

## Metabolic Syndrome: Comparison of Occurrence Using Three Definitions in Hypertensive Patients

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**Objective:** To compare the frequency of occurrence of metabolic syndrome using three international definitions and to study the distribution of cardiovascular risk factors among newly diagnosed hypertensive Nigerian subjects.

**Design:** Cross sectional study.

**Settings:** Cardiology unit of LAUTECH Teaching Hospital, Osogbo, Nigeria.

**Participants:** One hundred forty newly diagnosed hypertensive Nigerian subjects, and 70 normotensive controls (age- and sex-matched) were included in this study.

**Methods:** Clinical history and relevant laboratory investigations were performed on all study participants. The definition of metabolic syndrome was based on three international definitions: World Health Organization (WHO), International Diabetes Federation (IDF), and National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III). Ethical approval was obtained for the study. Statistical analyses were performed using SPSS 16.0.

**Results:** There was no difference in age and gender distribution between the hypertensive subjects and controls. ( $55.14 \pm 10.83$  years, females 53.6% vs.  $54.67 \pm 10.89$  years, females 52.9% respectively,  $P > 0.05$ ). The frequency of occurrence of metabolic syndrome among hypertensives was 34.5% according to WHO, 35.0% according to NCEP ATP III, and 42.5% according to IDF criteria. Visceral obesity and reduced high-density lipoprotein (HDL) were the other common cardiovascular risk factors among newly diagnosed hypertensive subjects. Female hypertensives had a higher prevalence of visceral obesity and low HDL.

**Conclusion:** Frequency of occurrence of metabolic syndrome was similar using the NCEP ATP III and WHO definitions. However, the IDF definition resulted in a higher frequency because of the lower cut-off for waist circumference used for identification of visceral obesity. Metabolic syndrome is present in a significant proportion of newly diagnosed hypertensive subjects. Therefore, appropriate screening and treatment are required.

**Keywords:** Frequency of occurrence; Hypertension; Metabolic syndrome; Obesity

**M**etabolic syndrome refers to the clustering or constellation of cardiovascular disease risk factors. The risk factors include elevated blood pressure, dyslipidemia (hypertriglyceridemia, low levels of high density lipoprotein [HDL] cholesterol), hyperglycemia, and central obesity.<sup>1,2</sup> Hypertension is a common cardiovascular disease risk factor worldwide.<sup>3,4,5</sup> Hypertension frequently coexists with many other cardiovascular disease risk factors such as obesity, dyslipidemia, impaired glucose tolerance (or hyperglycemia), and hyperuricemia.<sup>6-10</sup>

There are many definitions of metabolic syndrome, as recommended by the various working groups.<sup>11-13</sup> However, the core components of the syndrome which include increased waist circumference, impaired glucose tolerance, dyslipidemia, and hypertension, are commonly required by all the various groups for diagnosis.<sup>1,11-13</sup> Prevalence of metabolic syndrome varies in different populations and is influenced by several factors including age, race, gender, socio-economic status, work-related activities, and cultural views on body fat.<sup>14</sup> Although the various definitions measure similar components, each uses different combinations of cardiovascular disease risk factors. The World Health Organization (WHO) in 1999

made insulin resistance evaluated by the euglycemic study as the pivot for the diagnosis of metabolic syndrome.<sup>11,14</sup> The National Cholesterol and Education Program Adult Treatment Panel III (NCEP ATP III), International Diabetes Federation (IDF), and American Association of Clinical Endocrinology (AACE) adopted visceral obesity as the pivot for the diagnosis of metabolic syndrome. However, the European Group for the Study of Insulin Resistance (EGIR) suggested that the underlying etiology in the clustering of cardiovascular risk factors is insulin resistance.<sup>11-14</sup> The WHO, NCEP ATP III, and IDF criteria for diagnosis of metabolic syndrome are outlined in table 1.

