

Evaluation of metabolic syndrome and its biochemical parameters in individuals with gouty arthritis and asymptomatic hyperuricemia

Gut artriti ve asemptomatik hiperürisemisi olan bireylerde metabolik sendrom ve biyokimyasal parametrelerin değerlendirilmesi

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ABSTRACT

Objective: Hyperuricemia, which occurs as a result of high uric acid levels, the end product of purine metabolism, is related with asymptomatic hyperuricemia (ASH) when it does not show symptoms and gouty arthritis (GOUT) when urate crystals occur. Hyperuricemia may interact with metabolic syndrome components. Therefore, the aim of the study was to assess the relationship of GOUT and ASH with metabolic syndrome.

Methods: The study was conducted with 145 individuals diagnosed with GOUT and ASH. Data on general characteristics, biochemical test results (serum fasting insulin, fasting blood glucose, uric acid, and blood lipids (such as low-density lipoprotein, total cholesterol, triglyceride, and high-density lipoprotein)), anthropometric (waist and hip circumferences, body weight and height) and blood pressure (systolic and diastolic) measurement results were collected. Bioelectrical Impedance Analysis was used to measure body composition. The National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) diagnostic criteria were used for the detection of

ÖZET

Amaç: Pürin metabolizmasının son ürünü olan ürik asit düzeyinin yüksek olması sonucu ortaya çıkan hiperürisemi, semptom göstermediğinde asemptomatik hiperürisemi (ASH) ve ürat kristalleri oluştuğunda gut artriti (GUT) ile ilişkilidir. Hiperürisemi, metabolik sendrom bileşenleriyle etkileşime girebilir. Bu nedenle çalışmanın amacı, GUT ve ASH'nin metabolik sendromla ilişkisini değerlendirmektir.

Yöntem: Bu çalışma, GUT ve ASH tanısı alan 145 birey ile gerçekleştirilmiştir. Genel özellikler, biyokimyasal test sonuçları [serum açlık insülini, açlık kan şekeri, ürik asit ve kan lipitleri (düşük yoğunluklu lipoprotein, toplam kolesterol, trigliserit ve yüksek yoğunluklu lipoprotein gibi)], antropometrik (bel ve kalça çevresi, vücut ağırlığı ve boy uzunluğu) ve kan basıncı (sistolik ve diyastolik) ölçüm sonuçları ile ilgili veriler toplanmıştır. Vücut kompozisyonunu ölçmek için Biyoelektrik İmpedans Analizi kullanılmıştır. Metabolik sendromun saptanmasında Ulusal Kolesterol Eğitim Programı Erişkin Tedavi Paneli III (NCEP-ATP III) tanı kriterleri kullanılmıştır. Hastalardan yazılı

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metabolic syndrome. Written informed consent form was obtained from patients. Patients who were not volunteers, who were pregnant or lactating, diagnosed with cancer, chronic renal failure, chronic liver failure, and individuals using diuretic drugs were not included in the research. In the analyses of all hypothesis tests, $p < 0.05$ was accepted significant.

Results: The metabolic syndrome frequency was significantly higher in the GOUT group than in the ASH group ($p < 0.05$). The difference between body mass index (BMI) values according to gender and groups was statistically significant among women ($p < 0.05$). Mean body fat percentage values were significantly higher in women in both GOUT and ASH groups ($p < 0.05$).

Conclusion: The frequency of metabolic syndrome was significantly higher in the GOUT group. In addition, BMI and body fat percentage values were significantly higher in women. Abdominal obesity and possible hyperinsulinemia may cause more serious problems in the presence of hyperuricemia. Therefore, multiple parameters (various biochemical and anthropometric measurements) should be evaluated together.

Key Words: Uric acid, asymptomatic hyperuricemia, gout, metabolic syndrome

bilgilendirilmiş onam formu alınmıştır. Gönüllü olmayan, hamile veya emziren, kanser tanısı almış, kronik böbrek yetmezliği ve kronik karaciğer yetmezliği olan ve diüretik ilaç kullanan kişiler araştırmaya dahil edilmemiştir. Tüm hipotez testlerinin analizlerinde $p < 0.05$ anlamlı olarak kabul edilmiştir.

