

## Research Article

# Clinical Manifestations of Gout between Obese and Non-Obese Patients in Sub-Saharan Africa: A Cross-Sectional Study in Yaoundé, Cameroon

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## Abstract

**Background:** Gout is the most prevalent form of inflammatory arthropathy and is commonly associated with obesity which is strongly linked to hyperuricemia. Thus, we could think that the clinical signs of gout may be more severe in patients living with obesity. Few studies have evaluated the relationship between clinical signs of gout and obesity.

**Objective:** To study the clinical signs of gout in obese and non-obese patients.

**Methodology:** We performed a cross-sectional and comparative study for three months. We compared two pre-established groups, obese and non-obese, looking at the socio-demographic, history, clinical and para-clinical data. All statistical tests were two-tailed with type I error set at 0.05 and P<0.005 were considered statistically significant.

**Results:** We included 101 patients including 44 obese and 57 non-obese. Almost all the patients were living in an urban environment. The mean age was 59.5 ± 9.99 years. The diastolic blood pressure was significantly higher in the obese group (89.66 mmHg ± 13.05 mmHg vs. 84.05 mmHg ± 13.67 mmHg). The non-obese group significantly presented more tophi (56.1% vs. 29.5%); there was a fourfold risk of developing tophi in non-obese than in obese patients. Tophi preferred location was on the first metatarsophalangeal of the right foot in the non-obese group (35.1% vs. 9.1%); there was a fivefold risk of developing tophi on the first metatarsophalangeal joint of the right foot in non-obese compared to obese patients. Non-obese patients had significantly more joint deformities than obese patients (22.8% vs. 6.8%). There was a fourfold risk of having deformities in non-obese than in obese patients.

**Conclusion:** In our study, clinical signs are more severe in non-obese patients notably the predilection of tophi on the first metatarsophalangeal joint of the right foot, tophi and joint deformities.

**Keywords:** Gout; Obesity; Hyperuricemia; Metabolic syndrome; Obesity paradox

## Abbreviations

AC: Abdominal Circumference; ACR: American College of Rheumatology; ANOVA: Analysis of Variances; BMI: Body Mass Index; CVD: Cardiovascular Diseases; CI: Confidence Interval; CT: Computed Tomography; DBP: Diastolic Blood Pressure; DSO: Dismutase Superoxyde; EULAR: European League against

Rheumatism; FMPJRF: First Metatarsophalangeal Joint of the Right Foot; HDL: High Density Lipoproteins; IL-6: Interleukin 6; LDL: Low Density Lipoproteins; MDRD: Modification of Diet in Renal Disease; MRI: Magnetic Resonance Imaging; Mets: Metabolic Syndrome; RR: Respiratory Rate; SBP: Systolic Blood Pressure; SE: Standard Error; TCHT: Total Cholesterol; TG: Triglycerides; TNF-α: Tumour Necrosis Factor-alpha; WHO: World Health Organization; YGH: Yaoundé General Hospital; YTH: Yaoundé Teaching Hospital

## Introduction

Gout is the leading cause of arthritis in adults [1]. It is characterized by hyperuricemia with tissue deposition of sodium urate crystals [1]. Its global prevalence varies between 1% and 4% [2]. Data on its prevalence in Africa are characterized by their rarity, their age and their predominance in hospitals [2,3]. A study carried out in Cameroon at the Yaoundé General Hospital (YGH), found a prevalence of 5.9% [4]. It is frequently associated with co morbidities, in particular obesity, which is by far the most important in the face of High Blood Pressure (HBP), diabetes, and dyslipidemia [5]. Obesity can be defined as a

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disease in which there is an accumulation of excess body fat with adverse health effects [6]. In Africa, its prevalence is increasing and this is linked to the improvement of the socio-economic level and to the many changes caused by rapid urbanization [7].

Existing studies have been carried out mainly in Asia and found out that gout has an increasing prevalence with the stage of obesity, the onset age is earlier in obese and obesity is associated with a greater number of involved joints. Moreover, there is a positive relationship between biological features and body mass index, with only some country-related differences [8-10].

