. Bu nedenle, hastalar ürik asit ile ilişkili hastalıklar gelişimi açısından takip edilmelidir.
Anahtar Kelimeler: Metabolik sendrom, ürik asit, psoriazis

Introduction

Psoriasis is a chronic inflammatory skin disorder characterized by keratinocyte hyperproliferation and increased epidermal cell turnover. It is not limited to skin, it can also effects the joints[1]. Moreover, in recent studies, it has been shown that there was systemic inflammation and increased risk of metabolic syndrome and cardiovascular disease in patients with psoriasis[2-5].

Uric acid is a metabolic biomarker whose clinical significance is better understood recently. It is proposed to be associated with metabolic syndrome, hypertension and cardiovascular disease[6-9]. Increased uric acid levels in psoriasis have been commonly investigated[10,11]. It has been reported that increased uric acid levels were associated with the severity of psoriasis as well[11].

The pathogenesis of metabolic syndrome in psoriasis has not been sufficiently explained yet. The aim of this study was to investigate the relationship between metabolic syndrome and uric acid levels in psoriasis patients.

Materials and Methods

Psoriasis patients over 18 years old who attended the dermatology outpatient clinic in a university-affiliated hospital, and age- and sex-matched healthy individuals were included in the study. Healthy control group included healthcare employees and outpatient clinic patients who had no systemic inflammatory disease.

Patients with arthritis, systemic inflammatory diseases, and active malignancy and those who were on drugs, such as corticosteroids, thiazide diuretics, and allopurinol were excluded.

The severity of psoriasis was assessed via the Psoriasis Area and Severity Index (PASI)[12]. Waist circumference, height and weight in all individuals in patient and control groups were recorded. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared for all subjects. Serum levels of uric acid, urea, creatinine, C-reactive protein, fasting glucose, high-density lipoprotein (HDL) cholesterol, total cholesterol, triglycerides, and insulin were determined and recorded.

The metabolic syndrome diagnostic criteria which were determined by the guidelines by Diabetes Study group of the Society of Endocrinology and Metabolism of Turkey was used for the diagnosis of metabolic syndrome. Presence of type 2 diabetes mellitus, impaired glucose tolerance or insulin resistance in association with at least two or more of the following was required for the diagnosis of metabolic syndrome:

1) Central obesity (BMI >30 kg/m^2 or waist circumferences >88 cm in females and >102 in males),

2) Triglycerides ≥150 mg/dL, or HDL cholesterol <50 in females and <40 in males (or being on medicine for dislipidemia),

3) Blood pressure ≥130 (systolic)/85 (diastolic) mmHg (or being on medicine for pre-diagnosed hypertension)[13].

Insulin resistance was determined by the homeostasis model assessment of insulin resistance (HOMA-IR) which is done by multiplying fasting plasma glucose level (mg/dL) with fasting insulin level (mU/L) and then dividing this result by 405[13].

Local ethics committee approval was received for this case control study from Sakarya University (protocol number: 71522473/050.01.04/41).

Statistical Analysis

Analyses were performed using statistical software (IBM SPSS Statistics 20, SPSS Inc. an IBM Corp., Armonk, NY). Comparisons between the groups were performed with the chi-square or Fisher's exact test. The Kolmogorov-Smirnov test was used to determine the normal distribution of continues variables. Normally distributed variables were presented as mean±standard deviation and not normally distributed variables were presented as medium (range). The independent-samples t-test was used for normally distributed continuous variables, while the Mann-Whitney U test was applied for not normally distributed ones. Pearson's correlation coefficient was used to evaluate the correlation between continuous variables. A p-value of less than 0.05 was considered statistically significant.

Results

Seventy patients with chronic plaque psoriasis (37 females, 33 males) and 60 healthy individuals as controls were included in this study. The demographic and laboratory findings of patient and control groups are shown in Table 1. The prevalence of metabolic syndrome was significantly higher in psoriasis group than in control group (p=0.003). BMI, waist circumference, serum uric acid and fasting glucose levels were also significantly higher in psoriasis patients. Hyperuricemia was determined neither in psoriasis nor in the control group.

Psoriasis patients with and without metabolic syndrome were compared according to uric acid levels, PASI scores and duration of psoriasis (Table 2). Uric acid levels and PASI scores were found to be significantly increased in psoriasis patients with metabolic syndrome, but no difference was observed when duration of psoriasis was compared.

A significant positive correlation between waist circumference and uric acid level was observed with Pearson correlation analysis (p=0.003, r=350), but no correlation was found between HOMA-IR and uric acid level. There was no statistically significant difference in the prevalence of metabolic syndrome between female and male psoriasis patients (p=0.915).

Discussion

The salient findings of our study are that metabolic syndrome prevalence and uric acid levels were higher in psoriasis patients compared with those in healthy control group, and uric acid levels were higher in psoriasis patients with metabolic syndrome, than in those without metabolic syndrome.

Psoriasis is currently considered a systemic inflammatory disease by several authors, although the etiology is yet to be clarified[2]. Recently, there have been many studies reporting increased risk of obesity, metabolic syndrome and cardiovascular disease in psoriasis. It is suggested that increased inflammation in psoriasis leads to epithelial dysfunction, which drives the increased risk of cardiovascular disease[2,14-16].