Bulgular: GUT grubunda metabolik sendrom prevalansı ASH grubuna göre anlamlı derecede yüksekti ($p < 0.05$). Cinsiyet ve gruplara göre beden kütle indeksi (BKİ) değerleri arasındaki fark kadınlar arasında istatistiksel olarak anlamlı idi ($p < 0.05$). Ortalama vücut yağ yüzdesi değerleri hem GUT hem de ASH grubundaki kadınlarda anlamlı derecede yüksek olarak bulunmuştur ($p < 0.05$).

Sonuç: GUT grubunda metabolik sendrom prevalansı anlamlı derecede yüksekti. Ayrıca, kadınlarda BKİ ve vücut yağ yüzdesi değerleri anlamlı derecede yüksekti. Abdominal obezite ve olası hiperinsülinemi, hiperürisemi varlığında daha ciddi sorunlara neden olabilir. Bu nedenle, birden fazla parametrenin (çeşitli biyokimyasal ve antropometrik ölçümler) birlikte değerlendirilmesi gerekmektedir.

Anahtar Kelimeler: Ürik asit, asemptomatik hiperürisemi, gut, metabolik sendrom

INTRODUCTION

Gout is a type of arthritis that occurs when uric acid levels are irregular. It is a systemic disease that results in the accumulation of monosodium urate crystals in tissues. Elevated serum uric acid levels above a certain threshold cause the formation of uric acid crystals. The clinically gout is seen as acute gouty arthritis, asymptomatic hyperuricemia, chronic tophaceous gout, and intercritical period. Furthermore, many people with hyperuricemia may not develop gout, so uric acid crystals may not form (1). Uric acid, the metabolic end product of purine metabolism, has recently been related with many

chronic diseases, including metabolic syndrome (2).

There are numerous primary and secondary reasons of hyperuricemia. Modifiable factors that can cause hyperuricemia are: high purine diet, obesity, uncontrolled hypertension, alcohol consumption, hypertriglyceridemia, some drugs (such as thiazides and low-dose aspirin), and insufficient urine output (< 1400 ml/day). Chronic hyperuricemia is dangerous for health because it causes urate crystal accumulation, which can cause gout, urolithiasis, and uric acid nephropathy. Asymptomatic hyperuricemia is an elevated uric acid level (women: > 6 mg/dL or men: > 7 mg/dL). However, there are no symptoms associated with urate crystal formation. Detailed

health and nutritional history, physical examination, and laboratory findings are important in the treatment of asymptomatic hyperuricemia (3). The comorbidities of gout vary according to the affected system. Some of these are: stroke, hypertension, coronary heart disease, heart failure, atherosclerosis, nephrolithiasis, Alzheimer's and Parkinson's diseases, osteoporosis, chronic kidney disease, osteoarthritis, and diabetes. When evaluated in general, metabolic syndrome, which includes different metabolic components together, has an important place in gout (4). According to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria, metabolic syndrome prevalence was reported as 62.8% in gout patients and 25.4% in those without gout (5). Metabolic syndrome is a chronic low-grade inflammation status related with genetic or environmental factors. Insulin resistance or high blood glucose, visceral adiposity (high waist circumference), atherogenic dyslipidemia (especially declined high-density lipoprotein (HDL) and enhanced triglyceride (TG)), and increased blood pressure are the most important factors that cause metabolic syndrome (6). A significant correlation was found among metabolic parameters (TG, waist circumference, HDL-cholesterol, and blood pressure) and serum uric acid level. Especially, high triglyceride level was shown as the most effective parameter on serum uric acid level (7). Hyperuricemia is common in individuals with metabolic syndrome. It was suggested that there may be an increase in uric acid absorption secondary to hyperinsulinemia (8).

The purpose of this research was to examine the association of gouty arthritis and asymptomatic hyperuricemia with metabolic syndrome.

MATERIAL and METHOD

Patients

The study included volunteers diagnosed with gouty arthritis (GOUT) and asymptomatic hyperuricemia (ASH) and presented to the Internal

Medicine Outpatient Clinic within 5 months. The study included 145 individuals (52 men and 93 women) in 18-65 years old.

After the individuals were briefed about the research, a written informed consent form was obtained. Patients who were not volunteers, who were pregnant or lactating, diagnosed with cancer, chronic renal failure, chronic liver failure, and individuals using diuretic drugs were not included in the research.

In order to assess the socio-demographic features (age, gender, and educational status etc.) and general health information (such as smoking and alcohol use status) of the people, a questionnaire form with multiple-choice and open-ended items was administered by the researchers through face-to-face interviews.

Among the patients presented or consulted to the Internal Medicine Outpatient Clinic, persons with ASH or GOUT based on their biochemical and clinical findings were included in the study.