The actual studies suggest for most of them that clinical signs of gout are more severe in obese Caucasian individuals. Not knowing whether this is also true for black subjects and particularly in sub-Saharan Africa, we conducted this study to elucidate this area related-questions.

## Materials and Methods

This study was approved by the institutional ethical and research committee of the Faculty of Medicine and Biomedical Sciences. Our study consisted of 101 patients and was carried out from January 31<sup>st</sup>, 2019 to April 19<sup>th</sup> 2019.

Our source population was the adult patients with gout diagnosed or followed in our recruitment sites: Yaoundé central hospital, Essos hospital center, Biyem-Assi district hospital, Yaoundé Teaching Hospital and Efoulan district hospital.

### Inclusions criteria

We included:

- French/English speaking patients over 18 years
- Patients fulfilling the ACR/EULAR 2015 diagnostic criteria for gout,
- Patients with documented chronic gout coming for follow-up consultation or admitted to hospital in various departments of our recruitment sites
- Patients who read, understood and signed the informed consent form.

### Exclusions criteria

We did not include:

- Bedridden patients due to the difficulty in being able to measure their weights and sizes.

We excluded patients who withdrew their informed consent and those with another etiology of arthritis (chondrocalcinosis, hydroxyapatite rheumatism, septic arthritis, rheumatoid arthritis, systemic lupus erythematosus, and mixed connective tissue disease).

### Patients enrolment and follow-up

We collected data from history (sex, age, residency and co morbidities) and clinical exam (BMI, BP, presence of tophi or deformations).

### Assessment of body mass index

We measured height and weight at baseline. Body mass index was calculated as weight in kilograms divided by the square of height (kg/m<sup>2</sup>). We considered obese, people with BMI  $\geq$  30 Kg/m<sup>2</sup> according to the WHO criteria [7].

## Statistical analysis

We entered our data using Microsoft Excel 2013 and analysis was done with SPSS 22. Continuous variables were presented as mean  $\pm$  SE (Standard Error), comparisons among groups were tested by t-test or one-way ANOVA. Partial correlation analysis determined the relationship between obesity and related variables. Odds ratios were calculated to evaluate the correlation intensity between variables and the obese status. All statistical tests were two-tailed with type I error set at 0.05 and P<0.005 was considered statistically significant.

## Results

The study population consisted of 101 participants. In 91.1% of whom were male. The mean age was 59.5 (SE: 9.99); the mean age in obese was 57.45 (SE: 1.5) and 60.65 (SE: 1.27) in non-obese. Almost all the patients (90%) lived in urban areas and few of them (10%) in rural areas.

### History data

The most important co morbidity was HBP (40.6%), followed by dyslipidemia (39.6%), Mets (36.6%), osteoarthritis (20.8%) and diabetes (17.8%). Mets was significantly ( $p=0.001$ ) more frequent in obese subjects (54.5%) than in non-obese (22.8%).

### Clinical data

The body mass index was significantly higher in obese ( $34.04 \pm 4.27$  (30 Kg/m<sup>2</sup> to 45 Kg/m<sup>2</sup>)) than in non-obese ( $25.96 \pm 2.65$  (19 Kg/m<sup>2</sup> to 29.8 Kg/m<sup>2</sup>)) as well as the abdominal circumference ( $114.32 \pm 9.47$  (100 cm to 141 cm) vs.  $94.33 \pm 10.78$  (58 cm to 112 cm)).

The diastolic blood pressure was significantly increased in obese subjects ( $89.66 \pm 13.05$  (60 mmHg to 121 mmHg) vs.  $84.05 \pm 13.67$  (60 mmHg to 118 mmHg)).

Tophi were significantly ( $p<0.05$ ) more frequent in non-obese than in obese subjects (56.1% vs. 29.5%) and were also more likely to be found on the first metatarsophalangeal joint of the right foot of non-obese than in obese (35.1% vs. 9.1%).

Also, joint deformities were significantly ( $p<0.05$ ) more frequent in non-obese than in obese subjects (22.8% vs. 6.8%).