Metabolic syndrome has been associated with an increased tendency to develop type 2 diabetes mellitus and cardiovascular diseases.<sup>15-17</sup> The various criteria identify similar sets of people with cardiovascular risk factor clustering. The IDF definition includes a race-specific cut-off for visceral obesity. Abdominal obesity is race- and gender-specific as suggested by many population studies.<sup>1,10</sup> Information on the frequency of occurrence of metabolic syndrome in newly diagnosed hypertensive Black African patients is scarce. A comparative analysis of three standard international definitions for diagnosing metabolic syndrome is expected to give an

**Table 1.** Definition of metabolic syndrome based on different criteria used.

Clinical Measure	WHO (1999) <sup>11</sup>	ATP III (2001) <sup>12</sup>	IDF (2005) <sup>13</sup>
Insulin resistance	IGT, IFG, T2DM, or lowered insulin sensitivity, plus any 2 of the below listed features	None, but any 3 of the 5 features listed below	None
Body weight	Men: WHR > 0.90 Women: WHR > 0.85 and/or BMI > 30 kg / m <sup>2</sup>	WC ≥102 cm in men WC ≥88 cm in women	Increased WC (population specific) plus any 2 of the features listed below
Lipid	TG ≥150 mg/dL (1.7 mmol/L) and/or HDL-C <35 mg/dL (0.9 mmol/L) in men HDL-C <39 mg/dL (1.0 mmol/L) in women	TG ≥ 150mg/dL (1.7mmol/L) HDL-C <40 mg/dL (1.03 mmol/L) in men HDL-C <50 mg/dL (1.29 mmol/L) in women	TG ≥ 150mg/dL (1.7mmol/L) or on TG treatment HDL-C <40 mg/dL (1.03 mmol/L) in men HDL-C < 50 mg/dL (1.30 mmol/L) in women or on HDL-C treatment
Blood pressure	≥140/90 mmHg	≥130/85 mmHg	≥130 mmHg systolic or ≥ 85 mmHg diastolic or on hypertension treatment
Glucose	IGT, IFG, or T2DM	>110 mg/dL (6.1 mmol/L) (includes diabetes)	≥100 mg/dL (5.6 mmol/L) (includes diabetes)
Others	Microalbuminuria: UAE >20 µg/min or urinary ACR >30 mg/g		

WHO=World Health Organization; ATP III= Adult Treatment Panel III; IDF= International Diabetes Federation; IGT=impaired glucose tolerance; impaired fasting glycemia; T2DM=Type 2 diabetes mellitus; WHR=waist-hip ratio; BMI=body mass index; WC=waist circumference; TG=triglycerides; HDL-C=high-density lipoprotein cholesterol; ACR=albumin-creatinine ratio

**Table 2.** Clinical and demographic parameters of study participants.

Parameter	Hypertensives n=140	Controls n=70	P value
Age (years)	55.14 ± 10.83	54.67 ± 10.89	0.792
Female, n (%)	75 (53.6)	37 (52.9)	0.672
Mean WC, Male (cm)	92.5 ± 13.4	84.0 ± 7.3	0.000*
Mean WC, Female (cm)	94.3 ± 11.5	84.6 ± 10.7	0.000*
Mean HC (cm)	100.15 ± 11.63	92.79 ± 9.92	0.015*
Mean WHR	0.94 ± 0.082	0.91 ± 0.054	0.053
Mean BMI (kg/m <sup>2</sup> )	26.89 ± 5.31	23.86 ± 3.46	0.0045*

\* Statistically significant. WC=waist circumference; HC=Hip circumference; WHR=waist hip ratio; BMI=Body mass index

overview of the frequency of metabolic syndrome in a population. The aim of this study was to compare the frequency of occurrence of metabolic syndrome using three standard international criteria/definitions and to study the distribution of cardiovascular risk factors among newly diagnosed hypertensive Nigerians.

