



Metabolic syndrome: prevalence and risk factors in Korean gout patients

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Received: February 26, 2016
Revised: May 13, 2016
Accepted: May 23, 2016

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Background/Aims: We performed this study to investigate associations between metabolic syndrome, chronic kidney disease (CKD), and gout.

Methods: We reviewed the medical records of 151 patients with gout at the Department of Rheumatology in Korea University Ansan Hospital. The following measures were examined: waist circumference, blood pressure, alcohol consumption, and levels of triglyceride, high density lipoprotein cholesterol, fasting serum glucose, serum uric acid (SUA), creatinine, insulin, and C-peptide. We assessed metabolic syndrome by the homeostasis model assessment of insulin resistance (HOMA-IR) index and renal function by the Modification of Diet in Renal Disease equation; patients were classified according to World Health Organization Asia-Pacific obesity criteria.

Results: The prevalence of metabolic syndrome in gout patients (50.8%) was higher than in non-gout patients. The mean SUA level was significantly higher in gout patients with metabolic syndrome (9.13 ± 3.15 mg/dL) than in gout patients without metabolic syndrome (8.14 ± 2.07 mg/dL). The mean SUA level was also significantly higher in patients with gout and CKD (9.55 ± 2.86 mg/dL) than in patients with gout but no CKD (7.74 ± 2.27 mg/dL). In gout patients, HOMA-IR was positively correlated with waist circumference ($r = 0.409$, $p = 0.001$).

Conclusions: The prevalence of metabolic syndrome in patients with gout was 50.8%, which is higher than the prevalence in the general Korean population. Hyperuricemia in gout patients was correlated with metabolic syndrome and CKD. Insulin resistance may provide clues to better understand the relationship between metabolic syndrome, CKD, and gout.

Keywords: Metabolic syndrome; Gout; Renal insufficiency, chronic; Obesity, abdominal; Insulin resistance

INTRODUCTION

Gout is a disease caused by deposition of monosodium urate monohydrate crystals in joints. Gout is associated with metabolic syndrome related comorbidities such as obesity, hypertension, abnormal lipid metabolism, and impaired glucose tolerance [1]. Previous studies suggest

that the prevalence of metabolic syndrome is high among patients with gout, ranging from 30.1% to 82.0% [2]. In 2004, Rho et al. [3] showed that the prevalence of metabolic syndrome in Korean gout patients was 59.4% according to Adult Treatment Panel III (ATP III) criteria with World Health Organization (WHO) Asia-Pacific adjustment; the prevalence was 57.2% in 2005 [4]. Subsequently, Yoo et

al. [5] showed that the prevalence was 50.6% in 2009. Although the current exact prevalence of metabolic syndrome in Korean gout patients is not known, these results indicate that the prevalence may be decreasing.

The prevalence of metabolic syndrome in the Korean general population in 2012 was 28.2% according to ATP III criteria with WHO Asia-Pacific adjustment [6]. In Korea, the prevalence of metabolic syndrome has increased in recent years [7] and gout prevalence has also increased [8]. Thus, in this study we investigated the prevalence of metabolic syndrome in gout patients and determined whether the presence of metabolic syndrome affects serum uric acid (SUA) levels and if the prevalence of metabolic syndrome in Korean gout patients has changed since the last study published 5 years ago.

We also analyzed the relationship between alcohol consumption, chronic kidney disease (CKD), and gout. Multiple studies have shown an association between alcohol intake and hyperuricemia, which is a common precipitating cause of gouty arthritis [9]. Consistent with reports that the prevalence of gout is increasing worldwide, the prevalence of gout in Korea has also been shown to be increasing rapidly. Lee et al. [10] showed that an increase in the frequency and in the amount of alcohol consumption was associated with a higher prevalence of gout. In addition, CKD commonly occurs among gout patients [11]. To date, results from studies that have tested the correlation between metabolic syndrome and CKD [12,13] have reported that patients with greater diagnostic criteria for metabolic syndrome have a higher chance of CKD.

METHODS

Subjects

We reviewed the medical records of 151 patients (138 men and 13 women) with gout. All patients were seen between 2003 and 2014 at the Department of Rheumatology of Korea University Ansan Hospital. Patients satisfied the preliminary criteria of gout according to guidelines from the American College of Rheumatology [14]. Some patients came to the clinic for acute gout attack and were referred by their employers for the examination. Others were referred by their personal physicians or were self-referred.