The final adjusted odds ratio for non-obese compared to obese subjects concerning tophi was 4 (95% CI 1.6 - 9.10). This shows that there was a fourfold risk of having tophi in non-obese compared to obese subjects.

Also, the final adjusted odds ratio for non-obese compared to obese concerning the localization of tophi on the FMPJRF (first metatarsophalangeal joint of the right foot) was 5.4 (95% CI 1, 68 - 17.29). This shows that there was a fivefold risk of tophi occurrence on the FMPJRF in non-obese compared to obese subjects.

The final odds ratio for non-obese subjects compared to obese subjects concerning articular deformations was 4 (95% CI 1.1 - 15.2). This shows that there was a fourfold risk of having articular deformities in non-obese subjects compared to obese subjects (Tables 1-5).

## Discussion

This study reveals that clinical signs of gout are less severe in obese than in non-obese subjects. We excluded all the confounding factors and observed that both groups were similar ( $P>0.05$ ) regarding their socio-demographic features and even their treatments.

**Table 1:** Study population comorbidities.

Comorbidities	Obese (N=44)	Non-Obese (N=57)	P-Value
HBP	20 45.50%	21 36.80%	0.382
Dyslipidaemia	8 18.20%	32 56.14%	0.559
Mets	24 54.50%	13 22.80%	0.001
Osteoarthritis	12 27.30%	9 15.80%	0.176
Diabetes	8 18.20%	10 17.50%	0.934

HBP: High Blood Pressure; Mets: Metabolic Syndrome

**Table 2:** Anthropometric data of our study population.

	Obese		Non-Obese		P-Value
	Mean	SE	Mean	SE	
Weight (Kg)	104.18	15.56	79.67	11.36	0
Height (m)	1.75	0.82	1.75	0.77	0.912
BMI (Kg/m <sup>2</sup> )	34.04	4.27	25.96	2.65	0
AC (Cm)	114.32	9.47	94.33	10.78	0

BMI: Body Mass Index; AC: Abdominal Circumference

**Table 3:** Vital parameters of our study population.

	Obese		Non-Obese		P-Value
	Mean	SE	Mean	SE	
SBP (mmHg)	143.05	19.34	137.19	23.048	0.178
DBP (mmHg)	89.66	13.05	84.05	13.67	0.04
RR (cpm)	18.36	1.31	18.04	1.35	0.22

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; RR: Respiratory Rate

**Table 4:** Gout complications in our study population.

	Obese (N=44)	Non-obese (N=57)	P-Value
Tophi (%)	29.5	56.1	0.008
FMPJRF localisation of tophi (%)	9.1	35.1	0.002
Joint deformities (%)	6.8	22.8	0.029
Hallux-valgus (%)	0	7	0.073
Flessum (%)	6.8	19.3	0.072

FMPJRF: First Metatarsophalangeal Joint of the Right Foot

**Table 5:** Illustration of the power of the relationship between obesity and tophi in gout patients.

	Percentage (%)	Final adjusted odds ratio <sup>a</sup> (95%CI)	P-Value
<b>Tophi</b>			
Non-Obese	52.6	4(1.6-9.10)	0.002
Obese	22.7	1	
<b>Localisation of tophi on the FMPJRF</b>			
Non-Obese	35.09	5.4(1.68-17.29)	0.002
Obese	9.09	1	
<b>Deformations</b>			
Non-Obese	22.8	4(1.1-15.2)	0.029
Obese	6.8	1	

<sup>a</sup>Final adjusted odds ratio for body mass index, metabolic syndrome and diastolic blood pressure, FMPJRF: First Metatarsophalangeal Joint of the Right Foot

The mean age of our study population was 59.5 years (SE: 9.9). This result is similar to the one obtained by Singwe-Ngandeu et al. in 2007 and Ouedraogo et al. in 2009 in Burkina Faso [4]. Obese subjects were younger than non-obese [57.4 (SE: 1.5) vs. 60.6 (SE: 9.9)], but this difference was not statistically significant. This contrasts with Ma LD et al. [8] results which found that obese were significantly ( $p < 0.05$ ) younger than non-obese subjects [40 (31.50) vs. 45 (36.55) years old]. This difference is a reflection of the sample size difference.

