# Determining the Frequency of Metabolic Syndrome Among Patients with Gout

Elahe Elhami[a], Channaraya. V[b]

a   Pharm D, Visveswarapura Institute of Pharmaceutical Sciences, Bangalore, India
b   Professor and HOD, Medicine, KIMS Hospital, Bangalore, India

### Abstract

**Background:** *The metabolic syndrome describes a group of modifiable risk factors occurring in the same individual and associated with an increased risk of developing cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Increased serum urate concentration and gout were already recognised as important features. The aim of this study was to determine the prevalence of metabolic syndrome among patients with gout.*

**Methods:** *All patients who were diagnosed with gout referred to Kims Hospital and St. Philomenas hospital were studied according to the criteria of metabolic syndrome. The variables included age, sex, weight, height, body mass index (BMI), blood pressure, waist circumference, cigarette smoking, triglyceride, liver enzymes, and liver sonography. SPSS version 19 was used for statistical analysis.*

**Results:** *A total of 70 gout patients (62 men and 8 women) with a mean age of 46±14.2 years (range 75–34 years) and a mean period of 4.5 years of gouty arthritis; the prevalence of metabolic syndrome was 84% (59 patients). The prevalence of other abnormalities, such as BMI>24 (75.5%), central obesity (68.5%), hypertension (52.8%), fatty liver (37.2%), TG (31.4%), and T2DM (12.4%), was also studied. Also 38.5% of patients had a history of cigarette smoking. The mean BMI in this group of patients was 26 kg/m$^2$.*

**Conclusion:** *The prevalence of metabolic syndrome among patients with gout is very high. Efforts should be aimed to decrease the cardiovascular risk factors among these patients.*

**Keywords:** *metabolic syndrome, gout, patients with gout, prevalence*

## Introduction

The first description of patients with clustering of various metabolic abnormalities such as hypertension, hyperglycaemia, and hyperuricaemia, was observed as early as 1923, but it was more than five decades after this observation, in 1988, that Reaven coined the term 'syndrome X' for this conglomeration of various metabolic abnormalities, including glucose intolerance, hypertension, increased very low density lipoproteins (VLDLs), triglycerides, and decreased high-density lipoprotein cholesterol (HDL-C), with insulin resistance being the basic underlying pathophysiologic problem.[1–3] WHO defined metabolic syndrome (MS) in 1999: glucose

intolerance, impaired glucose tolerance (IGT), or diabetes mellitus (DM), and/or insulin resistance, together with two or more of the components listed below:

1. Raised arterial pressure, that is, ≥140/90 mm of Hg.

2. Raised plasma triglyceride (≥150 mg/dl) and/or low HDL-C (<35 mg/dl in men and <39 mg/dl in women).

3. Central obesity, that is, waist/hip ratio (WHR) >0.9 in men and >0.85 in women and/or body mass index (BMI) >30 kg/m$^2$.

4. Micro albuminuria, that is, urinary albumin excretion rate ≥20 μg/min or albumin/creatine ratio ≥30 μg/mg.[4]

The European Group for Study of Insulin Resistance (EGIR) proposed a modification of the WHO definition, using the term 'insulin resistance syndrome' rather than MS. According to the EIGR definition, the diagnostic criteria included elevated plasma insulin (>75$^{th}$ percentile) plus two other factors that are listed below:

1. Abdominal obesity: waist circumference (WC) ≥94 cm in men and ≥80 cm in women.

2. Hypertension: ≥140/90 mm Hg or on anti hypertensive treatment.

3. Elevated triglycerides (≥150 mg/dl) and/or reduced HDL-C (<39 mg/dl for both men and women).

4. Elevated plasma glucose: impaired fasting glucose (IFG) or IGT, but no diabetes.

In general, EGIR focused more on abdominal obesity than did WHO, but in contrast to WHO EGIR excluded patients with type 2 DM from their syndrome because insulin resistance was viewed primarily as a risk factor for diabetes.[5] This definition was followed by a simpler definition released by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III).[6] According to their definition, a subject has the MS if he or she has three or more of the following criteria:

1. Abdominal obesity: WC ≥102 cm in men and ≥88 cm in women

2. Hypertriglyceridaemia: ≥150 mg/dl (1.695 mmol/l).

3. Low HDL-C: <40 mg/dl in men and <50 mg/dl in women.

4. High blood pressure (BP): >130/85 mm Hg.

5. High fasting glucose: >110 mg/dl.

Identification of MS can be done more clinical by including clinical parameters such as age, family history, and personal history. Indian diabetes risk score (IDRS) is one such parameter comprising simple clinical information such as age, WC, family history of diabetes, and physical activity.[7] IDRS ≥60 has been found to be useful in predicting MS and cardiovascular disease.[8] Gout is an inflammatory arthritis that is associated with hyperuricaemia and is also widely known to be associated with obesity, dyslipidaemia, hyperglycaemia, and hypertension. Such metabolic abnormalities have recently been increasingly recognised as not being separate illnesses, but rather they are a clustered syndrome that has been termed the 'metabolic syndrome'.[9] Hyperuricaemia may be an asymptomatic condition, with an increased serum uric acid concentration as the only apparent abnormality. A urate concentration of >7.0 mg/dl is abnormal and is associated with an increased risk for gout. Acute attacks of gouty arthritis may be precipitated by stress, trauma, alcohol ingestion, infection, surgery, rapid lowering of serum uric acid by ingestion of uric acid-lowering agents, and ingestion of certain drugs known to elevate serum uric acid concentrations.[10] Treatment strategies include (1) reducing inflammation during acute attacks (with colchicines, non-steroid anti-inflammatory drugs (NSAIDs), or glucocorticoids), (2) accelerating renal excretion of uric acid with uricosuric drugs (probenecid or sulfinpyrazone), and (3) reducing (with allopurinol or febuxostat) the conversion of purines to uric acid by xanthine oxidase.[11] The objective of this study was to determine the frequency of MS, dyslipidaemia, fatty liver, smoking, diabetes, and high blood pressure in gout patients.

**MATERIALS AND METHODS**

This was a cross-sectional study conducted on both inpatients and outpatients who were diagnosed with gout of KIMS hospital and St. Philomena's,

Bangalore, from April 2015 to March 2016. We enrolled 70 patients with gout in our study. The studies were conducted in all individuals of either sex, irrespective of age, diagnosed with gout (joint swelling and joint tenderness, inflammation including redness, warmth, and blood urate level >0.7mg/dl). Data were extracted from the patient case sheets and laboratory reports (of blood sugar levels, blood lipids, and blood urate levels) and were collected using a data collection form. Information regarding socio-demographic details of the patients, pertaining to age, gender, height, weight, duration of gout, co-morbidity, smoking, and blood pressure was collected and recorded.

The laboratory test results of high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), fasting blood glucose (FBS), abdominal obesity, waist circumference, BMI, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were recorded.

## STATISTICAL ANALYSIS

Results were expressed as mean ± SD or percentage where appropriate statistical analyses were performed using the SPSS version. Chi-square tests and *t*-test were used to determine the relationship between variables. The relationships between serum uric acid levels and other variables were assessed using the Pearson's correlation coefficients.

## RESULT

Seventy patients (62 men and 8 women) with gout were enrolled in our study. The mean age of patients with gout in our study population was 46±14.2 years. Among our study population, the age range of gout patients was 34–75 years. The mean duration of gout observed was 4.5±7.3 years. A minimum duration of developing gout was 2 years, and a maximum duration of developing gout was 15 years. The mean height and weight of patients were 178±85 cm and 85±3.2 kg, respectively. In our study, the average BMI in gout patients was 26 kg/m². Patients with gout had 8.1±2.5 mg/dl uric acid, with minimum and maximum range of 3–13. The mean TG of patients with gout in our study was 173±84 mg/dl, with

| Table 1 \| Distribution of the characteristics of gout patients admitted to a hospital in 2015–2016 | | | |
|---|---|---|---|
| | Average | Standard deviation | Scope changes. |
| Age (years) | 46 | 14.2 | 34–75 |
| Duration of gout (years) | 4.5 | 7.3 | 2–15 |
| Height of patients (cm) | 178 | 8.5 | 165–190 |
| Weight of patients (kg) | 85 | 3.2 | 83–101 |
| BMI (kg/m²) | 26 | 1.6 | 23–31 |
| AST (mg/dl) | 22 | 42 | 8–124 |
| ALT (mg/dl) | 18 | 31 | 5–103 |
| TG (mg/dl) | 173 | 84 | 114–312 |
| Blood uric acid (mg/dl) | 8.1 | 2.5 | 3–13 |

minimum and maximum range of 114–312 (Table 1).

A total of 70 gout patients were admitted to a hospital in 2015–2016. Nine patients (12.8%) were with diabetes type 2, and 53 patients (75.7%) had a BMI>24. In our study, 37 patients (52.8%) had hypertension, 48 patients (68.5%) had abdominal obesity, 22 patients (31.42%) had dyslipidaemia (triglycerides >150 and HDL<40 in men or <50 in women), 27 patients (38.5%) were current smokers, and 26 patients (37.2%) had fatty liver (Table 2).

