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Original Research

Metabolic Syndrome in HIV: Prevalence, correlates, concordance of Diagnostic Criteria and relationship to Carotid Intimal Media Thickness in a Sub-Saharan Population

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Abstract

Background: The prevalence and usefulness of MetS in determining CVD risk in at-risk populations are influenced by its definition. In a cohort of HIV-positive Nigerians, we evaluated MetS based on various defining criteria, their agreement with one another, and their association to a CVD endpoint, Carotid-Intimal-Media-Thickness (CIMT).
Methodology: In this cross-sectional study, 145 HIV-positive individuals who were enrolled in HIV clinics at the Faith Alive Foundation and Jos University Teaching Hospital in Jos, Nigeria, were randomly chosen. Biophysical and anthropometric measurements including blood pressure, height, weight, waist circumference, and hip-circumference, as well as clinical records, CIMT, fasting plasma glucose, and lipid profile, were assessed.
Result: The median (Interquartile range) age of the participants was 41 (35-48) years, and the majority (71.7%) were females. The prevalence of metabolic syndrome (MetS) by the Adult Treatment Panel-III (ATP), International Diabetes Federation (IDF), and Joint Interim Statement (JIS) criteria were 30.3%, 32.4%, and 35.2% respectively. MetS by all criteria was more prevalent among females and participants ≥ 40 years, $p<0.05$. Low HDLc (93.6-95.5%), Central obesity (86.3-95.5%), and hypertension (80.9-86.4%) were the most frequent components of MetS. HIV-related parameters were not associated with MetS. The overall agreement among MetS criteria was almost perfect between IDF and JIS criteria (k=0.94); and strong between IDF vs., ATP (k=0.82) and ATP vs. JIS (k=0.89). There was no significant difference in the median CIMT in PLHIV with and without MetS across all defining criteria.
Conclusion: The prevalence of MetS in PLHIV is relatively high, particularly among females and older individuals. The correlations between the defining criteria were fairly strong and consistent across subpopulations of PLHIV. MetS based on these criteria, however, do not significantly correlate with rising CIMT.
Keywords: HIV, Metabolic Syndrome, Obesity, Cardiovascular disease risk, dyslipidaemia

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Introduction

The cardiovascular disease burden in Africa is widely accepted to be on the increase.[1,2] The growing tendency towards a more Westernized lifestyle in Sub-Saharan African populations is believed to underlie the epidemiological transition which is catalyzing a rise in the incidence of non-communicable diseases such as obesity, diabetes mellitus, cardiovascular diseases, and cancers in this region.[3] However, the association between HIV and cardio-metabolic risk factors is gaining more recognition as an alternative explanation for the rising cardiovascular disease burden in SSA.[4,5]HIV prevalence in SSA is the highest in the world, with an estimated 25.7 million people living with the disease, 1.1 million new infections and 470,000 dying from the disease in 2018, according to the World Health Organization (WHO).[6] The widespread use of Anti-retroviral Therapy (ART) in this region has resulted in an overall improvement in the quality of life in People living with HIV (PLHIV) and with increased longevity, an inadvertent increase in the risk of cardiovascular disorders in these individuals.

In order to mitigate the likely increase in mortality and morbidity due to CVDs in these individuals, the need for inclusion of cardiovascular risk assessment and management of cardiovascular disorder in routine integrated HIV care has been advocated.[7] However, cardiovascular risk assessment in HIV-infected individuals presents unique challenges when compared to non-infected populations. For instance, HIV infection and the effects of ART through several mechanisms, including inflammatory response to the virus, altered glucose metabolism, dyslipidaemia, and endothelial dysfunction increases the risk of CVDs.[8,9]ART may also cause differential fat deposition, which may affect the assessment of obesity and metabolic syndrome (MetS).The pattern, magnitude, and significance of these cardiometabolic risks in PLHIV vary across populations being modified by factors such as diet, smoking, alcohol intake, and genetics, among others which differ in pattern among people of different ethno-racial descent.[10]Therefore, the prevalence and significance of cardiovascular risk may vary in PLHIV of African descent compared to their European counterparts.