Clinical and biochemical investigations

At clinic visits, the body mass index (BMI) of each patient was calculated using the height and weight. In addition, waist circumference (WC) and blood pressure (BP) at systolic and diastolic phases were measured. Levels of triglycerides (TGs), high density lipoprotein cholesterol (HDL-C), fasting serum glucose, SUA, and creatinine after a 12-hour fast state were measured. In order to study insulin resistance, we measured the concentrations of insulin and C-peptide. Insulin resistance was assessed by the homeostasis model assessment of insulin resistance (HOMA-IR), which is calculated from fasting plasma glucose level and fasting insulin (insulin resistance index) [15]. Renal function in gout patients was evaluated by the estimated glomerular filtration rate (eGFR), calculated using the Modification of Diet in Renal Disease equation [16]. The eGFR was classified as normal, mildly impaired, moderately impaired, or severely impaired according to the following cutoffs: ≥ 90 , 60 to 89, 30 to 59, and < 30 mL/min/1.73 m², respectively. HOMA-IR and eGFR were calculated using the following equations: $\text{HOMA-IR} = \text{fasting insulin } (\mu\text{IU/mL}) \times \text{fasting glucose } (\text{mmol/L}) / 22.5$; $\text{eGFR} = 186 \times (\text{serum creatinine})^{-1.154} \times \text{age} - 0.203$.

In accordance with a report by the National Cholesterol Education Program, a patient was diagnosed with metabolic syndrome if more than three categories were satisfied among the following five criteria: (1) central obesity (WC greater than 102 cm in men and 88 cm in women); (2) concentration of TG greater than 150 mg/dL; (3) concentration of HDL-C less than 40 mg/dL in men and 50 mg/dL in women; (4) BP greater than 130/85 mmHg or under medical treatment of hypertension; or (5) concentration of serum glucose in fasting state greater than 100 mg/dL or under medical treatment of diabetes [17]. The first criterion for central obesity was re-evaluated to 90 cm in men and 80 cm in women, according to the Asia-Pacific obesity criteria (APC) by the WHO [18]. For patients without WC data, the first criterion for central obesity was substituted with a BMI greater than 25 kg/m², in accordance with modified criteria from ATP III [19].

As history of alcohol consumption was not consistently assessed in all patients, we divided patients into two groups: drinking and non-drinking. Patients who drank regularly and consumed more than one bottle a week were included in the drinking group, and the patients

who drank socially and less than one bottle a week were included in the non-drinking group [10].

Statistical analysis

Data was analyzed using the software IBM SPSS version 19.0 (IBM Co., Armonk, NY, USA) and results were presented in the form of mean \pm standard deviation. We performed descriptive statistics for general demographic characteristics and calculated the prevalence of metabolic syndrome. Incidence of metabolic syndrome in gout patients was assessed using the chi-square test for categorical data and Student *t* test for continuous data. We used a multivariate logistic regression model to estimate the odds ratios for clinical and laboratory findings. All confidence intervals were at 95%, and a *p* < 0.05 was considered significant.

Ethical statement

This study was performed in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Korea University Ansan Hospital. The informed consent was waived.

RESULTS

General characteristics of patients with gout

A total of 151 patients with gout were included in this study. There were a total of 138 male patients and 13 female patients (10.6:1). The mean age of gout onset was 51.28 ± 15.07 years, the mean weight was 70.72 ± 12.99 kg, the mean BMI was 25.07 ± 3.62 kg/m², and the mean WC was 91.86 ± 9.93 cm. The mean BMI indicated obesity according to APC by the WHO. The mean SUA level was 8.70 ± 2.64 mg/dL, mean concentration of creatinine was 1.59 ± 1.15 mg/dL, mean eGFR was 59.08 ± 19.79 mL/min/1.73 m² and mean HOMA-IR was 3.78 ± 5.93 . A total of 69.5% of patients had hypertension and 17.9% had diabetes mellitus (DM). Other general characteristics of study patients are described in Table 1.

