

# Comorbidities in patients with gout in rheumatology clinic Dr. Hasan Sadikin general hospital in 2012 - 2013

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## ABSTRACT

**Background:** Gout is a metabolic disease manifested mainly as an intense monoarticular inflammatory reaction which is strongly associated with hyperuricemia. Latest evidence showed that uric acid exerted effects on the development of other diseases. Many studies in developed countries had estimated the frequency of comorbidities associated with gout such as hypertension, obesity, diabetes mellitus, Chronic Kidney Disease (CKD), and Myocardial Infarct (MCI). However, no data regarding these frequencies have been found in Indonesia up to now to the best of the author's knowledge. This study aimed to establish the frequency of these comorbidities in patients with gout in Rheumatology Clinic Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.

**Methods:** All medical records of patients with gout in Rheumatology Clinic Dr. Hasan Sadikin General Hospital from January 2012 to December 2013 were collected. The data on blood pressure; Body Mass Index (BMI); random blood glucose, fasting blood glucose or 2 hours post prandial blood glucose; history of myocardial infarction; and creatinine were taken and analyzed to determine the presence of comorbidities

**Results:** Among all patients with gout in Rheumatology Clinic Dr. Hasan Sadikin General Hospital, 53.08% had chronic kidney disease, 42.73% had hypertension, 25.39% had diabetes mellitus, 15.70% had myocardial infarction and 12.22% had obesity.

**Conclusions:** Comorbidities commonly found in patients with gout in order of frequency were chronic kidney disease, hypertension, diabetes mellitus, myocardial infarct, and obesity.

**Keywords:** gout, comorbidities, frequency.

## Introduction

Gout is a chronic disease affecting multiple systems which is caused by increased serum uric acid level (hyperuricemia). This condition contributed by error in purine metabolism or excretion is commonly further worsened by excessive purine intake.<sup>1</sup> Hyperuricemia leads to deposition and nucleation of uric acid into Monosodium Urate (MSU) crystals in synovial space which induces an inflammatory reaction and clinically manifested as an acute and very painful arthritis commonly known as gouty arthritis. Extremely or chronically elevated serum uric acid level also can lead to several derangements in the renal including chronic

urate nephropathy, acute uric acid nephropathy, and uric acid nephrolithiasis which eventually result in renal failure.<sup>2</sup>

Increasing concern into this disease was brought by the fact that the prevalence of gout and hyperuricemia remain large and had risen in the past 2 decades.<sup>3</sup> During its natural course of disease, patients with gout and hyperuricemia are also associated with many comorbidities such as hypertension, Chronic Kidney Disease (CKD), obesity, diabetes, and Myocardial Infarct (MCI) probably due to recently found role of uric acid in pathogenesis of these comorbidities.<sup>4</sup> Several studies had been performed in United States, United Kingdom, and Germany to estimate the frequency of comorbidities in gout population.<sup>5,6</sup> However, to the best of the author's knowledge, similiar data in Asia, particularly in Indonesia hasn't been documented. To address this issue, this study was designed to identify the frequency of comorbidities in patients with gout in Rheumatology Clinic Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.

## Methods

In order to know the pattern of comorbidities in patients with gout, cross sectional study using all medical records of such patients in Rheumatology Clinic Dr. Hasan Sadikin General Hospital were carried out. The medical record of a patient would be included if the time of admission was between January 2012 – December 2013 and the patient was diagnosed with gout by attending physician or given code as ICD (International Classification of Disease) M10. Diagnostic criteria used for gout in Rheumatology Clinic Dr. Hasan Sadikin General Hospital were based on American College of Rheumatology guidelines. Several data were recorded for data analysis purpose such as age, gender, weight in kilograms, height in centimeters, blood pressure at the time of admission, blood glucose test (fasting blood glucose, random blood glucose, or 2 hours post prandial blood glucose), serum creatinine level, and history of myocardial infarction. All the data collected were then inserted into Microsoft Excel for analysis. Patients without any of the data above were excluded