Uric acid is a metabolic marker which has been shown to be associated with conditions like hypertension, metabolic syndrome and atherosclerotic heart disease[6-8]. There are different opinions on cause and effect relationship between uric acid and metabolic syndrome and its components, but it is widely admitted that higher uric acid levels are associated with increased risk of metabolic syndrome and cardiovascular disease[17,18]. Oxidative stress and inflammation are proposed for this interaction[19]. Serum uric acid levels increase with insulin resistance; by both directly enhancing uric acid production and indirectly inhibiting renal excretion. An increased uric acid level then aggravates insulin resistance and associated conditions, such as hypertension, endothelial dysfunction and dyslipidemia leading to increased risk of cardiovascular disease[17].

Increased levels of uric acid have been well-known in psoriasis. This finding was attributed to increased epidermal cell turnover at first, but it is currently suggested that uric acid increases in association with the presence of metabolic syndrome in psoriasis[20,21]. In a recent population-based cross-sectional study, it has been reported that the evidence is limited about psoriasis being an independent risk factor for hyperuricemia, besides, higher uric acid levels in psoriasis was likely a result of metabolic syndrome[21]. Nevertheless, increased uric acid due to increased epidermal cell turnover may be the triggering factor for metabolic syndrome in psoriasis.

In a study, a correlation of serum uric acid levels with waist circumference, BMI and serum triglyceride levels in psoriasis patients was reported. Another significant finding of this study was that the risk of metabolic syndrome was higher in female patients with higher uric acid levels. They also stated that the risk for metabolic syndrome was higher with even normal uric acid levels than lower levels in male patients[22]. Another study from Korea demonstrated a correlation between uric acid levels and BMI in psoriasis patients[11].

The findings of our study showed that the prevalence of metabolic syndrome and uric acid levels were higher in psoriasis patients compared with those in healthy controls. Furthermore, uric acid levels were higher in psoriasis patients with metabolic syndrome than in those without metabolic syndrome. A correlation was observed between waist circumference and serum uric acid levels. No correlation was present between HOMA-IR and uric acid levels. This suggests that uric acid may not take part alone in pathophysiology of metabolic syndrome and insulin resistance in psoriasis. Uric acid levels in patients with metabolic syndrome were higher than in ones without metabolic

Table 1. Demographic features, and laboratory values of psoriasis patients and healthy volunteers

	Psoriasis group (n=70)	Control group (n=60)	p value
Sex (n) Female Male	 37 (52.9%) 33 (47.1%)	 31 (51.7%) 29 (48.3%)	0.892
Metabolic syndrome frequency (n)	25 (%35,7)	8 (%13.3)	**0.003**
Age (year)	45.0±14.4	43.4±10.6	0.470
BMI (kg/m^2)	28.1±6.4	25.8±4.2	**0.024**
Waist circumference	96.0±15.6	89.3±13.8	**0.012**
Uric acid (mg/dL)	4.86±1.24	4.29±1.11	**0.008**
eGFR (mL/min/1.73 m^2)	106.5±21.6	105.4±16.1	0.740
Glucose (mg/dL)	102.5±29.8	91.9±9.5	**0.006**
HDL (mg/dL)	46.4±10.9	47.2±11.2	0.707
Triglycerides (mg/dL)	137.4±66.1	138.5±93.1	0.932
Total cholesterol (mg/dL)	197.9±37.5	193.6±41.1	0.541
HOMA*	1.9 (0.3-19.6)	1.8 (0.5-4.1)	0.159
CRP (mg/L)*	3.7 (1.0-34.3)	3.4 (1.0-10.4)	0.272

*Median value and range of these parameters were given because of not normal distribution of them, BMI: Body mass index, eGFR: Estimated glomerular filtration rate, CRP: C-reactive protein, HOMA: Homeostasis model assessment, HDL: High-density lipoprotein

Table 2. Comparison of serum uric acid levels, Psoriasis Area and Severity Index scores, and duration of disease of psoriasis patients with and without metabolic syndrome

	Psoriasis patients with metabolic syndrome (n=25)	Psoriasis patients without metabolic syndrome (n=45)	p value
Uric acid (mg/dL)	5.3±1.1	4.6±1.3	**0.041**
PASI	8.7 (3.3-29.5)	5.8 (1.2-31.0)	**0.024**
Duration of disease (month)	240 (4-456)	144 (9-684)	0.197

*Median value and range of these parameters were given because of not normal distribution of them, PASI: Psoriasis Area and Severity Index

syndrome although all of them were within the normal range.

A similar pathogenic mechanism and inflammation pathway was reported in both psoriasis and atherosclerosis[2,15]. This is important for early intervention on subclinical atherosclerosis to prevent cardiovascular events in psoriasis patients.

Study Limitations

There are some limitations deserve mention in our study. The number of patients was relatively small. Moreover, it was not possible to draw a cause and effect relationship between metabolic syndrome development and high serum uric acid levels. Nonetheless, there have been a limited number of studies evaluating this subject. This study is valuable that it represents the data in our country and it may be a guide for future studies concerning the subject.

Conclusion

In conclusion, the findings of the current study demonstrate that uric acid levels are elevated in psoriasis patients with metabolic syndrome. The prevalence of metabolic syndrome was also significantly higher. Hence, patients should be followed up for the development of uric acid-related disorders.

Ethics

Ethics Committee Approval: The study were approved by the Sakarya University of Local Ethics Committee (protocol number: 71522473/050.01.04/41).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.S., Design: B.S., Data Collection or Processing: B.S., B.S.D., T.E., Analysis or Interpretation: B.S., Literature Search: B.S., B.S.D, T.E., Writing: B.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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