The prevalence rate of metabolic syndrome

Using the WHO APC, we diagnosed 66 of 130 (50.8%) with metabolic syndrome. Table 2 shows the prevalence of the criteria for metabolic syndrome. Among all patients, 78.8% had hypertension, 54.7% had hyperglycemia, 46.5% had low HDL-C, and 33.1% had high fast-

Table 1. Descriptive characteristics of gout patients

Factor	Mean \pm SD
Age, yr	51.28 \pm 15.07
Male	50.33 \pm 15.11
Female	61.38 \pm 10.69
Height, m	167.67 \pm 7.34
Male	169.04 \pm 5.83
Female	153.38 \pm 6.29
Weight, kg	70.72 \pm 12.99
Male	71.75 \pm 12.96
Female	59.92 \pm 7.19
Body mass index, kg/m ²	25.07 \pm 3.62
Male	25.03 \pm 3.66
Female	25.56 \pm 3.39
Waist circumference, cm ^a	91.86 \pm 9.93
Male	91.45 \pm 10.03
Female	96.17 \pm 8.28
Systolic blood pressure, mmHg	129.00 \pm 16.31
Diastolic blood pressure, mmHg	81.71 \pm 14.03
Fasting serum glucose	108.26 \pm 39.01
Insulin, μ IU/mL	13.98 \pm 17.91
Insulin resistance (HOMA-IR)	3.78 \pm 5.93
Total cholesterol, mg/dL	186.59 \pm 42.86
Triglyceride, mg/dL	200.49 \pm 132.76
HDL-C, mg/dL	41.87 \pm 14.61
Uric acid, mg/dL	8.70 \pm 2.64
Creatinine, mg/dL	1.59 \pm 1.15
eGFR, mL/min/1.73 m ²	59.08 \pm 19.79

Total number of male patients was 138 and female patients was 13 (10.6:1).

HOMA-IR, homeostasis model assessment of insulin resistance; HDL-C, high density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate.

^aOnly 69 values present (males 67, females 2).

ing glucose. Finally, central obesity was diagnosed in 49.3% (APC) of the patients. The number of normal body weight, overweight, and obese patients was 42 (28.4%), 44 (29.7%), and 62 (41.9%), respectively. The prevalence of metabolic syndrome according to age is presented in Table 3.

The average HOMA-IR in gout patients was 3.78 ± 5.93 . We compared clinical factors between the non-drinking and drinking groups. The mean TG level was higher in

Table 2. Prevalence rate of each metabolic syndrome criterion in gout patients compared to control groups (n = 150)

Variable	No. (%)
Obesity	
BMI > 25	148 (41.9)
WC ^a	69 (56.5)
APC	150 (49.3)
TG ≥ 150	128 (54.7)
HDL-C ^b	127 (46.5)
Fasting serum glucose ≥ 110	145 (33.1)
BP ≥ 130/85	150 (78.8)

BMI, body mass index; WC, waist circumference; APC, Asia-Pacific obesity criteria; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; BP, blood pressure.

^a> 90 Males, > 80 females.

^b< 40 Males, < 50 females.

Table 3. The prevalence of metabolic syndrome according to age

Variable	Metabolic syndrome (APC)
Age, yr	
≤ 29	4/10 (40.0)
30–39	9/26 (34.6)
40–49	18/38 (47.4)
50–59	14/30 (46.7)
60–69	12/24 (50.0)
70–79	9/20 (45.0)
80–89	0/3
Total	66/151 (43.7)

Values are presented as number (%).

APC, Asia-Pacific obesity criteria.

Table 4. Mean serum uric acid level in gout patients according to metabolic syndrome and chronic kidney disease

Variable	No.	SUA, mg/dL	p value
MS			
MS+	65	9.13 ± 3.15	0.024
MS–	63	8.14 ± 2.07	
CKD			
CKD+	67	9.55 ± 2.86	0.001
CKD–	63	7.74 ± 2.27	
MS CKD			
MS+CKD– ^a	31	8.15 ± 2.45	0.161
MS–CKD– ^b	32	7.34 ± 2.04	
MS+CKD+ ^c	35	10.14 ± 3.50	0.073
MS–CKD+ ^d	32	8.91 ± 1.78	

Values are presented as mean ± SD.

SUA, serum uric acid; MS, metabolic syndrome; CKD, chronic kidney disease.