Based on the MS criteria (ATPIII), of 70 patients with gout enrolled in our study, 3 patients (4.2%) had one MS criteria, 8 patients (11.5%) had two MS criteria, 30 patients (42.8%) had three MS criteria, thus, the MS was positive in this group, and a total of 29 patients (41.4%) had more than three MS criteria – thus, this group had a very high risk to develop cardiovascular disease (Fig. 1).

| Table 2 \| Frequency distribution characteristics of gout patients admitted to a hospital in 2015–2016 based on the metabolic syndrome criteria | | |
|---|---|---|
| | Frequency | % |
| Men | 62 | 88.5 |
| Women | 8 | 11.5 |
| Diabetics | 9 | 12.8 |
| BMI>24 | 53 | 75.7 |
| BP≥130/85 | 37 | 52.8 |
| Smoking | 27 | 38.5 |
| Fatty liver | 26 | 37.2 |
| Central obesity (waist circumference >95 cm) | 48 | 68.5 |
| Dyperlipidaemia | 22 | 31.4 |
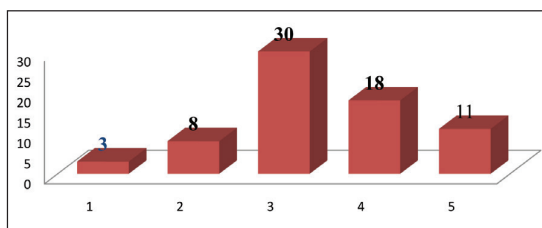
**Figure 1** | Distribution of the number of criteria of metabolic syndrome in gout patients.

Of 70 gout patients enrolled in our study show that serum uric acid levels had positive correlations with waist circumference, BMI, BP, aspartate aminotransferase, alanine aminotransferase, and triglycerides. Age was negatively correlated with serum uric acid in men but positively correlated with that in women (Fig. 2).
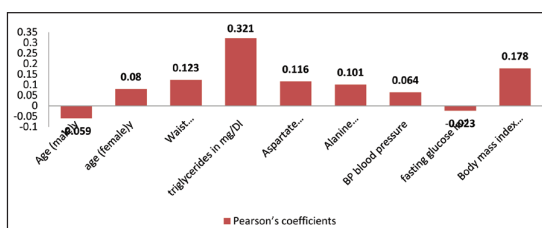


**Figure 2** | Correlation between serum uric acid and investigated variables

## Discussion

It was shown in this study that of 70 gout patients, 62 (88.57%) were men and 8 (11.42%) were women (Table 2). The mean age of patients with gout in our study population was 46±14.2 years (range 34–75 years; Table 1). The duration of gout plays an important role in its management. The mean duration of gout observed was 4.5±7.3 years. In this study, the prevalence of MS was 84% (*n*=59). The maintenance of a healthy body weight should remain the cornerstone of gout. Body mass index (BMI) was calculated by dividing the weight of the patients in kilogram by the square of their height in metres. Furthermore, the prevalence of other metabolic disorders in this group was as follows: BMI>24 (75.7%), abdominal obesity (68.5%), high blood pressure (52.8%), dyslipidaemia (31.4%), diabetes (2.4%), and fatty liver (37.2%). Also 38.5% patients were smokers, which is one of the risk factors for cardiovascular disease. Of the total population,

the mean BMI of patients with gout in our study population was 26 kg/m$^2$. The mean age of patients with gout in our study population was 46+14.2 years. This was also similar to the results of the other studies conducted worldwide.[12] The prevalence of gout increases with age, and the peak incidence age is 55–64 years.[12] In our study, a high proportion of gout in male patients is 88.5%. The high prevalence of the MS has also seen worldwide. In a study conducted in USA by Ford ES, 24% of adult patients had MS,[13] while in other studies conducted in Europe by Balkau and Ozsahin, 13%–33% patients had MS.[14,15] The prevalence of MS was increased with age to about 50% in people who are over 60 years. In our study, the prevalence of MS in gout patients was 84%. This was also similar to the results of a study conducted in Mexico by Melladoet al., where they found that the prevalence of MS was 82% in gout patients,[16] which was comparable with a study conducted by Hyonin the USA – their results showed that the prevalence of MS in gout patients was 62.5%.[17] However, a study conducted in Spain by Cuevaset al. showed that in 90%, the first attack of gout preceded the diagnosis of the features of MS.[18] Most probably, racial differences and the special diet are cause for reducing the prevalence of MS in Japan by Inokuchi[19] and in Spain by Fraile[20] in less than these values (36% and 51%, respectively). The prevalence of MS in South Korea is very similar to Japan. Probably this is due to a close race between the Japanese and the Koreans. As a result, the difference in the prevalence of MS in gout patients due to differences in sample size and methods sometimes slight differences in the study populations and definitions of MS. The study found that the prevalence of MS in gout patients is very high that can confirm the relationship between these two pathologies. In this study, 12.4% of diabetic patients had abnormal. As we know, high insulin levels can reduce the renal excretion of urate.[21–23] For example, it has been shown that the exogenous insulin reduces excretion of urate in healthy subjects and patients with high blood pressure.[24] Perhaps insulin increases the reabsorption of urate in the proximal tubule. In a study conducted in the USA,[17] 50% patients had the

