Original Article

Prevalence and Pattern of Metabolic Syndrome in Patients Presenting with Gouty Arthritis in a Tertiary Health Centre in Zaria, North Western Nigeria

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ABSTRACT

Objective: The aim of the study was to determine the prevalence and pattern of metabolic syndrome (MetS) in patients presenting with hyperuricemia and gouty arthritis to the rheumatology clinic of Ahmadu Bello University Teaching Hospital (ABUTH) Zaria. Methods: The study is a retrospective study of patients that presented to the rheumatology clinic of ABUTH Zaria with gouty arthritis. We reviewed the medical records of patients that presented to the rheumatology clinic and medical wards of Ahmadu Bello University Teaching Hospitals with gouty arthritis over 10 years period (January 2011- December 2020). The following parameters: demographic variables, pattern of joint involvement, duration of gouty arthritis, anthropometric measures, and blood pressure. Results of fasting blood glucose, fasting lipid profile, electrolyte urea and creatinine were also retrieved. Diagnosis of gouty arthritis was based on American College of Rheumatology Classification Criteria. Metabolic syndrome was defined using National Cholesterol Education Program- Adult Treatment Panel III (NCEP-ATP III) classification criteria. Of the 160 patients with gout seen in the period under review, 22 patients were excluded from the study on account of incomplete results. Data was analyzed using SPSS version 20 and p value of <0.05 was considered as significant. Results: A total of 160 gout arthritis patients were seen in the period under review of a total of 1520 rheumatology patients, thereby constituting 10.5% of all Rheumatic Musculoskeletal Diseases (RMDs). However only 138 gout patients that had complete data were studied. This consisted of 94 (68.1%) males and 44 (31.9%) females. The mean age at presentation of gouty arthritis patients was 56.5 ± 10.6 years. The mean serum uric acid was 566.5 ± 170.1 μ mol/L. Hypertension was recorded in 86 (62.3 %), Diabetes Mellitus in 19 (13.8%), abnormal waist circumference in 72 (52.2 %), low HDL in 49(35.5%) and hypertriglyceridemia in 83 (60.1%) of patients. Metabolic syndrome was diagnosed in 59 (42.8%) patients and the prevalence of Metabolic syndrome was higher in males compared to female gouty arthritis patients. Conclusion: The prevalence of metabolic syndrome in gouty arthritis patients is 42.8%. Efforts should be intensified at screening patients presenting with gouty arthritis for metabolic syndrome to forestall adverse cardiovascular outcome.

Keywords- Metabolic syndrome, gouty arthritis

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INTRODUCTION

Gouty arthritis is an ascending inflammatory arthritis due to persistent hyperuricemia with consequent deposition of monosodium urate salt in articular cartilage. It is the most common cause of inflammatory arthritis. Though, presentation with acute severe joint pain is often the primary reason why gouty arthritis patients seek medical attention; the disease is often a red flag sign for the presence of one or more component diseases of metabolic syndrome, with the latter adversely affecting overall outcome in concert with gouty arthritis.

Metabolic syndrome (MetS) is the occurrence of metabolically related (cardiometabolic) disease cluster such as: hypertension, diabetes mellitus, visceral obesity and dyslipidemia in an individual. [2] The presence of MetS in an individual is associated with heightened risk of adverse cardiovascular outcome and increased mortality. [2,3] Epidemiological studies have alluded to a close association between gouty arthritis and MetS, [3-5] with hyperuricemia thought to be the link. Hyperuricemia is a well-established independent risk factor for MetS [6,7] and high levels of serum uric acid level have been shown to be associated with higher prevalence of MetS in gout patients in a 'concentration-severity-dependent effect [8,9] Insulin resistance appears to be a common denominator and possible link between hyperuricemia and MetS. Insulin resistance is an established risk factor for MetS. [2,10] Insulin resistance predisposes to hyperuriceamia by reducing the renal clearance of uric acid.[11] Regardless of the cause-effect relationship that exist between hyperuriceamia and MetS, the concurrence of MetS in patients with gout has been shown to be associated with higher morbidity and increased mortality [2-5]

Most studies on MetS in Nigerians have been conducted on general population [12,13] and patients with diabetes mellitus, hyperthyroidism and hypertension [14,15] with no study focused on the

burden of MetS in patients with hyperuricemia/gouty arthritis. This study is aimed at ascertaining the prevalence and pattern of MetS amongst patients presenting with gouty arthritis in a Tertiary Hospital in Nigeria.