### Materials and Methods

This study was carried out in the Department of Medicine of Ladoké Akintola University of Technology Teaching Hospital (LAUTECH), Osogbo, Nigeria. Institutional ethical approval was obtained for the study from the LAUTECH Teaching Hospital research and ethical board. It was a cross-sectional study consisting of 140 consecutive newly diagnosed hypertensive subjects and 70 normotensive controls. The controls were hospital staff, patients' relatives, and students who voluntarily gave their consent to participate. The control subjects were age- and sex-matched with the hypertensive subjects. The diagnosis of hypertension was made according to standardized criteria<sup>18</sup> (subjects with systolic blood pressure of  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg taken twice after at least five minutes of rest in the clinic). Subjects with mild hypertension defined by the Joint National Committee Report VII (JNC7 Stage 1) were asked to return after two weeks for further review and confirmation. Those with moderate and severe hypertension (JNC7 Stage 2) were recruited for the study immediately. Exclusion criteria included evidence of chronic renal impairment, pregnancy,

current illnesses, and those with previously diagnosed diabetes mellitus. Subjects' socio-demographic data, clinical history, examinations, and investigations were taken.

Waist circumference (in centimeters) was measured at the mid-point between the lowermost rib and the iliac crest on expiration. The hip circumference (in centimeters) was taken across the greater trochanters. The waist-to-hip ratio (WHR) was determined. Blood samples were collected after at least eight hours overnight fast for serum biochemistry, lipid profile (including total cholesterol [TC], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C] and triglycerides [TG]), and plasma glucose in all participants. Laboratory analysis of fasting serum lipids was performed using the Randox laboratories lipid profile kit (United Kingdom). Hypertriglyceridemia was defined as serum triglycerides  $>1.7$  mmol/L, hypercholesterolemia as serum cholesterol  $>6.5$  mmol/L, reduced HDL as serum HDL  $<1.30$  mmol/L (females) and  $<1.03$  mmol/L (males). Fasting plasma glucose was done by the glucose oxidase method.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software (version 16, SPSS, Inc, Chicago, IL, USA). Continuous and categorical variables were displayed as means  $\pm$  standard deviation (SD) and percentages, respectively. The student's *t*-test was used to assess the differences between means. Differences between

**Table 3.** Distribution of other cardiovascular risk factors and frequency of occurrence of metabolic syndrome in the study population.

Parameter	Hypertensives n=140	Controls n=70	P value
WC $>102$ cm (males)	16 (24.6%)	1 (3.0%)	$<0.05^*$
WC $>88$ cm (females)	48 (64.0%)	12 (32.4%)	$<0.05^*$
HDL-C $<1.03$ mmol/L (males)	25 (38.5%)	9 (27.3%)	$<0.05^*$
HDL-C $<1.30$ mmol/L (females)	42 (56.0%)	20 (54.1%)	$<0.05^*$
TG $>1.7$ mmol/L	21 (15.0%)	7 (10%)	$<0.05^*$
FPG $>6.1$ mmol/L	29 (20.7%)	2 (2.9%)	$<0.05^*$
FPG $>5.6$ mmol/L	60 (42.9%)	7 (10.0%)	$<0.05^*$
WC $>94$ cm (Males)	32 (49.2%)	3 (9.1%)	$<0.05^*$
WC $>80$ cm (females)	64 (85.3%)	20 (54.1%)	$<0.05^*$
WHR $>0.9$ (Males)	46 (70.8%)	13 (39.4%)	$<0.05^*$
WHR $>0.85$ (females)	45 (60.0%)	19 (51.4%)	$<0.05^*$

\* Statistically significant. WC=Waist circumference; HDL-C=High density lipoprotein cholesterol; TG=Triglycerides; FPG-Fasting plasma glucose; WHR=waist-hip ratio.