^aWith only MS. ^bWithout MS or CKD. ^cWith both metabolic syndrome and CKD. ^dWith only CKD.

the drinking group (43.22 ± 11.84 mg/dL) compared to the non-drinking group (39.83 ± 16.40 mg/dL); however, this result was not statistically significant, and there were no significant differences between the two groups according to other clinic factors.

Serum uric acid level, chronic kidney disease, and metabolic syndrome

Table 4 compares SUA levels between gout patients with metabolic syndrome and gout patients without meta-

bolic syndrome. We observed that mean SUA levels in gout patients with metabolic syndrome differed significantly from those in gout patients without metabolic syndrome (9.13 ± 3.15 mg/dL vs. 8.14 ± 2.07 mg/dL, respectively; *p* = 0.024). We also determined whether SUA levels differed between gout patients with and without CKD. Presence of CKD was defined as having an eGFR less than 60 mL/min/1.73 m² [11]. The mean SUA level in patients with gout and CKD was significantly higher than that of patients with gout but no CKD (9.55 ± 2.86

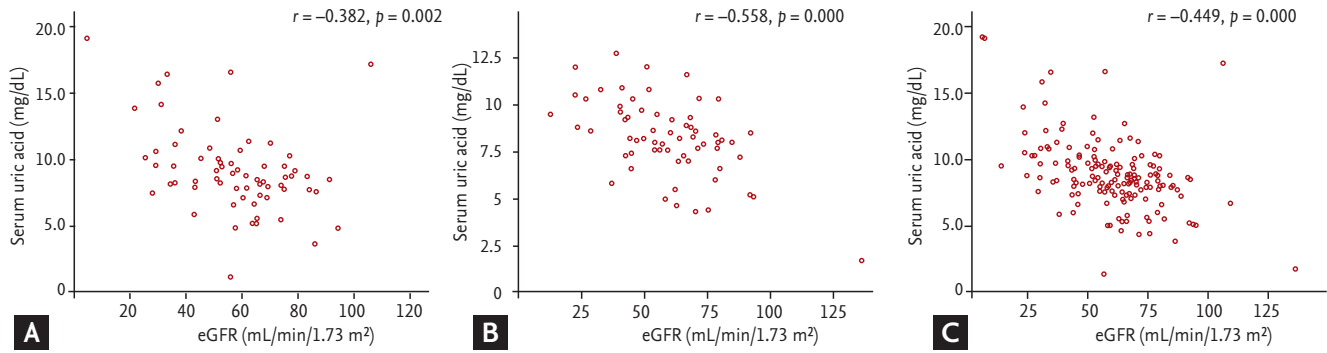


Figure 1. Correlation between serum uric acid level and eGFR among subjects (A) with gout and metabolic syndrome (n = 66), (B) with gout and without metabolic syndrome (n = 64), and (C) with gout (n = 151) by Pearson correlation.

mg/dL vs. 7.74 ± 2.27 mg/dL, $p = 0.001$).

Based on the results shown in Table 4, we classified patients into four groups: (1) those with both metabolic syndrome and CKD (MS+CKD+); (2) those with only CKD (MS-CKD+); (3) those with only metabolic syndrome (MS+CKD-); and (4) those without metabolic syndrome or CKD (MS-CKD-). We observed differences between the MS+CKD- and MS-CKD- groups, and between the MS+CKD+ and MS-CKD+ groups; however, these differences were not statistically significant.

We analyzed the correlation between SUA levels and eGFR among gout patients with and without metabolic syndrome. There was a negative correlation between SUA level and eGFR for patients with metabolic syndrome as well as those without metabolic syndrome (Fig. 1). This correlation was stronger in the patients without metabolic syndrome than in patients with metabolic syndrome.