METHODOLOGY

The study was a retrospective study conducted via review of medical records of 160 adult patients presenting to the rheumatology clinic and medical wards of Ahmadu Bello University Teaching Hospital with gouty arthritis over a 10-year period (January 2011 – December 2020). One hundred and thirty-eight patients were eventually studied, as 22 patients (15 males and 7 females) had incomplete data such as missing anthropometric measurements and absent results of blood sugar or fasting lipid profile were excluded from the study. Diagnosis of gout was attained using the American College of Rheumatology Classification Criteria for gouty arthritis. [16] Information retrieved manually from the medical records included: patients biodemographic data at 1st presentation, duration of articular symptoms, number and type of joint affected. History of hypertension or usage of antihypertensives, diabetes or usage of antidiabetic medications, dyslipidemia or use of cholesterol lowering drugs. Findings on general physical examination at 1st presentation such asanthropometric examination, musculoskeletal, systemic examination and blood pressure, were also retrieved. Results of urea, creatinine and uric acid, fasting blood sugar and lipid profile at 1st presentation were also retrieved for all patients. Metabolic syndrome was determined using the National Cholesterol Education Program Adult Treatment Panel-III (NCEP-ATP-III) Criteria. [2] Ethical approval for the study was obtained from ABUTH Health Research and Ethics Committee. Statistical analysis was done using statistical software for social sciences (SPSS) version 20, Inc Chicago, Illinois, USA.

Demographic and baseline characteristics were presented as tables. Univariate analyses were carried out and presented as range, mean (standard deviation) for numerical variables and count/percentages for categorical variables. Differences in the anthropometric and baseline characteristics between the gender groups were done by an independent sample t-test. Chi-square was used to differentiate the proportions of categorical variables. P-value of ≤ 0.05 was considered as significant.

RESULTS

The baseline characteristic of gouty arthritis patients is shown in table 1. A total of 160 gout arthritis patients were seen in the period under review of a total of 1520 rheumatology patients, thereby constituting 10.5% of all Rheumatic Musculoskeletal Diseases (RMDs). The 138 gout patients studied, consisted of 94 male (68.1%) and 44 females (31.9%), with a male to female ratio of 2.1:1. The mean age at presentation of gouty arthritis patients is 56.5 ± 10.6 years, with an age range of 32-90 years. The mean age at presentation for male gouty arthritis patients is 56.12 ± 10.27

Table 1; Sociodemographic characteristic of patients with gout

No of patients studied = 138. Sex distribution: males = 94, females=34: sex ratio: M: F = 2.1:1 Mean(sd) age at presentation (all patients) = 56.5 ± 10.6 years Mean (sd) age at presentation (males) = 56.12 ± 10.27 years Mean (sd) age at presentation (females) = 57.2 ± 11.46 years Mean age (sd) of patients with MetS = 56.1 ± 9.95 Mean age (sd) of patients without MetS = 56.3 ± 10.84 Median (IQR) duration of symptoms prior to presentation = 2 (4) years Alcohol ingestion: No =118 (85.5%), Yes = 20 (14.5%)

years, while the mean age for female gouty arthritis patient is 57.3 ± 11.46 years.

There was no statistically significant difference between mean ages at presentation for male and female patients with gouty arthritis, (p= 0.065). The mean ages of patients with and without MetS was 56.1 ± 9.95 and 56.3 ± 10.84 respectively. There was no significant difference between ages of patients with MetS when compared to patients without MetS, (p=0.071)

The mean duration between disease onset and presentation to the rheumatology clinic was 3.52 ± 3.34 years, with a median (IQR) of 2 (4) years. Majority of our patients never used alcohol.