Cardio-metabolic risk factors such as obesity and metabolic syndrome have been previously studied in PLHIV in Nigeria and SSA.[11–13]However, there are wide disparities in their reported burdens due to differing parameters of assessment or definition. Several studies have highlighted the pros and cons of each classification system.[10,14]Given that the classification criteria for metabolic syndrome have been largely extrapolated from data obtained in HIV-uninfected individuals, especially in Western countries, it is unclear if these definitions are valid for PLHIV and how they relate to cardiovascular disease endpoint such as Carotid Intimal Thickness (CIMT). In this study, we assessed some criteria for MetS and their concordance with one another and their relationship with Carotid Intimal Thickness (CIMT) in PLHIV in a Nigerian population.

Methods

Study Design

This was a cross-sectional study involving participants chosen from HIV clinics supported by the AIDS Prevention Initiative in Nigeria at the Faith Alive Foundation (FAF) and Jos University Teaching Hospital (JUTH), both in Jos, North-Central Nigeria. Jos, the capital city of Plateau State, is home to both the JUTH and FAF HIV clinics, which together care for over 16000 HIV-positive people. The same National AIDS Control Agency treatment protocol is used for HIV care at both clinics.

Study Population

The study participants include 145 randomly selected HIV-infected adults on ART between ages 20 and 70 years (inclusive) enrolled at JUTH and FAF HIV clinics. Selected HIV-infected adults had undetectable viral load (plasma HIV-1 RNA < 20 copies per milliliter) within 1 year before the study. We excluded very ill patients, pregnant women, and those on current ARV regimen for less than 6 months. In addition, confirmed CVD (stroke, myocardial infarction, and/or peripheral vascular disease), malignancy, and active

infection (documented in the medical records), receiving glucocorticoids, growth hormone, or other anabolic agents within the past 6 months were excluded from the study.

Study Procedure

We collected pertinent socio-demographic information and clinical information from each participant with the aid of a pretested semi-structured questionnaire. HIV-related history was obtained from patients' records, such as known duration of HIV infection, the start date of ART, current ARV regimen, and previous changes in regimen, as well as the latest CD4+ cell count, and HIV viral load were recorded if done within the last 12 months. The relevant history of CVD risk factors, prior illnesses, co-morbidities (such as hypertension, diabetes mellitus and dyslipidemia), and co-medications (such as steroid and non-steroidal anti-inflammatory agents), as well as lifestyle factors like exercise, diet, smoking, and alcohol use were also sought. Biophysical measurements were obtained according to standard procedures. These included height, weight, hip and waist circumference measurements, and blood pressure readings (BP).

Blood sample collection and biochemical analysis

Following an 8–12 hour overnight fast, each subject had four millilitres (mls) of blood taken from them into a plain vacutainer tube for the lipid profile and three mls into a fluoride oxalate vacutainer tube for the glucose assay. The supernatant, plasma, or serum was removed from the specimens after 10 minutes of centrifugation at 4000 revolutions per minute. While samples for aliquots for lipid profile assays were kept at -20°C in a carefully maintained freezer for one month prior to the analyses, plasma glucose was assessed on the day that samples were collected.

Fasting plasma glucose concentration was measured using the Hexokinase method; triglyceride (TG) and high-density lipoprotein cholesterol (HDLc) were analyzed with standard enzymatic methods. All assays were analyzed on a Roche Cobas C111 analyzer (Roche Diagnostics, Germany). Quality control was assured by simultaneous analysis of control specimens.

Carotid Intima-Media Thickness (CIMT) Measurement

This was conducted by a radiologist using a high-resolution real-time GE Logiq® C5 color Doppler ultrasound scanner (2017 model) (GE Healthcare Chicago, Illinois, USA) fitted with a 7.5MHz linear probe. The subject was positioned supine, with the neck hyperextended (with the aid of a soft pillow under the shoulders. The head was turned to the opposite side to examine the right and left carotid arteries for each scan.The common carotid artery (CCA) was found at its origin, and the probe was then moved along the artery's long axis at various scanning angles (anterior and lateral) until it reached the carotid bifurcation (bulb) and the proximal 10 mm of the internal carotid artery (ICA). The Intimal Media Thickness (IMT) was taken in the longitudinal plane at the point of maximal thickness on the far wall of the CCA, (within 10mm proximal to the bifurcation), the bulb, and at the ICA (within 10mm distal to the bifurcation). The machine was frozen and using its caliper markers, the distance between the inner echogenic line, which represents the intima-blood interface, and the outer echogenic line, which represents the media-adventitia junction, was measured as the IMT. The images were magnified to improve the accuracy of the caliper placement. For quality assurance, individuals were rescanned at random. According to the protocol used in the Atherosclerosis Risk In Communities (ARIC) study, the mean of the maximum IMT from the far wall of the distal common carotid artery, the carotid bifurcation, and the proximal internal carotid on the right and left sides (mean of 6 sites) was recorded as the mean CIMT.[15]