**Table 4.** Prevalence of metabolic syndrome among hypertensives according to three standard definitions/criteria.

Criteria	Male (n= 65)	Female (n= 75)	Total
ATP III	20 (30.8%, CI 19.6-42.0%)	28 (37.3%, CI 26.6-48.0%)	48 (34.3%, CI 26.4-42.2%)
WHO	22 (33.8%, CI 22.31-46.3%)	27 (36.0%, CI 25.2-46.8%)	49 (35.0%, CI 27.1-42.9%)
IDF	23 (35.4%, CI 23.8-47.0%)	37 (49.3%, CI 38.1-60.5%)	60 (42.9%, CI 34.7-51.1%)

ATP III=National Cholesterol Education Programme Adult Treatment Panel III; WHO=World Health Organization; IDF=International Diabetes Federation

categorical variables were analyzed by chi-square test and the analysis of variance (ANOVA) for continuous variables. *P* values <0.05 were considered to be statistically significant.

### Results

Hypertensive subjects and normal controls were matched well in age and gender distribution. Hypertensive subjects had a higher mean waist circumference (94.3 ± 11.5 cm [females]) than normotensive controls (84.6± 10.7cm [females]), respectively. Body mass index (BMI) and hip circumference were significantly higher among hypertensive subjects than normal controls as shown in table 2.

Table 3 shows the pattern of distribution of major cardiovascular risk factors among the study population. Hypertensive subjects had a higher prevalence of all cardiovascular risk factors. Visceral obesity was the most prevalent of the other cardiovascular risk factors using the IDF population-based classification, followed by low-HDL and impaired fasting glucose in the study population.

Table 4 shows the prevalence of metabolic syndrome based on the three standard definitions. The ATP III and the WHO definitions gave similar prevalence (34.3% vs. 35%, respectively), while the IDF definition gave a higher prevalence of 42.9%.

Table 5 shows the comparison of clinical and laboratory characteristics between male and female hypertensive subjects.

Female hypertensive subjects had a higher mean waist circumference (103.7 ± 11.52 cm vs. 93.4 ± 12.4 cm, *P*<0.05) and BMI (27.7 ± 5.7 vs. 25.7± 4.5 kg/m<sup>2</sup>, *P*<0.05) respectively, compared to their male counterparts. Female subjects had a higher systolic blood pressure (148.4 ± 24.2 vs. 142.4 ± 29.8 mmHg, *P*>0.05), and pulse pressure (59.7±18.2 vs. 53.6±30.4 mmHg, *P*>0.05) than their male counterparts, respectively; however, these were not statistically significant.

### Discussion

This study demonstrated that the prevalence of metabolic syndrome among newly diagnosed, non-diabetic, hypertensive Nigerian subjects was similarly high using the WHO and the NCEP ATP III criteria. The IDF criteria, however, resulted in a higher prevalence. This was because of the lower cut-off value for waist circumference required to diagnose visceral obesity that is population-specific according to the IDF criteria. Using any of the three criteria, at least one third of newly diagnosed, non-diabetic, hypertensive subjects were diagnosed with metabolic syndrome in this study. The three definitions have been shown to identify individuals who have metabolic syndrome and are at an increased risk for cardiovascular diseases. This study agrees with other reports that have shown that the prevalence of metabolic syndrome is similar among a particular group using these various criteria/definitions.<sup>19-21</sup>

The prevalence of metabolic syndrome among hypertensive subjects in this study was between 34.3% and 42.9%,

**Table 5.** Clinical and laboratory characteristics of male and female hypertensive subjects.

Variable (mean)	Male (n=65)	Female (n=75)	<i>P</i> value
Age (years)	54.9±11.5	54.5±10.7	0.862
SBP (mmHg)	142.4±29.8	148.4±24.2	0.191
DBP (mmHg)	88.8±17.7	88.7±16.5	0.828
WC (cm)	93.4±12.4	103.7±11.52	0.013*
FBS (mmol/L)	5.7±2.3	5.3±1.6	0.105
TG (mmol/L)	1.2±0.4	1.2±0.5	0.648
TC (mmol/L)	4.7±1.53	4.4±1.2	0.216
HDL (mmol/L)	1.2±0.43	1.2±0.48	0.383
BMI (kg/m <sup>2</sup> )	25.7±4.5	27.7±5.7	0.007*
PP (mmol/L)	53.6±30.4	59.7±18.2	0.116