Biochemical Indicators

The serum fasting insulin, fasting blood glucose, uric acid, and blood lipids (such as low-density lipoprotein (LDL), total cholesterol, TG, and HDL) values were recorded from patient files. In the evaluation of biochemical indicators, reference ranges of the Private Lokman Hekim Ankara Hospital Laboratory were exerted. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) amounts were counted for the detection of insulin resistance. A HOMA-IR of ≥ 2.7 was defined as insulin resistance (9).

Measurement of Blood Pressure

Blood pressures were measured with a manual sphygmomanometer by a nurse assigned by hospital. Blood pressures (systolic and diastolic) were recorded by receiving the mean of two consecutive measurements while at rest. Hypertension is described as systolic blood pressure-140 mm Hg and greater and/or diastolic blood pressure-90 mm

Hg and greater and/or receiving anti-hypertensive treatment (10).

Anthropometric Measurements and Body Composition

Waist-hip circumferences, body weight, height, and body composition measurements were taken. Bioelectrical Impedance Analysis (BIA) was used for body weight measurement, while the patients were in thin clothes, without socks and shoes. Height was measured with a Seca stadiometer. While taking the height measurements of the individuals, they were in the Frankfort plane (eye and auricle are at the same level) and their feet were together. Body weights and heights were calculated using the body mass index (BMI) formula: $[BMI (kg/m^2) = Body Weight (kg) / Height (m)^2]$, and the outcomes were classified in accordance with the World Health Organization (WHO) classification. Accordingly, $<18.50 kg/m^2$ was evaluated as underweight, $18.50-24.99 kg/m^2$ -normal, $25.00-29.99 kg/m^2$ -overweight, and $\geq 30.00 kg/m^2$ -obese (11).

Waist circumference measurement was made by measuring the circumference through the midpoint between the lowest rib and the crista iliaca with an inflexible tape measure. According to the WHO classification, waist circumference values were evaluated as <94 cm-normal, ≥ 94 cm-risk, and ≥ 102 cm-high risk in men; <80 cm-normal, ≥ 80 cm-risk, and ≥ 88 cm-high risk in women (12).

The hip circumference was measured from the

highest point, parallel to the ground, and standing on the side of the individual with an inflexible tape measure. Waist/hip ratio was calculated with this formula: $[Waist/Hip Ratio = Waist Circumference (cm) / Hip Circumference (cm)]$. The outcomes were assessed according to the WHO classification. Accordingly, waist/hip ratio was determined as <0.90 normal and ≥ 0.90 risk in men; <0.85 normal and ≥ 0.85 risk in women (12).

Detection of Body Composition

The body composition of individuals (body fat percentage etc.) was assessed using BIA. The individuals were asked not to eat at least two hours before the measurement, not to drink much water before the measurement, not to drink tea/coffee 4 hours before the measurement, not to perform heavy physical activity, and not to consume alcohol 24 hours before. Body fat percentage was classified as $\leq 5\%$ lean, $6-24\%$ normal, and $\geq 25\%$ risk in men; $\leq 8\%$ lean, $9-31\%$ normal, and $\geq 32\%$ risk in women (13).

Metabolic Syndrome Diagnostic Criteria

The NCEP-ATP III diagnostic criteria were used for the detection of metabolic syndrome (Table 1) (14).

Informed Consent

The authors declare that they obtained a written informed consent from the patients and/or volunteers included in the article and that this report does not contain any personal information that could lead to their identification.

Table 1. NCEP-ATP III diagnostic criteria for metabolic syndrome (14)

- Abdominal obesity (waist circumference: >102 cm-men, >88 cm-women)
- Hypertriglyceridemia (≥ 150 mg/dL for TG)
- Low HDL (HDL: <40 mg/dL-men, <50 mg/dL-women)
- Hypertension ($\geq 130/85$ mm Hg for blood pressure)
- Hyperglycemia (≥ 110 mg/dL for fasting blood glucose)

*Exhibiting at least three of the parameters is necessary for metabolic syndrome.

NCEP-ATP III: National Cholesterol Education Program-Adult Treatment Panel III, TG: triglyceride, HDL: high-density lipoprotein.