Working Definitions

Metabolic syndrome (MetS) was defined according to the criteria of the International Diabetes Federation (IDF), National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII), and Joint Interim Statement (JIS).

Metabolic syndrome (MetS) was defined according to the International Diabetes Federation (IDF 2005) guidelines as the constellation of at least three abnormalities–abdominal obesity (abdominal circumference

≥ 94 cm in males and ≥ 80 cm in females), raised blood pressure (SBP ≥130 mmHg and or DBP ≥85 mmHg), FBG ≥100 mg/dL, triglycerides ≥1.70 mmol/L and HDLc< 1.03mmol/Lin males and <1.30mmol/L in females.[16]

The National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII, 2005 Revision) defined MetS as presence of any three of the following: waist circumference over ≥ 102cm (men) or 88cm (women) and at least two of the following: blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women) and fasting blood sugar over 100 mg/dl.[17]

The Joint Interim Statement JIS (2009), a harmonized definition of MetS proposed in 2009 by several international organizations: at least three of five criteria including waist circumference over 40 inches (men) or 35 inches (women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women) and fasting blood sugar over 100 mg/dl.[18]

MetS was defined by the WHO 1998 criteria as Insulin resistance or diabetes, plus two of the following criteria: Waist/hip ratio: >0.90 (M), >0.85 (F); or BMI >30 kg/m2; TG 150 mg/dl or HDLc<35 mg/dl (M), <39 mg/dl (F); Hypertension ≥ 140/90 mmHg and Microalbuminuria.[19] These criteria were not used in this study because insulin and microalbumin were not assayed.

Statistical Analysis

Data was entered into Microsoft Excel® version 2.0 (Microsoft Corp., Redmond, Washington, USA) and exported to SPSS® software version 23.0 (IBM Corp., Chicago, Illinois, USA) for analysis. Descriptive statistics are presented as medians with interquartile ranges (IQRs) for non-parametric continuous variables, and proportions (as percentages) for categorical variables. Mann-Whitney U test was used to test the difference in medians of continuous variables between groups and Chi-square and Fisher's exact where appropriate were used to test relationships among variables. The significance level was set at $p \leq 0.05$. The agreement between the diagnostic criteria for the metabolic syndrome was assessed with the use of Kappa statistics. Kappa statistics values were interpreted as none (≤ 0.2), minimal (0.21- 39), weak (0.40-0.59), moderate (0.60-0.79), strong (0.80-0.90) and "almost perfect" (> 0.90).[20]

Ethical consideration

The ethical committee of Jos University Teaching Hospital and Faith Alive Foundation approved the study (JUTH/DCS/ADM/127/XXV/168). Written Consent for participation in the research was obtained from all participants.

Results

One hundred and four (71.7%) from a total of 145 participants in the study were women. The overall median (IQR) age was 41 (35-49) years with men significantly older than women. (p=0.001). Women had a higher median BMI of 26.0 (23.0-29.0) compared to males 23.5 (21.3-27.3), p=0.019 while men had higher WHR than females, (0.88 (0.86-0.94) and 0.85 (0.82-0.96) respectively), p=0.002.The fasting glucose and lipid profiles were similar among male and female participants although the median LDL cholesterol was slightly higher among females. The Carotid intimal medial thickness (CIMT); and intimal medial thickness calculated by CCA and BULB measurement IMT (CCA and BULB) were significantly higher in males than females. p=0.001. The overall median known duration of infection and ARV use were 5 years and 4 years. This was significantly higher in males than females. p=0.027 and0.029 respectively. The latest CD4 counts were higher in females than their male counterparts, 487.0 (320.0-674.5) and 375.0 (278.5-491.0) respectively, p=0.015, see Table 1.