DISCUSSION

Results from this study showed that the prevalence of metabolic syndrome among Korean gout patients is higher than among the general Korean population and not lower than that of previous studies. Elevated mean SUA levels were found to be significantly increased by the component number of metabolic syndrome [20]; furthermore, the prevalence of metabolic syndrome also increased significantly with SUA level [13]. Although it has been reported that weight loss helps in achieving target SUA level in hyperuricemia or gout patients [21],

Table 5. Correlation between insulin resistance (HOMA-IR) and criterion of metabolic syndrome

Variable	HOMA-IR	
	R	p value
Body mass index	0.317	0.000
Waist circumference	0.409	0.001
Systolic blood pressure	0.078	0.392
Diastolic blood pressure	0.053	0.559
Triglyceride	-0.092	0.344
HDL-C	0.014	0.890

HOMA-IR, homeostasis model assessment of insulin resistance; HDL-C, high density lipoprotein cholesterol.

weight loss was found to be less effective than medicines that reduced SUA levels. In addition, results from previous studies have suggested that weight loss may prevent the recurrence of acute gout attack [9], weight gain increases the occurrence of gout, and weight loss has a protective effect against gout [22].

Gout is rare in people of younger age and increases in frequency with age, but has recently been observed to be increasingly prevalent in younger adults. The prevalence of gout in adults under 30 years of age was 6.62% (10 patients among total 151 patients) in our study. Among these 10 patients, four patients had metabolic syndrome; systolic BP in these patients was greater than 135 mmHg. The increasing incidence of gout in younger adults may be related to metabolic syndrome, especially hypertension [1].

The HOMA-IR is a simple method for evaluation of

insulin sensitivity and is correlated with results of the glucose clamp test in subjects with mild diabetes without significant hyperglycemia [23]. The average HOMA-IR in gout patients was 3.78 ± 5.93 , which was higher than non-gout populations; in a previous study of 7,057 adults, average HOMA-IR was 1.85 ± 0.96 [12]. In correlation analyses between HOMA-IR and each diagnostic criterion of metabolic syndrome, BMI and WC showed the most significant positive correlation (Table 5). We concluded that, among the diagnostic criteria for metabolic syndrome, central obesity is most associated with increased insulin resistance in gout patients. As type 2 DM is associated with insulin sensitivity representing HOMA-IR, future studies should test the correlation between DM and gout.

We investigated the prevalence of metabolic syndrome and CKD. We also observed that patients with metabolic syndrome are more likely to have increased SUA levels, as eGFR is low. In this study, we found that CKD is an independent risk factor for hyperuricemia and gout, and CKD combined with metabolic syndrome was a stronger risk factor. As both metabolic syndrome and CKD are increasing in prevalence in Korea [24,25], prevention of these diseases is important to decrease gout occurrence. Gout is also a risk factor of CKD. In animal studies, injection of hypouricemic agents suppressed the progression of renal disease [26]. Administration of allopurinol to patients with CKD to control hyperuricemia prevents decline of kidney function [27]. For gout patients, allopurinol, febuxostat, or benzbromarone are used as hypouricemic agents.

The strong association between insulin resistance in gout patients and central obesity should be seriously considered. Control of metabolic syndrome is expected to be more useful when medication is limited due to impaired renal function. For gout patients, we suggest combining lifestyle modifications, such as exercise and diet, with medication to reduce risk factors such as occurrence and progression of renal disease, metabolic disease, and cardiovascular disease, which can be achieved with less expense.

This study has several limitations. First, it was a retrospective study conducted at a single center. In addition, the study population was too small for the study to have statistical power. Finally, as gout occurs more frequently in males, the proportion of female patients in this study

was small.

In conclusion, the prevalence of metabolic syndrome was higher in patients with gout than in the general Korean population. Hyperuricemia in gout patients has been correlated with metabolic syndrome and CKD, and insulin resistance may provide clues to better understand the relationship between gout, metabolic syndrome, and CKD. Further studies are underway to test the correlation between SUA and kidney function in gout patients under aggressive control of metabolic syndrome. We expect that in gout patients receiving limited medication due to impaired renal function, control of metabolic syndrome will lead to reductions in SUA levels and slow the deterioration of kidney function.

KEY MESSAGE

1. The prevalence of metabolic syndrome in patients with gout is higher than that in the general Korean population.
2. Hyperuricemia in gout patients is correlated with metabolic syndrome and chronic kidney disease.
3. Average insulin resistance was higher in gout patients, and central obesity had the greatest impact on insulin resistance.
4. Insulin resistance may provide clues to better understand the relationship between gout, metabolic syndrome, and chronic kidney disease.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

This study was funded by a grant from Korea University Medical College.

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