The Metabolic Syndrome (Mets) was significantly ( $p < 0.05$ ) more

frequent in obese than in non-obese subjects (54.5% vs. 22.8%). This predominance of the Mets in obese subjects can be explained by the fact that obesity is a major determinant of Mets as described in many study, particularly by Sherling et al. [11] in 2017 in the United States of America.

The diastolic blood pressure was significantly ( $p < 0.05$ ) higher in obese subjects than in non-obese [89.6 mmHg (SE: 13) vs. 84.05 (SE: 13.6)]. This result is similar to the one obtained by Moulin et al. [12].

The lack of significance in the Systolic Blood Pressure (SBP) elevation ( $p > 0.05$ ) in obese compared to non-obese subjects [143 (SE: 19.3) vs. 137 (SE: 23)] as opposed to Ma LD et al. [8,9] who found out that the SBP was significantly increased in obese can be explained by our relative few number of patients.

Major complications of gout which are tophi and joint deformities were significantly ( $p < 0.05$ ) more frequent in non-obese subjects than in obese subjects with (52.6% vs. 22.7%) for tophi and (22.8% vs. 6.8%) for joint deformities. This result allow us to suggest the effectiveness of obesity paradox in patients with gout [13,14].

This obesity paradox firstly described in patient living with cardiovascular diseases explains that although the obesity is associated with incident Cardiovascular Diseases (CVD) including Heart Failure (HF), it paradoxically leads to a more favorable prognosis in patients with chronic heart failure [15]. In the same way, Nguyen et al. [16] observed that the effect of static obesity value as the exposure on the risk of recurrent attacks gout was entirely mediated through its effect on incident gout and conversely there was no direct effect of obesity independent of its effect on incident gout. We can explain the obesity paradox in patients with gout, using the same argument as the study describing obesity paradox in CVD especially by incriminating: The limiting factor of BMI, metabolic factors particularly the oxidative stress and genetic factors [15,16].

Concerning the limiting factor of BMI, it is recognized as being a practical method in measuring body fat, but this method does not take into consideration the distribution of body fat which may be involved in the inflammatory process that leads to the formation of tophi [1]. We suggest that more precise evaluation methods of the body fat like Magnetic Resonance Imaging (MRI), Computed Tomography (CT), dual energy x-ray absorptiometry, bio-electrical impedance and the weighing under water may bring more convincing results [15,17].

Regarding the metabolic factors and particularly the oxidative stress, we are thinking that this one may play a role in the formation of tophi. Indeed, obesity is associated to hyperuricemia and this one may be a protective factor against oxidative stress given the fact that obesity could be associated to a preponderant production of Dismutase Superoxide (DSO) which herself seems to be negatively correlated with IL-6 and TNF- $\alpha$ , this may reduce the chronic inflammatory process that lead to the formation of tophi [18-20].

Talking of genetic factors, there may be some genetic anomalies with a protective effect in obese subjects and this keep them out of gout complications like tophi and articular deformities [21,22].

We demonstrated in our study that there was a linear correlation ( $r = 0, 4$ ;  $P = 0, 00$ ) between tophi and deformities as observed by Tsuyoshi et al. [23].

## Conclusion

Non-obese subjects develop more complications of gout

compared to obese subjects, particularly with regard to tophi and joint deformities. Tophi have a predilection for the first metatarsophalangeal joint of the right foot of non-obese compared to obese subjects.

## Declaration

Ethical approval and consent to participate, All participants received an information leaflet and signed informed consent. Research authorization have been obtained from different hospitals. Ethical clearance was obtained from the ethical and research committee of the faculty of medicine and biomedical sciences of the University of Yaoundé I.

## Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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## Author's Contributions

DAA, MSN, VJAM, JB designed the study; DAA, VJAM, MSN, JB, CN, VAE, LSS, ME, NOC, AJ, NJR collected data; AMJ, DAA, JRN performed statistical analysis; DAA, VJAM, JB, PJY wrote the manuscript. This work was under the supervision of MSN. All authors have read and approved the manuscript.

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