Statistical Analysis

Number (n) and percentage (%) were used for categorical variables. Mean, standard deviation (SD), minimum, and maximum values were used for continuous variables. Whether the data were normally distributed was assessed with the Kolmogorov-Smirnov Test and histograms. In the assessment of categorical variables, the Pearson's Chi-square (χ^2) Test was performed when the assumptions were met; the Fisher's Exact (χ^2) Test was performed when the number of samples in the crosstab was insufficient and the assumption could not be met. Statistical Package for Social Sciences 22.0 was applied in the statistical assessment of the data. In the analyses of all hypothesis tests, $p < 0.05$ was accepted significant.

This study was approved by the Baskent University Non-Interventional Clinical Research Ethics Committee (Date: 12.04.2016 and Number: 94603339-604.01.02/12438).

RESULTS

Basic Information of the Individuals

In the study, 63.4% (n=92) of the individuals were women and 36.6% (n=53) were men. The mean age of all individuals was 37.2 ± 12.8 years; 34.0 ± 12.7 years for the ASH group and 41.0 ± 12.0 years for the GOUT

group. In the ASH group, 15.0% were housewife, 7.5% were civil servant, 17.5% were worker, 13.8% were self-employed, 1.3% were retired, and 45.0% were in other professions. In the GOUT group, 21.5% were housewife, 18.5% were civil servant, 1.5% were worker, 21.5% were self-employed, 15.4% were retired, and 21.5% were in other professions (Data not shown).

In the ASH group, 71.3% were non-smokers, 10.0% had been smokers before and quit smoking, and 18.8% were current smokers; 50.8% of the GOUT group were non-smokers, 1.5% had been smokers before and quit smoking, and 47.7% were current smokers. In the ASH group, 11.3% consumed alcohol, whereas 26.2% of the GOUT group consumed alcohol. It was observed that 88.8% of the ASH group and 73.8% of the GOUT group did not consume alcohol (Data not shown).

Metabolic Syndrome Frequency

The metabolic syndrome frequency was statistically significantly higher than the ASH group. The metabolic syndrome frequency of the individuals participating in the study is shown in Table 2.

The distribution of metabolic syndrome frequency by age and the groups (ASH and GOUT) is shown in Table 3. The highest metabolic syndrome frequency was 47.6% in individuals aged 20-29 for ASH group and 41.4% in individuals aged 40-49 for GOUT group (Table 3).

Table 2. Comparison of metabolic syndrome in accordance with ASH and GOUT groups and gender

| Metabolic Syndrome | | ASH (n= 80) | | GOUT (n= 65) | | Total (n= 145) | | p |
|--------------------------------|-------|----------------|-------|-----------------|-------|-------------------|-------|---------|
| | | n | % | n | % | n | % | |
| Presence of metabolic syndrome | Women | 15 | 71.4 | 13 | 44.8 | 28 | 56.0 | 0.061 |
| | Men | 6 | 28.6 | 16 | 55.2 | 22 | 44.0 | |
| | Total | 21 | 100.0 | 29 | 100.0 | 50 | 100.0 | |
| Absence of metabolic syndrome | Women | 51 | 86.4 | 13 | 36.1 | 64 | 67.4 | <0.001* |
| | Men | 8 | 13.6 | 23 | 63.9 | 31 | 32.6 | |
| | Total | 59 | 100.0 | 36 | 100.0 | 95 | 100.0 | |

ASH: asymptomatic hyperuricemia, GOUT: gouty arthritis.

Table 3. Metabolic syndrome frequency according to ASH and GOUT and age groups

| Disease Group | | Metabolic Syndrome | |
|---------------|-------|--------------------|------|
| | | n | % |
| ASH | 20-29 | 10 | 47.6 |
| | 30-39 | 4 | 19.0 |
| | 40-49 | 2 | 9.6 |
| | 50-59 | 4 | 19.0 |
| | 60-65 | 1 | 4.8 |
| GOUT | 20-29 | 5 | 17.2 |
| | 30-39 | 4 | 13.8 |
| | 40-49 | 12 | 41.4 |
| | 50-59 | 7 | 24.2 |
| | 60-65 | 1 | 3.4 |

ASH: asymptomatic hyperuricemia, GOUT: gouty arthritis.

Distribution of Anthropometric Measurements of ASH and GOUT Groups

In the ASH group, 42.9% of men and 42.4% of women were obese, 57.1% of men and 28.8% of women were overweight, and 0.0% of men and 28.8% of women were normal. In the GOUT group, 73.1% of women were obese, 19.2% were overweight, and 7.7% had normal BMI; these values were 56.4%, 41.0%, and 0.0% in men, respectively. The difference among BMI values according to gender and groups was statistically important among women ($p=0.021$) (Table 4).