Table I: General Characteristics of the study Participants by Gender

Variable (Median; IQR)	Total (n=145)	Female (n=104)	Male (n=41)	p-value
Age (years; (median; IQR)	41.0 (35.0-49.0)	40.0 (33.0-47.0)	48.0 (41.0-55.0)	0.001
Systolic BP (SBP) mmHg (median; IQR)	122.0 (110.0-131.5)	120.0 (110.0-130.0)	130.0 (109.0-144.0)	0.111
Diastolic BP (SBP) mmHg (median, IQR)	80.0 (70.0-86.0)	78.5 (70.0-85.0)	80.0 (70.0-90.0)	0.403
BMI (kg/m^2) (median; IQR)	25.4 (22.2-28.3)	26.0 (23.0-29.0)	23.5 (21.3-27.3)	0.019
Waist circumference (cm) (median; IQR)	86.0 (77.5-94.0)	87.0 (78.0-96.0)	85.0 (77.0-90.0)	0.124
Waist-to-hip ratio (WHR) (median; IQR)	0.86 (0.83-0.92)	0.85 (0.82-0.96)	0.88 (0.86-0.94)	0.002
Fasting Plasma Glucose (mmol/L) (median, IQR)	5.1 (4.7-5.5)	5.0 (4.7-5.5)	5.3 (4.9-5.6)	0.158
Total Cholesterol (mmol/L) (median; IQR)	4.9 (4.2-5.8)	5.1 (4.3-5.9)	4.7 (3.9-5.4)	0.054
Triglyceride (mmol/L) (median; IQR)	1.0 (0.7-1.5)	1.0 (0.7-1.5)	1.0 (0.8-1.5)	0.495
HDL Cholesterol (mmol/L) (median; IQR)	1.0 (0.8-1.2)	1.0 (0.8-1.2)	0.9 (0.7-1.2)	0.414
LDL Cholesterol (mmol/L) (median; IQR)	2.5 (1.8-3.1)	2.7 (1.9-3.1)	2.0 (1.5-2.9)	0.044
CIMT (median; IQR)	0.57 (0.52-0.65)	0.57 (0.50-0.62)	0.63 (0.56-0.67)	0.002
IMT (CCA and BULB) (median; IQR)	0.65 (0.58-0.75)	0.63 (0.58-0.70)	0.73 (0.63-0.80)	0.001
IMT (CCA) (median; IQR)	0.60 (0.50-0.65)	0.55 (0.50-0.60)	0.60 (0.55-0.73)	0.002
Known duration of infection (years) (Median; IQR)	5.0 (3.0-10.0)	5.0 (3.0-9.0)	8.0 (4.0-11.5)	0.027
Duration of ARV (years) (Median; IQR)	4.0 (3.0-9.5)	4.0 (3.0-8.0)	7.0 (3.5-11.0)	0.029
Nadir CD4 count (cells/ul) (Median; IQR)	167.0 (100.0-240.0)	198.5 (90.3-244.5)	143.0 (102.0-215.5)	0.251
Latest CD4 count (cells/ul) (Median, IQR)	487.0 (304.5-613.0)	487.0 (320.0-674.5)	375.0 (278.5-491.0)	0.015

Prevalence of Metabolic Syndrome and associated factors

The prevalence (95% CI) of metabolic syndrome (MetS) by theATPIII 2005, IDF, and JIS criteria were 30.3 (23.4-37.9),32.4 (24.1- 40.0), and 35.2 (27.1-42.3) respectively. Females were proportionally more likely to have MetS compared to males by all criteria; IDF criteria (38.5% vs. 17.1%), p=0.013, NCEF-ATP criteria (35.6% vs. 17.1%), p=0.029 and JIS Criteria (40.4% vs 17.6%), p=0.036. In relation to age,MetS was proportionally more common in the participants who were ≥ 40 years by all criteria; IDF criteria (40.9% vs. 19.3%), p=0.007, NCEF-ATP criteria (39.8% vs. 15.8 %), p=0.029 and JIS Criteria (43.4% vs 21.1%), p=0.003.

Table 2: Prevalence (95% confidence interval) of the metabolic syndrome by the IDF, NCEF-ATP III 2005 and JIS criteria presented by gender and relationship with demographic and HIV-related factors.