Anthropometric measures of patients with gouty arthritis patients are presented in table 2. The mean weight and mean height were significantly higher in male patients with gouty arthritis compared to female patients. The mean BMI was 30.9± 6.4 Kg/m^2 for all patients, with mean BMI being $30.1 \pm$ 6.67 and 32.7 \pm 5.39 in male and female patients respectively. The difference in mean BMI between male and female gouty arthritis was statistically significant, (t=1.98, p=0.0029). Thirty-two (23.2%) of patients had normal body mass index (BMI) on presentation, 35 patients (25.3%) were overweight. Overall,71 (51.5%) patients presented with various degree of obesity composed of - 37 (26.8%) with class I obesity. 26(18.8%) with class II obesity and 8 (5.8%) had class III obesity.

The mean waist circumference for all patients was

Table 2: Anthropometric and blood pressure parameters of patients with gouty arthritis by gender. Values are presented as Mean (standard deviation), p values determined using student t-test.

Parameter		Number (%)		D. Walna
	All (N=138)	Male (n=94)	Female (n=44)	P- Value
Weight (kg)	84.2 (19.2)	85.8 (20.8)	80.8 (14.9)	0.042
Height (cm)	1.66 (0.5)	1.66 (0.28)	1.49 (0.35)	0.001
BMI (Kg/m^2)	30.9 (6.4)	30.1 (6.67)	32.7 (5.4)	0.0029
Waist Circ. (cm)	100.3 (16.8)	102.1 (17.4)	95.9 (14.9)	0.001
Hip Circ. (cm)	106.2 (12.9)	104.2 (13.2)	111.1(11)	0.002
Waist Hip ratio	0.95 (0.1)	0.98(0.08)	0.86 (0.09)	0.001
SBP (mmHg)	150.6 (10.5)	146.8(9.8)	144.9 (8.7)	065
DBP (mmHg)	92.8 (9.5)	90.7 (8.4)	88.7 (8.2)	0.56

 100.3 ± 16.4 cm, the mean waist circumference is 102 ± 17.43 cm and 95.93 ± 14.94 cm for male and female patients respectively. There was significant difference in mean waist and hip circumferences between male and female patients with gouty arthritis.

The mean serum uric acid was $566.5 \pm 170.1 \mu mol/L$ with a range of $405\text{-}1151 \mu mol/L$, the mean serum uric acid for male patients with gouty arthritis was $584.1 \pm 174.8 \mu mol/L$, while that of female patients with gouty arthritis was $531.3 \pm 158.6 \mu mol/\mu L$, with the difference being statistically significant, (p < 00.2). Mean serum uric acid level for gouty arthritis patients with MetS was $542.7 \pm 151.8 \mu mol/L$, while the mean serum uric acid level for gouty arthritis patients without MetS was $504.2 \pm 105 \mu mol/L$ (p<0.001).

Mean values of components of MetS evaluated in the patients is shown in table 3. There was no significant difference in mean fasting blood sugar values between male and female patients with gouty arthritis. The total cholesterol levels and other components of lipid profile were higher male patients with gouty arthritis compared to female patients.

The prevalence of components of MetS is shown in table 4. Using the ATP III criteria, 59 (42.8%) of patients with gouty arthritis had MetS. The metabolic syndrome was diagnosed in 42 (44.7%)