While the mean waist circumference of the men was 106.3±20.29 cm in the ASH group, it was 104.1±17.26 cm in the GOUT group. It was 90.3±21.85 cm in women in the ASH group and 95.0±12.50 cm in women in the GOUT group. There was no signification among the mean values of waist circumference between the groups ($p=0.691$ for men, $p=0.302$ for women) (Data not shown). In the ASH group, 50.0% of the men and 45.5% of the women were in the high-risk group. In the GOUT group, 56.5% of men and 65.4% of women were in the high-risk group. There was no significant differentiation between the groups by

waist circumference classification ($p=0.105$) (Table 4).

Mean hip circumference of men was 109.2±11.20 cm in the ASH group and 110.0±11.67 cm in the GOUT group; it was 103.6±12.24 cm in women in the ASH group and 107.8±10.51 cm in women in the GOUT group. There was no statistical signification among the mean hip circumference values between the groups ($p=0.832$ for men, $p=0.126$ for women) (Data not shown).

Mean waist/hip ratio was 0.97±0.10 for men and 0.84±0.10 for women in the ASH group. The mean waist/hip ratio was 0.93±0.09 for men and 0.87±0.06 for women in the GOUT group. There was no statistical signification among the mean values of waist/hip ratio between the groups ($p>0.05$) ($p=0.215$ for men, $p=0.103$ for women). According to the mean waist/hip ratio classification, in the ASH group, 21.4% of the men were in the normal group and 78.6% of the men in the risk group, while 48.5% of the women were in the normal group and 51.5% in the risk group. In the GOUT group, 28.2% of the men were in the normal group and 71.8% in the risk group; 30.8% of the women were in the normal group and 69.2% were in the risk group. There was no

significant difference among waist/hip ratio values according to gender and groups ($p=0.123$) (Table 4).

The mean body fat percentage (%) was 29.9 ± 4.42 for men and 35.4 ± 6.77 for women in the ASH group. In the GOUT group, mean body fat percentage (%) for men was 30.7 ± 7.80 and 39.2 ± 4.22 for women. In both GOUT and ASH groups, mean body fat percentage values were higher in women and the

difference among them was statistically important ($p=0.008$) (Data not shown). In terms of the body fat percentages, 92.9% of men and 72.7% of women in the ASH group were in the risky class, while 92.3% of both gender in the GOUT group were in the risky class. There was a significant differentiation between the groups by gender ($p=0.040$) (Table 4).

Table 4. Distribution of anthropometric measurements of ASH and GOUT groups by gender

| Anthropometric Measurements | Men | | | | Women | | | | Total | Men | Women | |
|---------------------------------|-----|------|------|------|-------|------|------|------|-------|------|--------|--------|
| | ASH | | GOUT | | ASH | | GOUT | | | | | |
| | n | % | n | % | n | % | n | % | | | | p |
| BMI (kg/m²) | | | | | | | | | | | | |
| Underweight | - | - | 1 | 2.6 | - | - | - | - | 1 | 0.7 | 0.021* | |
| Normal | - | - | - | - | 19 | 28.8 | 2 | 7.7 | 21 | 14.5 | | |
| Overweight | 8 | 57.1 | 16 | 41.0 | 19 | 28.8 | 5 | 19.2 | 48 | 33.1 | | |
| Obese | 6 | 42.9 | 22 | 56.4 | 28 | 42.4 | 19 | 73.1 | 75 | 51.7 | | |
| Waist circumference (cm) | | | | | | | | | | | | |
| Normal | 2 | 14.3 | 9 | 23.1 | 25 | 37.9 | 4 | 15.4 | 40 | 27.6 | 0.105 | |
| Risk | 5 | 35.7 | 8 | 20.4 | 11 | 16.6 | 5 | 19.2 | 29 | 20.0 | | |
| High risk | 7 | 50.0 | 22 | 56.5 | 30 | 45.5 | 17 | 65.4 | 76 | 52.4 | | |
| Waist/hip ratio | | | | | | | | | | | | |
| Normal | 3 | 21.4 | 11 | 28.2 | 32 | 48.5 | 8 | 30.8 | 54 | 37.2 | 0.735 | 0.123 |
| Risk | 11 | 78.6 | 28 | 71.8 | 34 | 51.5 | 18 | 69.2 | 91 | 62.8 | | |
| Body fat percentage (%) | | | | | | | | | | | | |
| Normal | 1 | 7.1 | 3 | 7.7 | 18 | 27.3 | 2 | 7.7 | 24 | 16.6 | 1.000 | 0.040* |
| Risk | 13 | 92.9 | 36 | 92.3 | 48 | 72.7 | 24 | 92.3 | 121 | 83.4 | | |

ASH: asymptomatic hyperuricemia, GOUT: gouty arthritis, BMI: body mass index.