Variables Overall Prevalence (%) 95% CI n=145	MetSYN (IDF) 32.4 (24.1-40.0) n=47/145			MetSYN (NCEF-ATP) 30.3 (23.4-37.9) n=44/145			MetSYN (JIS) 35.2 (27.1-42.3) n=51/145		
	No	Yes	p-value	No	Yes	p-value	No	Yes	p-value
Demographic data									
Female, n (%)	64 (61.5)	40 (38.5)	0.013	67 (64.4)	37 (35.6)	0.029	62 (59.6)	42 (40.4)	0.036
Male, n (%)	34 (82.9)	7 (17.1)		34 (82.9)	7 (17.1)		32 (78.0)	9 (17.6)	
Age group < 40 years, n (%)	46 (80.7)	9 (19.3)	0.007	48 (84.2)	9 (15.8)	0.002	45 (78.9)	12 (21.1)	0.003
Age group ≥ 40 years, n (%)	52 (69.1)	36 (40.9)		53 (60.2)	35 (39.8)		49 (55.7)	39 (43.3)	
Dyslipidemia									
HIV-Related parameters									
Receiving First-line ARV, n (%)	93 (68.4)	43 (31.6)	0.668	95 (69.9)	41 (30.1)	1.000	89 (65.4)	47 (34.6)	0.809
Receiving Second-line ARV, n (%)	5 (55.6)	4 (44.4)		6 (66.7)	3 (33.3)		5 (55.6)	4 (44.4)	
Known duration of infection (years) (Median; IQR)	5.0 (3.0-10.0)	4.0 (3.0-10.0)	0.355	6.0 (3.0-10.0)	4.5 (3.0-8.8)	0.350	6.0 (3.0-10.0)	4.0 (3.0-9)	0.287
Duration of ARV (years) (Median; IQR)	5.0 (3.0-10.0)	4.0 (3.0-9.0)	0.377	5.0 (3.0-10.0)	4.0 (3.0-8.0)	0.271	5.0 (3.0-10.0)	4.0 (3.0-8.0)	0.289
Nadir CD4 count (cells/ul) (Median; IQR)	193.5 (105.8-270.8)	146.0 (65.0-222.0)	0.069	193.0 (102.0-257.5)	153.5 (72.8-220.0)	0.176	193.5 (102.0-270.8)	151.0 (66.0-220.0)	0.118
Latest CD4 count (cells/ul) (Median; IQR)	445.0 (326.7-610.0)	410.0 (273.0-625.0)	0.389	444.0 (324.5-627.0)	413.0 (266.8-605.5)	0.365	444.5 (329.8-621.5)	401.0 (273.0-610.0)	0.269
CIMT (cm) (Median, IQR)	0.57 (0.52-0.65)	0.58 (0.52-0.65)	0.576	0.57 (0.51-0.65)	0.59 (0.52-0.65)	0.653	0.57 (0.52-0.65)	0.60 (0.52-0.65)	0.455
IMT (CCA and BULB) (Median; IQR)	0.63 (0.58-0.75)	0.68 (0.58-0.73)	0.524	0.63 (0.58-0.75)	0.65 (0.58-0.70)	0.764	0.63 (0.58-0.75)	0.68 (0.58-0.73)	0.460

The use of first-line or second-line ARVs was not related to MetS by any criteria. The association of WHO criteria with duration of HIV infection or ARV, nadir CD4 counts, latest CD4 counts, and intimal media thickness were similar in MetSand non-MetS groups by all criteria, p> 0.05, see Table 2.The least common component of MetS was abnormal triglyceride (36.2-40.9%) followed by impaired fasting glucose (46.8-47.7%). Central obesity and low HDLc were joint highest in occurrence in the IDF criteria followed by hypertension (93.6%). Low HDLc was the most prevalent in the ATP (95.5%) and JIS (94.1%) followed by hypertension (86.4%) in ATP criteria and central obesity (86.3%) in the JIS criteria, (see Figure 1).