prevalence of IFG (FBS>100 mg/dl), which is much higher than that in our results. The same situation is even among the control group who did not develop gout was 27%. Most probably, high-calorie diet is responsible for pre-diabetes. In a study conducted in Mexican, it was found that out of population enrolled in the study, 20% patients had ischaemic heart disease (FBS=129).[16] This rate reflects that the American population is on a high level of risk, because the prevalence of abnormal FBS in American was equal to the Mexican population with gout and lipid disorder. In the gout patients, obesity can be observed in the form of either higher BMI or central obesity. Most probably, urate and leptin together will be increased.[25,26] Some researchers have suggested that leptin may affect the renal reabsorption of urate. It should be noted that obesity and insulin resistance are associated with each other. However, insulin resistance syndrome disrupts the oxidative phosphorylation cycle and increases the levels of adenosine in the blood. This would eventually cause retention of water, sodium, and urate in the body. The studies conducted on obesity in the gout patients were as follows: America 63%, Spain 50%, British 28%, and South Korea 53%. In our study, 52.8% of patients had blood pressure >130/85. The prevalence of high blood pressure in other studies was as follows: America 70%, Mexico 67%, Spain 73%, and South Korea 47%. Hypertension is a high risk factor for heart disease – cardiovascular mortality and morbidity. In our study, approximately 38.5% of them were smokers. In a study conducted in South Korea,[27] about 70% of patients consume a high and medium amount of alcohol. In our study, abnormal TG had a stronger association with increasing serum UA level than all other components that are commonly seen in association with individual cardiovascular risk factors. This finding is in agreement with studies conducted in the Indian Ocean region by Conen, in the Japan by Nakanishi, and in the Italy by Bonora,[28–30] in which they have consistently found that TG correlates independently with UA level. The mechanism for the strong association between TG and UA concentrations has not been elucidated. Although genetic factors are associated with the concurrence of gout and hypertriglyceridaemia,[31,32] investigators have generally concluded that hyperuricaemia and hypertriglyceridaemia reflect the lifestyle of the patient more than genetic factors because obesity is also associated with these characteristics.[33]

## Conclusion

The prevalence of MS among patients with gout is so high. Efforts should be aimed to decrease the cardiovascular risk factors among these patients.

## References

1) Parikh RM, Mohan V. Changing definitions of metabolic syndrome. *Indian J Endocr Metab*. 2012; 16:7–12.

2) Kylin E. Studies of the hypertension hyperglycemia hyperuricemia syndrome. *ZentralblInnere Med*. 1923; 44:105–27.

3) Reaven GM. Banting Lecture 1988: Role of insulin resistance in human disease. *Diabetes*. 1988; 37:1595–607

4) Part 1: diagnosis and classification of diabetes mellitus. World Health Organization: Geneva, Switzerland; 1999. [Last accessed on 2011 Jun 03]. World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications: Report of a WHO Consultation.

5) Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). *Diabet Med*. 1999; 16:442–3.

6) National Institutes of Health: Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary. Bethesda, MD, National Institutes of Health, National Heart, Lung and Blood Institute. 2001 (NIH publ. no. 01-3670)

7) Mohan V, Deepa R, Deepa M, et al. A simplified Indian diabetes risk score for screening for undiagnosed diabetic subjects. *J Assoc Physicians India*. 2005; 53:759–63.

8) Mohan V, Sandeep S, Deepa M, et al. A diabetes risk score helps identify metabolic syndrome and cardiovascular risk in Indians – the Chennai Urban Rural Epidemiology Study (CURES-38). *Diabetes Obes Metab*. 2007; 9:337–43.

9) Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002; 106:3143–421.