Metabolic Syndrome Frequency according to ASH and GOUT Groups (Presence of Insulin Resistance and Dyslipidemia)

In Table 5, the metabolic syndrome frequency was evaluated by groups, the presence of dyslipidemia, and insulin resistance of the individuals participating in the study. While 71.4% of women and 28.6% of men in the ASH group had metabolic syndrome, 86.4% of women and 13.6% of men did not have metabolic syndrome. In the GOUT group, there was metabolic syndrome in 44.8% of women and 55.2% of men; metabolic syndrome was not found in 36.1% of women and 63.9% of men. Insulin resistance was

72.7% in men with metabolic syndrome, while it was 57.1% in women. The differentiation between the groups was not important ($p=0.061$) (Table 5).

In terms of dyslipidemia status, 40.9% of men with metabolic syndrome had total cholesterol ≥ 200 mg/dL, 68.2% LDL ≥ 100 mg/dL, 18.2% HDL < 35 mg/dL, and 36.4% TG ≥ 150 mg/dL. In women with metabolic syndrome, 28.6% had total cholesterol ≥ 200 mg/dL, 53.6% had LDL ≥ 100 mg/dL, 25.0% had HDL < 35 mg/dL, and 28.6% had TG ≥ 150 mg/dL. However, no statistical significance was found among these values ($p=0.361$ for total cholesterol, $p=0.295$ for LDL, $p=0.561$ for HDL, $p=0.558$ for TG) (Table 5).

Table 5. Metabolic syndrome frequency according to ASH and GOUT groups, presence of insulin resistance and dyslipidemia

| Hospital Reference Values | Metabolic Syndrome | | | | | | | | | |
|------------------------------------|--------------------|----|---------------|----|-------------|------------|---------------|----|-------|---------------|
| | Yes (n= 50) | | | | | No (n= 95) | | | | |
| | Men (n= 22) | | Women (n= 28) | | Men (n= 31) | | Women (n= 64) | | p^1 | p^2 |
| % | n | % | n | % | n | % | n | | | |
| ASH | 28.6 | 6 | 71.4 | 15 | 13.6 | 8 | 86.4 | 51 | 0.061 | 0.644 |
| GOUT | 55.2 | 16 | 44.8 | 13 | 63.9 | 23 | 36.1 | 13 | | |
| Insulin resistance | | | | | | | | | | |
| HOMA-IR < 2.7 | 27.3 | 6 | 42.9 | 12 | 32.3 | 10 | 67.2 | 43 | 0.352 | $< 0.001^*$ |
| HOMA-IR ≥ 2.7 | 72.7 | 16 | 57.1 | 16 | 67.7 | 21 | 32.8 | 21 | | |
| Dyslipidemia | | | | | | | | | | |
| Total cholesterol < 200 mg/dL | 59.1 | 13 | 71.4 | 20 | 51.6 | 16 | 82.8 | 53 | 0.361 | 0.010* |
| Total cholesterol ≥ 200 mg/dL | 40.9 | 9 | 28.6 | 8 | 48.4 | 15 | 17.2 | 11 | | |
| LDL < 100 mg/dL | 31.8 | 7 | 46.4 | 13 | 29.0 | 9 | 53.1 | 34 | 0.295 | 0.027* |
| LDL ≥ 100 mg/dL | 68.2 | 15 | 53.6 | 15 | 71.0 | 22 | 46.9 | 30 | | |
| HDL < 35 mg/dL | 18.2 | 4 | 25.0 | 7 | 6.5 | 2 | - | - | 0.561 | 0.010* |
| HDL 35-55 mg/dL | 59.1 | 13 | 64.3 | 18 | 83.8 | 26 | 59.4 | 38 | | |
| HDL > 55 mg/dL | 22.7 | 5 | 10.7 | 3 | 9.7 | 3 | 40.6 | 26 | | |
| TG < 150 mg/dL | 63.6 | 14 | 71.4 | 20 | 83.9 | 26 | 100 | 64 | 0.558 | 0.030* |
| TG ≥ 150 mg/dL | 36.4 | 8 | 28.6 | 8 | 16.1 | 5 | - | - | | |

p^1 : Men and women with metabolic syndrome.

p^2 : Evaluation of the metabolic syndrome frequency by men and women without metabolic syndrome.