The presence of particular comorbidities was checked according to the following definitions. Hypertension was defined as systolic blood pressure

more than or equal to 140 mmHg or diastolic pressure more than or equal to 90 mmHg.<sup>7</sup> Obesity was defined as Body Mass Index (BMI)  $\geq 30$  kg/m<sup>2</sup> where BMI is body weight divided by height in meters squared.<sup>8</sup> Diabetes was defined as either fasting blood glucose  $\geq 126$  mg/dl or the presence of diabetic symptoms (polydipsia, polyuria, polyphagia) and random blood glucose  $\geq 200$  mg/dl or 2 hours post prandial blood glucose  $\geq 200$  mg/dL.<sup>9</sup> Chronic kidney disease was defined as estimated Glomerular Filtration Rate (eGFR) below 60 ml/min/1.73 m<sup>2</sup> where eGFR =  $((140 - \text{age}) \times \text{weights (kg)}) / (72 \times \text{serum creatinine})$ .<sup>10</sup> History of myocardial infarction of each patients is recorded. Patients without the necessary data were not included in the data analysis of corresponding comorbidities.

## Results

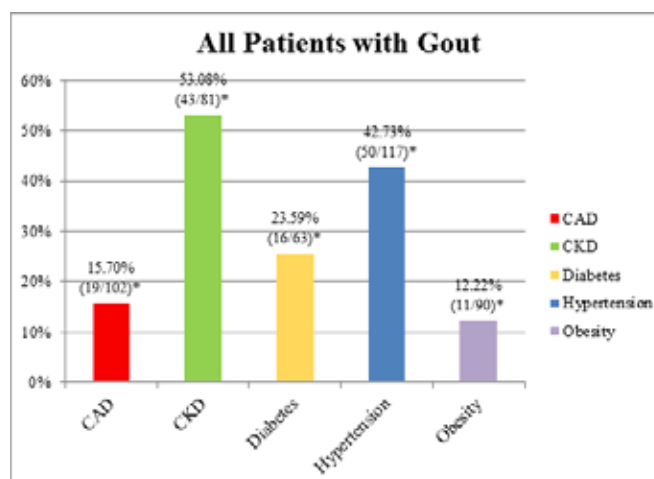
There were 128 patients who attended the Rheumatology clinic during period January 2012 – December 2013 and diagnosed with gout or ICD 10 code M10. Six patients were excluded from the data analysis due to the lack of data of interest. From these patients, 100 (81.96%) patients were male and 22 (18.03%) patients were female. Mean age of patients with gout was 58 with standard deviation 11.25 (Table 1).

**Table 1** Patients Characteristic

Variable	n (%)
<b>Gender</b>	
Male	100 (81.96%)
Female	22 (18.03%)
<b>Age</b>	58 (SD 11.25)*

\* Mean (SD)

There were 5 patients whose data were incomplete for blood pressure. Out of 117 patients, 50 patients (42.73%) that composed of 40 male and 10 female got hypertension. For BMI purpose, there were 32 patients who didn't have their height or weight measured. From 90 patients, 11 patients (12.2%) who consisted of 7 male and 4 female were obese. Fifty nine patients got no data about either blood glucose measurement or Diabetes history thus weren't included in the analysis of Diabetes. Among 40 patients which included, 16 patients (25.39%) consisted of 13 male and 3 female had Diabetes. There were 42 patients whose data were incomplete for determining eGFR, thus only 81 patients were included in the data analysis. From 43 patients (53.08%), there were 30 men and 6 women suffered from CKD. Coronary Artery Disease (CAD) was found in 13 male and 6 female (15.70%) out of 121 patients. (Figure 1)



\*Numbers displayed (patients with comorbidities/ all patients with particular data regarding the comorbidities)

**Figure 1** Comorbidities in Patients with Gout

## Discussions

In this study, patients with gout had mean age of 58 (11.25) years. Nearly similar data also were presented by Mikuls *et al.* in their study of gout epidemiology that the mean age of patients with gout is 60.5 (15.4) years. Male predominance in this study, as commonly known in gout patients, was stated in that study as well (79.6%).<sup>11</sup>