\* Statistically significant. SBP=Systolic blood pressure; DBP=Diastolic blood pressure; WC=waist circumference; FBS=Fasting blood sugar; TG=triglycerides; TC=Total cholesterol; HDL=High density lipoprotein; BMI=Body mass index; PP=Pulse pressure.

depending on the criteria used. This is similar to what was reported among newly diagnosed South African hypertensive subjects.<sup>22</sup> It is, however, lower compared to values reported from developed countries like the United States and many European countries.<sup>23,24</sup> Farsang et al<sup>23</sup> reported that the prevalence of metabolic syndrome in hypertensive subjects across Europe varies between 50% to 68%, with the highest reported from Central Europe and the lowest reported from the Mediterranean. This inter-regional difference has been suggested to be due to nutritional factors, exercise, and genetics. In a report from Spain, 52% of a hypertensive cohort fulfilled the criteria for the diagnosis of metabolic syndrome.<sup>25</sup> The variation observed in prevalence is likely due to the interplay of many factors such as impact of genetics/race, lifestyle, and prevalence of the constituent cardiovascular risk factors.<sup>1,26</sup> Dyslipidemia has been reported to be lower among Black Africans than Caucasians.<sup>27</sup> The prevalence rate of obesity continues to increase worldwide which may lead to an increase in the prevalence rate of metabolic syndrome unless aggressive primary and secondary prevention strategies are implemented. The reported lower frequency of occurrence of metabolic syndrome among our study participants compared to Caucasians is suggested to be due to racial factors and possibly a lower prevalence of obesity and dyslipidemia among native Black Africans.

Obesity was the most common of the other cardiovascular risk factors present among hypertensive and normotensive patients. Obesity has been suggested as the major underlying risk factor driving the presence of metabolic syndrome. There were more females than males with metabolic syndrome, although this was not statistically significant. This was due to higher a proportion of obesity among females. Visceral obesity engenders insulin resistance that can precipitate dyslipidemia and other components of metabolic syndrome. This may be deduced because clinical and demographic characteristics are similar among male and female hypertensives, except in terms of indicators of obesity both in terms of waist circumference and BMI. Therefore, the higher prevalence of metabolic syndrome among females is likely to be significantly related to the differential prevalence of obesity between the male and female hypertensive subjects.

However, it should be a serious public health concern that at least a third of newly diagnosed hypertensive patients can be diagnosed as having the cardiometabolic syndrome. This places them already at increased risk for cardiovascular disease and events. The WHO predicts that the prevalence of cardiovascular disease worldwide will double by the year 2020, and most of the increase will come from the developing countries.<sup>5</sup> Therefore, efforts should be initiated toward appropriate public health interventions and early identification of individuals at risk of cardiovascular disease. There is, therefore, the need to adequately screen newly diagnosed hypertensive patients for other cardiovascular risk factors and to institute appropriate strategies for the control of obesity in order to achieve improved cardiovascular care and reduce the

burden of cardiovascular diseases among them. Furthermore, identification of multiple cardiovascular risk factors among obese individuals, those with hyperlipidemia, and those with a family history of cardiovascular disease as a population-based health intervention strategy will improve cardiovascular care and ultimately reduce the cardiovascular risk burden among the population at large.

## Conclusion

Clustering of cardiovascular risk factors was common among newly diagnosed hypertensive subjects. The WHO and NCEP ATP III definitions resulted in similar prevalence of metabolic syndrome. However, the IDF criteria resulted in a higher prevalence due to the race-specific definition of visceral obesity.

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