ASH: asymptomatic hyperuricemia, GOUT: gouty arthritis, HOMA-IR: Homeostasis Model Assessment of Insulin Resistance, LDL: low-density lipoprotein, HDL: high-density lipoprotein, TG: triglyceride.

DISCUSSION

The current study provides insights into the relationship of ASH and GOUT with metabolic syndrome. We used the biochemical, blood pressure, anthropometric, and body composition measurements to assess the all participants with ASH, GOUT, and metabolic syndrome. Hyperuricemia, abdominal obesity, low HDL, hypertension, hypertriglyceridemia, and hyperglycemia were the parameters used in this research to determine the association of ASH and GOUT with metabolic syndrome. In both gout and asymptomatic hyperuricemia, metabolic syndrome components may be affected. Thus, factors that may cause hyperuricemia and metabolic syndrome components should be evaluated together.

The mean of waist circumference, one of the indicators of abdominal obesity, was 106.3 ± 20.29 cm in men and 90.3 ± 21.85 cm in women in the ASH group in this study and it was concluded that both values were higher than the reference values (12). In another study conducted with 83 patients with ASH, a significant relationship was found among hyperuricemia with glucose intolerance, abdominal obesity, and hypertriglyceridemia, which are components of metabolic syndrome, excluding hypertension and HDL (15). Therefore, blood lipid and glucose controls, and certain anthropometric measurements (such as waist and hip circumference) should be routinely performed in treatment approaches in hyperuricemia.

In the cross-sectional study, there were 174 gout patients, 48.3% women and 51.7% men. The metabolic syndrome prevalence was 54.6% and no significant difference was found between women (59.5%) and men (50.0%) (16). In this study, 44.8% of women and 55.2% of men in the GOUT group had metabolic syndrome. Unlike the previous study (16), the metabolic syndrome frequency was greater in men with gout in this study.

In this study, the men/women ratio was 3/2 among gout patients. In the research carried out by Jung et al. (17) in Korean gout patients and investigating the metabolic syndrome prevalence,

the men/women ratio was 10.6/1, which was higher than our study. Furthermore, the mean age of gout patients was 51.28 ± 15.07 years in the same study (17) and it was 41.0 ± 12.68 years in our study, which was lower. The variation in the prevalence of gout according to age may be due to the socio-demographic features of the persons participating in the study.

According to a cross-sectional study of 9,206 Chinese individuals, when compared with BMI and waist circumference, waist/height ratio was accepted as the independent variable in the estimation of the presence of hyperuricemia (18). In a study conducted in Taiwanese men, a significant and linear relationship was found between waist/height ratio and gout. In addition, it was emphasized that waist/height ratio is a better anthropometric measurement in defining gout when compared to BMI, waist/hip ratio, and waist circumference (19). In this study, it was noted that all of the men (100.0%) and 71.2% of the women in the ASH group, 97.4% of the men and 92.3% of the women were overweight and obese in the GOUT group. In both groups, it was detected that men were more in the overweight and obese classes. In addition, it was found that 50.0% and more of men in both groups (ASH and GOUT) were in the high-risk group in terms of waist circumference measurements. Therefore, the evaluation of different anthropometric measurements together rather than a single anthropometric measurement and the fact that alcohol consumption is higher in men in nutritional habits should not be ignored in treatment protocols.

In terms of body fat percentages, 92.9% of men and 72.7% of women in the ASH group; 92.3% of both men and women in the GOUT group were in the risk group in this study. In a study examining the relationship between body fat distribution and uric acid metabolism, visceral fat accumulation elevated the hyperuricemia risk in elderly and middle-aged individuals, independent of neck circumference, BMI, and waist circumference (20). In a study of Vietnamese men with primary gout ($n=107$) and healthy ($n=107$) Vietnamese men, mean total body and trunk fat

masses in gout patients were found to be significantly higher than control group. Therewithal, it was stated that there was a strong and positive correlation between BMI and total body fat mass; a strong and positive correlation between trunk fat mass and waist circumference in gout patients. In addition, in accordance with the original and revised NCEP-ATP III criteria, the metabolic syndrome prevalence was significantly greater in gout patients (21). The balance of body fat composition and fat distribution can be shown among the factors included in the pathogenesis of systemic and metabolic diseases.