10) www.*Pharmacotherapy-Pathophysiologic-Approach-Joseph-Di Piro*

11) Bertram G. Katzung, MD, PhD, Professor Emeritus of Pharmacology Department of Cellular & Molecular Pharmacology, University of California, San Francisco. pg no 322-326.

12) Wong R, Davis AM, Badley E, et al. Prevalence of arthritis and rheumatic diseases around the world. *Models of Care in Arthritis, Bone and Joint Disease*. 2010.

13) Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among us adult. *JAMA*. 2002; 287:356–0.

14) Balkau B, Venay M, Mhamdi L, et al. The incidence and persistence of metabolic syndrome. *Diabetes Metab*. 2003; 29:526–32.

15) Ozsahin AK, Gokcel A, Sezgin N, et al. Prevalence of the metabolic syndrome in a Turkish adult population. *Diabetes Nutr Metab* 2004; 17:230–4.

16) Vázquez-Mellado J, García CG, Vázquez SG, et al. Metabolic syndrome and ischemic heart disease in gout. *J Clin Rheumatol*. 2004; 10:105–10.

17) Choi HK, Ford ES, Li C, Curhan G. Prevalence of the metabolic syndrome in patients with gout: The Third National Health and Nutrition Examination Survey. *Arthritis Rheum*. 2007; 57(1):109–15.

18) Hernández-Cuevas CB, Roque LH, Huerta-Sil G, et al. First acute gout attacks commonly precede features of the metabolic syndrome. *J Clin Rheumatol*. 2009; 15(2):65–7.

19) Inokuchi T, Tsutsumi Z, Takahashi S, et al. Increased frequency of metabolic syndrome and its individual metabolic abnormalities in Japanese patients with primary gout. *J Clin Rheumatol*. 2010; 16:109–12.

20) Fraile JM, Torres RJ, de Miguel ME, et al. Metabolic syndrome characteristics in gout patients. *Nucleosides Nucleotides Nucleic Acids*. 2010; 29:325–9.

21) Ter Maaten JC, Voorburg A, Heine RJ, et al. Renal handling of urate and sodium during acute physiological hyperinsulinaemia in healthy subjects. *Clin Sci* (*Lond*). 1997; 92(1):51–8.

22) Muscelli E, Natali A, Bianchi S, et al. The effect of insulin on renal sodium and uric acid handling in essential hypertension. *Am J Hypertens*. 1996; 9(8):746–52.

23) P H Dessein, E A Shipton, A E Stanwix, et al. Beneficial effects of weight loss associated with moderate calorie/carbohydrate restriction, and increased proportional intake of protein and unsaturated fat on serum urate and lipoprotein levels in gout: a pilot study. *Ann Rheum Dis*. 2000; 59:539–43.

24) Emmerson B. Hyperlipidaemia in hyperuricaemia and gout. *Ann Rheum Dis*. 1998; 57:509–10.

25) Bedir A, Topbas M, Tanyeri F, et al. Leptin might be a regulator of serum uric acid concentrations in humans. *Jpn Heart J*. 2003; 44(4):527–36.

26) Fruehwald-Schultes B, Peters A, Kern W, et al. Serum leptin is associated with serum uric acid concentrations in humans. *Metabolism*. 1999; 48(6):677–80.

27) Rho YH, Choi SJ, Lee YH, et al. The prevalence of metabolic syndrome in patients with gout. *J Korean Med Sci*. 2005; 20:1029–33.

28) Conen D, Wietlisbach V, Bovet P, et al. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. *BMC Public Health*.2004; 4:1–9.

29) Nakanishi N, Suzuki K, Kawashimo H, et al. Serum uric acid: correlation with biological, clinical and behavioural factors in Japanese men. *J Epidemiol*. 1999; 9:99–106.

30) Bonora E, Targher G, Zenere MB, et al. Relationship of uric acid concentration to cardiovascular risk factors in young men: role of obesity and central fat distribution. The Verona Young Men Atherosclerosis Risk Factors Study. *Int J Obes Relat Metab Disord*. 1996; 20: 975–80.

31) Ferns GA, Lanham J, Dieppe P, Galton DJ. A DNA polymorphism of an apoprotein gene associated with the hypertriglyceridaemia of primary gout. *Hum Genet*.1988; 78:55–9.

32) Moriwaki Y, Yamamoto T, Takahashi S, et al. Apolipoprotein E phenotypes in patients with gout: relation with hypertriglyceridaemia. *Ann Rheum Dis*.1995; 54:351–4.

33) Lai SW, Ng KC. Which anthropometric indices best predict metabolic disorders in Taiwan? *South Med J*. 2004; 97:578–82.

*We know what we are, but know not what we may be.*
— William Shakespeare