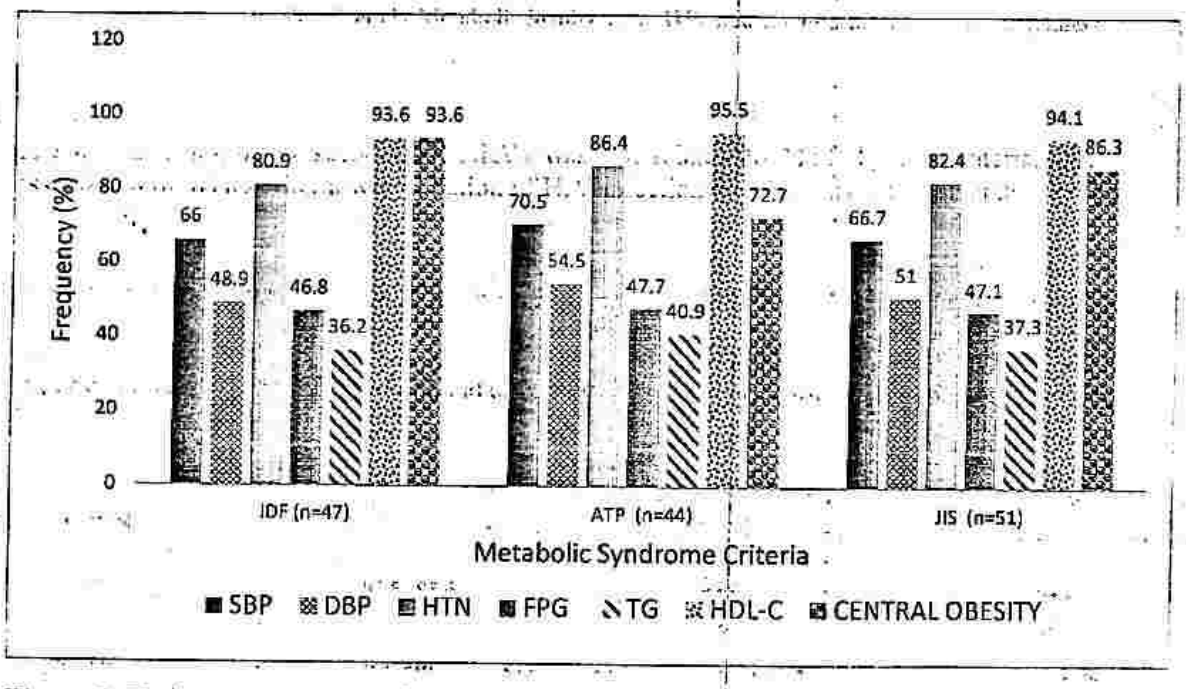

Figure 1: Frequency of components of Metabolic syndrome across different criteria.

Concordance between Different MetS Criteria

Overall, the strongest concordance was between the IDF and JIS criteria with a kappa value of 0.94 (95%CI: 0.87 – 0.99). This was accentuated among females, kappa= 0.96 (95%CI: 0.90 – 1.00), while among males, the agreement between JIS and IDF on one hand and JIS and ATP on the other were similar with a kappa of 0.85 in both instances. In relation to age, the agreement between the IDF and JIS was stronger in the group below 40 years kappa = 0.95 (0.84 – 1.00) compared to those 40 years and above, kappa = 0.93 (0.84 – 1.00), see table 3.

Table 3: Kappa statistics and 95% confidence interval for the concordance between the BMI, IDF, and ATPIII 2005 and WHR Metabolic Syndrome criteria presented by gender and age group

		MetSYN (JIS)	MetSYN (NCEF-ATP)	MetSYN (IDF)
Overall	MetSYN (IDF)	**0.94 (0.87– 0.99)** $p<0.001$	0.82 (0.72 – 0.92) $p<0.001$	1.0
	MetSYN (NCEF-ATP)	0.89 (0.79 – 0.96) $p<0.001$	1.0	
	MetSYN (JIS)	1.0		
Female	MetSYN (IDF)	**0.96 (0.90 – 1.00)** $p<0.001$	0.86 (0.74 – 0.96) $p<0.001$	1.0
	MetSYN (NCEF-ATP)	0.90 (0.81 – 0.98) $p<0.001$	1.0	
	MetSYN (JIS)	1.0		
Male	MetSYN (IDF)	0.85 (0.55– 1.00) $p<0.001$	0.66 (0.23 – 0.93) $P=0.006$	1.0
	MetSYN (NCEF-ATP)	**0.85 (0.52 – 1.00)** $p<0.001$	1.0	
	MetSYN (JIS)	1.0		
Age < 40 years	MetSYN (IDF)	**0.95 (0.80 – 1.00)** $p<0.001$	0.76 (0.48 – 0.95) $p<0.001$	1.0
	MetSYN (NCEF-ATP)	0.83 (0.57– 1.00) $p<0.001$	1.0	
	MetSYN (JIS)	1.0		
Age ≥ 40 years	MetSYN (IDF)	**0.93 (0.84 – 1.00)** $p<0.001$	0.84 (0.70– 0.95) $p<0.001$	1.0
	MetSYN (NCEF-ATP)	0.90 (0.82 – 1.00) $p<0.001$	1.0	
	MetSYN (JIS)	1.0		