Gout patients in this study, 18.5% were in the age range of 20-29, 24.6% were 30-39, and 30.8% were 40-49 and it was specified that the gout frequency increased with age. On the contrary, according to the results of a cross-sectional study, a significant and negative relation was detected between age and uric acid concentrations in 653 individuals with gout (22).

In a study of 348 men gout patients, the dyslipidemia prevalence was significantly greater in those with excess fat (body fat percentage $\geq 25.0\%$) compared to those with normal body fat percentage (70.1%, 54.0%, respectively) (23). In a study of 41 primary gout patients to examine the metabolic syndrome prevalence and its constituents, 21 gout patients (51.0%) exhibited three or more of the metabolic syndrome components. Dyslipidemia was determined as one of the most common metabolic syndrome criteria with a rate of 73.17% (30/41) (24). In this study, when the components of dyslipidemia were examined, 40.9% of men with metabolic syndrome had total cholesterol ≥ 200 mg/dL, 68.2% had LDL ≥ 100 mg/dL, 18.2% had HDL < 35 mg/dL, and 36.4% had TG ≥ 150 mg/dL. In women with metabolic syndrome, these values were determined as 28.6%, 53.6%, 25.0%, and 28.6%, respectively. The higher HDL levels in men than in women can be demonstrated by the fact that men are physically more active. The metabolic syndrome prevalence in gout patients was significantly greater (43.6%) than the Korean control group. In

comparison to the control group, gout patients had more metabolic syndrome components. At the same time, BMI and HDL were stated as important factors in the emergence of metabolic syndrome in gout patients (25). In order to prevent cardiometabolic complications that may occur in gout patients with metabolic syndrome, metabolic syndrome components should also be targeted in the treatment.

It was noticed that individuals with insulin resistance had a substantially greater rate of metabolic syndrome. The mean serum uric acid level was greater in those with insulin resistance than in those without insulin resistance, but this differentiation was not important. Similarly, the mean serum uric acid level was greater in those with metabolic syndrome in comparison to those without metabolic syndrome, but it was not statistically important. It was revealed that there was no relationship among serum uric acid level with metabolic syndrome and insulin resistance (26). In the study in which 46 patients (men) with primary gout were classified according to the presence of metabolic syndrome, gout patients had significantly greater HOMA-IR levels. Furthermore, those with metabolic syndrome had significantly greater uric acid levels. In addition, gout patients with metatarsophalangeal (big toe joint) joint erosion had significantly higher insulin resistance values (27). In another study, the metabolic syndrome prevalence in gout patients was found to be 30.1% according to ATP III criteria and 50.6% according to WHO Asia-Pacific criteria. In addition, the mean HOMA-IR value in gout patients was determined as 2.63 ± 1.36 and it was observed that it was significantly greater than the control group (28). In this study, insulin resistance was found in more than half of men and women with metabolic syndrome. Since there are common factors that can cause hyperinsulinemia and hyperuricemia, care should be taken when questioning a nutritional history.

The individuals in both (ASH-GOUT) groups were selected by the determined criteria and data were collected through the questionnaire in face-

to-face interviews, which increased the originality of the data. These were the strengths of the study.

The limitations of the study incorporated the smaller sample size and it was a single centre study. We recommend that further population-based studies (epidemiological, meta-analysis etc.) and also multicenter studies should be carried out in future to evaluate the association of gouty arthritis and asymptomatic hyperuricemia with metabolic syndrome.

In conclusion, while gout is seen more with increasing age, asymptomatic hyperuricemia can also occur at younger ages. As there is an increase in blood uric acid levels without symptoms in

asymptomatic hyperuricemia, urate crystals formed in gout may adversely affect the prognosis and treatment approaches of the disease. In both gout and asymptomatic hyperuricemia, metabolic syndrome components (waist circumference, HDL, TG, blood pressure, and blood glucose) may be affected. Therefore, factors that may cause hyperuricemia and hyperinsulinemia should be evaluated together. Furthermore, the development of metabolic syndrome can be prevented by evaluating various anthropometric measurements, biochemical tests, and nutrition and health history together in gout and asymptomatic hyperuricemia treatment.

ETHICS COMMITTEE APPROVAL

* This study was approved by the Baskent University Non-Interventional Clinical Research Ethics Committee (Date: 12.04.2016 and Number: 94603339-604.01.02/12438).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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