male and 17(38.6.%) female patients with gouty arthritis respectively. There is no significant gender difference in the prevalence of MetS (p= 0.503). Of the 59 patients with MetS: 30 patients (50.8%) had 3 criteria for MetS, 19 (32.2%) had 4 criteria for MetS and 10 patients (16.9%) had all 5 criteria for MetS. Thirty-seven (39.3%) males had waist circumference above the cut off value of 102cm, while 35 (79.5%) female patients had waist circumference above the cut off value of 88cm. Eighty-six (62.3%) of patients with gout had hypertension at presentation, this consisted of 59 male patients (62.8%) and 27 female patients (61.4%). Twenty-eight (21.9%) patients presented with type 2 diabetes mellitus, this consisted of 20 males (20.3 %) and 8 females (18.1%). There was a statistically significant difference in the proportion of female and male gouty arthritis patients that attained threshold for MetS with regards to parameters such as increased waist circumference and dyslipidemia. There was no difference in the proportion of male and female gouty arthritis patients with hypertension and hyperglycemia in the MetS range. Increased waist circumference and low HDL were more prevalent determinants of MetS in female patients, with hypertriglyceridemia, hypertension and hyperglycemia being more prevalent in male patients with gouty arthritis.

Table 3: Metabolic profile of patients with gouty arthritis by gender. Values are presented as Mean(standard deviation), p values determined using student t-test.

Parameter	Number (%)			P- Value
	All (N=138)	Male (n=94)	Female (n=44)	
FBS (mmol/L)	5.4 (2)	5.7 (1.0)	5.1 (2.3)	0.007
Total Cholesterol	5.1 (1.44)	5.39 (1.35)	4.26 (1.45)	0.046
HDL-C	1.34(0.64)	1.42 (0.63)	1.1 (0.66)	0.038
LDL-C	3.12 (1.11)	3.29 (1.13)	2.58 (1.0)	0.044
Triglyceride	1.96 (0.89)	2.01 (0.91)	1.8 (0.9)	0.042

Parameter	Number (%)			* P- Value
	All (N=138)	Male (n=94)	Female (n=44)	
Increased WC	72(52.2)	37 (39.3)	35 (79.5)	0.00001
Hypertension	86 (62.3)	59 (62.8)	27 (61.4)	0.8728
Hyperglycemia	28 (21.9)	20 (21.3)	8 (18.1)	0.6744
Low HDL-C	49 (35.5)	28 (29.8)	21 (47.7)	0.0404
High Triglyceride	83 (60.1)	69 (73.4)	14 (31.8)	0.0001
Metabolic syndrome	59 (42.8)	42 (44.7)	17 (38.6)	0.053

Table 4: Determinants of Metabolic syndrome in patients with gouty arthritis by gender. P value determined suing Chi square

DISCUSSION

One hundred and thirty-eight patients were evaluated in this study, with the bulk of the patients (68%) being males. The mean age at presentation of female patients with gouty arthritis was higher than that of male patients. Gouty arthritis is more prevalent, and presents at a lower mean age in males compared to females. This is due the lower mean age at peak serum uric acid level in males compared to females and the uricosuric effect of estrogen, thereby causing delayed onset of disease until after menopause in females. The same physiologic factor could also account for the lower mean serum uric acid level seen in female patients in this study compared to males

The median duration of symptoms prior to presentation was in excess of 2 years in our patients. Delayed presentation of gouty arthritis was also noted in previous studies of gouty arthritis patients. [17,18] Despite gout being an intensely painful condition, tendency to spontaneous resolution of pain after days of symptoms and good response to and widespread usage of NSAIDs could contribute to delay in presentation of patients with gouty arthritis. Normal body weight was recorded in less than a guarter of our patients (23.4%), with 24.5% being overweight and the rest (51.5 %) having various degree of obesity. High prevalence of obesity has been reported in patients with hyperuricemia and gout. [17] Studies have established a link between obesity and raised serum uric acid. [18,19] With obesity perceived as one of the predisposing factors for the development of gouty arthritis. [17] Abnormal waist circumference was noted in over half (56%) of all patients. With abnormal waist circumference being more prevalent in female patients than in male patients. Central obesity has been shown to be more prevalent in females with MetS and contributes more significantly to the burden of MetS in females compared to males. [12] Perhaps the difference in waist circumference threshold values for MetS in males and females could partly be responsible for female preponderance. An association between increased waist circumference and hyperuricemia has been reported in studies. [19]