The most prevalent comorbidity in this study was CKD (53.08%) characterized by eGFR  $< 60$  ml/min/1.73.<sup>2</sup> Different results were presented in studies carried out in United States by Zhu *et al.* in which hypertension (74%) was the leading comorbidities in gouty patients in the United States (US) while CKD (71%) was the second most.<sup>5</sup> Many incomplete data in the analysis of CKD frequency could be the factor that influencing this discrepancies. Nevertheless, CKD had strong relation with gout based on the knowledge up to now. Kidneys act as the main excretory organs of these metabolism end products in such way that disturbance in the kidney function will decrease uric acid clearance and thus increase serum uric acid level.<sup>1</sup> Besides that, hyperuricemia could cause a downfall in kidneys' function through urate nephropathy, uric acid nephropathy, or nephrolithiasis which terminally lead to renal failure.

Hypertension occurred in 42.73% of patients with gout in this study compared with 74%, 17.5%, and 18.5% which stated in studies of gout comorbidities in US, United Kingdom (UK), and Germany respectively.<sup>5,6</sup> These differences occurred probably due to the lack of data regarding anti-hypertension medication used which probably decrease the number of hypertensive patients in this study. Lifestyle variation in the population studied also contributed to these variations. Nevertheless, increased serum uric acid level is constantly associated with hypertension and many data and evidence support this. Pathogenesis of hypertension in hyperuricemia is related to the biological effects of uric acid in vascular such as to decrease Nitric Oxide (NO), increase Reactive Oxygen Species (ROS), induce vascular inflammation, and to induce proliferation of vascular smooth-muscle cells thus promote to vascular narrowing. In addition to vascular effects, uric acid

also exerts impacts towards renal such as increased renin, decreased NO, interstitial inflammation, interstitial fibrosis which all leads to vasoreactive hypertension.<sup>4,12</sup>

Diabetes which occurred in 25.39% of all gout patients in this study is concordant with other study in Germany and US which was 25.9% and 26% respectively.<sup>5,6</sup> Many studies had linked hyperuricemia with Diabetes Mellitus. One meta-analysis study had associated serum uric acid level with the risk of developing type 2 Diabetes and found that each 1 mg/dl increase in serum uric acid resulted in 17% higher risk of having type 2 Diabetes Mellitus.<sup>13</sup> Uric acid had been found as mediator of proinflammatory imbalance in adipose cells by inducing ROS production via stimulation of NADPH oxidase and decreasing adiponectin production which is an important insulin sensitizer and anti-inflammatory substance.<sup>14,15</sup>

Obesity was found in 12.22% patients with gout in this study which was smaller in frequency compared with the study in US (53%) and UK (27.7%).<sup>5,6</sup> This discrepancy probably contributed by the lifestyle and socioeconomic level differences between the population studied. However, obesity had been associated with gout in study by Chen *et al.* who stated that obesity in women and hypertriglyceridemia in men could precipitate gout attacks in the absence of saturated serum uric acid level.<sup>16</sup> It is also proved from the study in the United Kingdom general population that obesity was associated with higher risk of developing gout.<sup>17</sup>

The presence of CAD in 15.7% patients with gout in this study also stated by the studies in US, UK, and Germany (11.6%, 7.4%, and 5.8% respectively).<sup>5,6</sup> Relationship between gout and coronary artery disease could be explained by the effects of uric acid towards vascular which is to cause endothelial dysfunction through reduction of NO and production of ROS.<sup>12</sup>

The results of this study are consistent with previous study carried out in US, UK, and Germany about comorbidities in patients with gout such as CKD, hypertension, diabetes mellitus, CAD, and obesity even though there were slight differences in the results obtained. Data regarding comorbidities of gout in Asia are lacking. These discrepancies probably caused by the differences in lifestyle and socioeconomic status of the population studied. Besides that, the incompleteness of data could be one of the factors affecting the differences. This study only address the most common comorbidities occurred in gout patients, while for the cause and effect relationship between gout and its comorbidities or vice versa cannot be determined. The results of this study can be used in the future as a step for further research about association between gout and its comorbidities. The consistent presence of comorbidities in patients with gout found in this study necessitates more meticulous comprehensive approach to gout management through early detection of these reported comorbidities and furthermore considering those comorbidities treatments' effects towards serum uric acid level and vice versa.

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