Discussion

Our study showed that the prevalence of metabolic syndrome by ATPIII 2005, IDF, and JIS criteria were 30.3%, 32.4%, and 35.2% respectively. This is higher than the prevalence in rural Nigerian communities which ranged from 8% to 28.1%,[21–24] but slightly lower than the overall prevalence by ATP criteria (35.1%), obtained in the general population in urban communities in North-Western Nigeria.[25] Among individuals living with HIV and on ART, the prevalence of MetS in our study was higher across diagnostic criteria, as compared to the prevalence of metabolic syndrome by ATPIII 2005, IDF and JIS criteria, (12.7%, 17.2%, and 21.0% respectively) found in a previous Nigerian study.[26] However, other studies in Nigeria reported higher values. Ojong et al, among HIV-infected individuals on ART in Calabar, Nigeria reported 32.0 %, and 50.3% for NCEP-ATP III and IDF criteria respectively,[27] while Salawu et al, obtained a prevalence of metabolic syndrome as 35.2% according to NCEP-ATP III criteria, 36.8% according to IDF criteria and 43.2% using the JIS criteria.[28] The prevalence was relatively higher in the JIS criteria. JIS criteria is similar to the IDF in all respects except that the demonstration of central obesity is not a requirement in the JIS criteria, and this most likely accounted for the higher prevalence of MetS by JIS criteria. Similar to the findings of Ayodele et al, the prevalence of metabolic syndrome was lower by the ATP III criteria compared to the IDF and JIS criteria and in part due to higher cut-off points for abdominal obesity.[26] The higher prevalence of MetS by all criteria compared to previous studies about a decade earlier underscores the reports of the increasing prevalence of cardio-metabolic risk factors in Sub-Saharan Africa particularly among PLHIV.

The pattern of frequency of the different components of metabolic syndrome has varied considerably in previous studies. We found dyslipidaemia represented by low HDL was the most prevalent component of MetS.At least nine out of ten individuals with metabolic syndrome had low HDLc. However, the overall rate of low HDLc was 71%. A previous study in Calabar, Nigeria showed that 90.6% of HIV patients on ART had low HDLc compared to 52% among those not on ARV.[27] Low HDLc was also the most prevalent component of MetS in the non-HIV infected population in Nigeria although the frequency was much lower (56.1-87.5%).[22,25]However, increased triglyceride and blood pressure were the criteria withthe highest occurrence among HAART-exposed individuals with MetS in one study, but central obesity followed by HDLc was the most prevalent in another, while hypertension was the most prevalent component of MetS in a Sub-Saharan African meta-analysis.[28–30]This implies that whereas it is imperative to carry out a comprehensive MetS screening, in resource-constrained circumstances, we could consider prioritizing HDLc measurement in our setting.
HIV-infected individuals have significantly decreased HDL levels, particularly those subjects with higher viral load and lower CD4+ T-cell counts and this phenomenon is thought to be associated with elevated inflammatory markers.[31] Another plausible explanation for the very high abnormal HDLc is the very high proportion of women in this study many of whom are in the postmenopausal age group. HDLc is known to be generally reduced in this population, approximating the levels in men.[32]However, other studies suggest that low HDLc is not strongly associated with menopause and not a main characteristic of metabolic syndrome in postmenopausal women.[33,34]The significance of this form of dyslipidaemia in women living with HIV as it relates to the risk of CVDs is not fully known but worth considering.