Hypertension was the most prevalent comorbidity associated with gouty arthritis in our patients, occurring in 62.3% of patients. Hypertension has been shown to be the most common comorbidity associated with gouty arthritis, with prevalence rates ranging between 49.3-62.9%. amongst Nigerian patients with gout. [17,20] The relationship between hypertension and gouty arthritis appears complex. On one hand, the occurrence of hypertension induced renal injury can result in reduced renal clearance of uric acid and consequent hyperuricemia. Conversely, there is growing evidence that hyperuricemia is an independent risk factor for hypertension in patients. [21,22]

Mean serum uric was high in our patients with

values being significantly higher in male patients with gouty arthritis compared to females. Mean serum uric acid level was also significantly higher in gouty arthritis patients diagnosed with metabolic syndrome than in patients without MetS. Hyperuricemia has been shown to be an independent risk factor for MetS ^[6,7] with high levels of serum uric acid correlating with the prevalence of metabolic syndrome in gout patients. ^[8,9]

The prevalence of MetS amongst our patients was 42.8%. With prevalence of MetS being non-significantly higher in male gout patients (44.7%) compared to female patients (38.6%). Studies done in Asian and in the United States has shown a wide range prevalence figures of MetS of 30.1-62.8%. [5.23,24] In a study done in Cameroun the prevalence of MetS amongst gouty arthritis patients, using International Diabetic Federation criteria, was 54.6%, with metabolic syndrome noted to be non-significantly more prevalent in females with gouty arthritis (59.5%) compared to males (50%) [25]

A number of longitudinal studies have demonstrated close association between elevated serum urate levels and MetS and also hinted at elevated serum uric acid as forerunner and an independent predictor of MetS in both population-based and hospital-based studies. [26,27] Furthermore, a dose-response relationship between the prevalence of MetS and uric acid quartiles have been alluded to in studies. [26,28]

The prevalence of MetS amongst our gout patients is markedly higher than prevalence of MetS in general population in a rural community in South West Nigeria (12.1% overall, 12.7% males, 11.8% females) [12], and an urban population in North-Western Nigeria (35.1% overall, 27.36%- males, 42.86%-females) [13] and also higher than the prevalence of Metabolic syndrome in out-patients of a tertiary hospital (overall- 28.04%, 15.3%-males, 38.8%- females). [29]. The prevalence of MetS in gout arthritis patients is however less than the reported prevalence of MetS in patients

diagnosed with type II diabetes mellitus (66.7%-overall, 41.9%-males, 58.1%-females). [14]

With regards to the component diseases of MetS, hypertension was the most common component of MetS in our patients, occurring in 61.3% of patients, it was more frequent in male patients. Abnormal waist circumference was noted in 52.2%, with prevalence being more significantly higher in women. Variety of dyslipidemia was diagnosed in patients with gouty arthritis, with hypertriglyceridemia being the most prevalent (59.4%) and low HDL (31.1%) being the least prevalent.

Diabetes mellitus was least prevalent component of MetS diagnosed in patients with gouty arthritis, occurring in 21.9% of patients. The distribution of components of Mets differs from findings in Cameroonian patients where central obesity was the most prevalent component of MetS (84.5%), followed by hypertension (74.1%). With the exception hypertriglyceridemia that was more prevalent amongst our patients, other components of MetS was more in Cameroonian gouty arthritis patients compared to Nigerian patients. The differences in diagnostic criteria of MetS and also difference in population studied could be responsible for the disparity in prevalence rates between the 2 populations.

The prevalence of individual components of MetS were also higher amongst gouty arthritis patients compared to value derived from study of metabolic syndrome in Nigerian general population, [12.13] thereby further underscoring the close association between MetS and gouty arthritis.

CONCLUSION

The prevalence of metabolic syndrome in Nigerian patients with gouty arthritis is 42.8%, with MetS being more prevalent in male patients compared to females.hypertension, hypertriglyceridemia and visceral obesity were the most prevalent component of MetS in our patients.

Recommendations

Patients presenting with gout should be routinely screened for components of metabolic syndrome and offered appropriate treatment to reduce adverse cardiovascular outcome associated with m e t a b o 1 i c s y n d r o m e.

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