Assessing the correlates of MetS, we found that metabolic syndrome was more common in women and older persons, and this wasconsistent with previous reports.[27,28,30]This is not surprising given that central obesity and low HDLcare the key components of MetS in this study and were most prevalent among the female participants. This may be related to biological, hormonal, and environmental factors that are thought to contribute to the occurrence of metabolic syndrome in women.[16] Incorporating gender differences in screening and managing obesity and MetS has therefore been suggested, more so, among PLWA.[35]

The impact of HIV-related parameters on MetShas remained controversial. HIV-related parameters were not significantly associated with MetS in our study. For instance, the use of first line ARVs or second-line ARVs did not significantly affect the Mets rates. The duration of infection and use of ARVs as well as the latest or lowest CD4 count was not different in those who had MetS and those who did not. A previous report from Nigeria showed that longer duration of HIV diagnosis, use of ARV, and exposure to PIs were significantly associated with MetS.[29]Nguyen et al,showed that MetS is associated with the use of second-line drugs and longer duration of HIV infection but not CD4 count.[36]Similarly, CD4 counts were not associated with MetS in some other reports[28,36]

We examined the concordance of MetS criteria in our study population. The overall agreement was almost perfect between IDF and JIS criteria (k=0.94) and strong between IDF vs., ATP (k=0.82) and ATP vs JIS (k=0.89). This is consistent with a previous report by Nguyen et al who obtained kappa of 0.96, 0.84, and 0.89 respectively. The agreement in our study was better than what was reported among a Nigeria population by Ayodele et al, k= 0.88, 0.0.58, and 0.71 respectively. Subgroup analysis in this study showed that the agreement was strongest among females but equally strong in younger and older age groups. The import of this finding is that

the same individuals are generally classified as MetS or non-MetS by these sets of criteria. This is not surprising since all three criteria are based on the same components but differ slightly by the threshold for central obesity or having central obesity as a compulsory criterion. Nguyen had earlier reported that the agreement was not affected by HIV-related factors. This implies that MetS can be assessed with these common set of criteria in the general population and for cardiovascular risk assessment among PLHIV.

The relationship between MetS and CIMT, a cardiovascular endpoint, was assessed in this present study. Our results showed that there was no significant difference in the median CIMT in PLHIV with and without MetS and this was consistent across all criteria of MetS.Schoffelen and colleagues on the other hand, reported that MetS was significantly and independently associated with increased CIMT.[37]Our finding may not be surprising considering that in a previous study among PLHIV in our setting, male gender, hypertension, and increasing age were the main predictors of increased CIMT among HIV patients whereas dyslipidaemia and obesity were not related to increased CIMT.[38]However, in the present study, abnormal HDLc, and obesity were the most common component of MetS.This calls to focus the debates on the adequacy of the threshold for dyslipidaemia and obesity, moreso, in PLHIV and among Africans.[10,30]Thefindings from our study beg to question of whether the threshold for dyslipidaemia and obesity in PLHIV is not too generous given that HIV infection is known to affect these parameters and whether a more stringent threshold should be considered for PLHIV for them. Also, should more weight be accorded to hypertension which has been shown to be an independent marker of CVD? For instance, what would be the impact of making hypertension a compulsory marker for MetS or a tool for assessing CVD risk in PLHIV?

Our study as designed, would not have sufficient power to do justice to these questions. These are questions that should be addressed in future studies. Another limitation ofthis study is that we could not establish a causal association given the cross-sectional nature of this study. Also, we did not assess metabolic syndrome by WHO criteria because we did not assess insulin and microalbumin levels in the present study. Nonetheless, these limitations had no bearing on the assessment of the prevalence of metabolic syndrome and its correlates among HIV-infected patients by the criteria we employed. This study has brought out the peculiarities of metabolic syndrome presentation among HIV patients in North-Central Nigeria

In conclusion, in this HIV-infected population in North-Central Nigeria, the prevalence of metabolic syndrome is relatively high and more common among females and older individuals. There was a fair amount of agreement among the defining criteria and similar correlations across the general and subpopulations of HIV-positive individuals. These criteria can therefore be used in CVD screening programs for a larger population of HIV-positive patients. MetS based on these criteria, however, does not significantly correlate with rising CIMT.

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