

Assessment of Metabolic syndrome among adult human immunodeficiency virus/acquired immunodeficiency syndrome patients in a tertiary health facility in Southeast Nigeria

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ABSTRACT

Context: Metabolic syndrome (MS) on the background of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome has not been reported from Southeast Nigeria. **Aims:** We sought to determine the prevalence of MS among HIV-infected Nigerians seen at the Federal Medical Centre, Umuahia, its correlation with highly active antiretroviral therapy (HAART) and other demographics. A total of 105 HAART-treated and 60 HAART-naïve patients were reviewed. **Settings and Design:** This study was cross-sectional, and the data were prospectively collected. **Methodology:** They were matched for sex and age. Anthropometric data including current weight and height, waist circumference, blood pressure, as well as blood lipids and fasting glucose were measured. MS was determined using National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III criteria. **Statistical Analysis Used:** SPSS version 17.0 (Chicago IL, USA) was used for data collection and analysis. **Results:** There was 24.3% overall prevalence of MS in the study population, 28.8% in HAART-treated, and 25% in HAART-naïve patients ($P = 0.554$). The prevalence of MS components was as follows: hypertension (49.7%), impaired fasting glucose (9.62%), hypertriglyceridemia (32.0%), low high-density lipoprotein-cholesterol (44.2%), and central obesity (22.1%). Correlation of MS with female gender was highly significant ($r = -0.306$, $P = 0.002$). **Conclusions:** MS was not significantly associated with the use of HAART in our patients but correlated with female gender.

Key words: Correlation with highly active antiretroviral therapy, human immunodeficiency virus/acquired immunodeficiency syndrome, metabolic syndrome, Southeast Nigeria, tertiary hospital

INTRODUCTION

Metabolic syndrome (MS) has been reported among patients with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), and more so among patients with HIV infection who are on highly active antiretroviral therapy (HAART). Most studies have been carried out in the developed

nations,^[1-5] with few local studies.^[6,7] This would be the first report from the Southeast Nigeria.

Jayasuriya *et al.*^[8] studied MS among black African patients in the United Kingdom. The prevalence of MS was 22.1% by International Diabetes Federation (IDF) criteria and 15.5% by National Cholesterol Education Program (NCEP) criteria. Muhammad *et al.*^[7] described

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the cardiovascular risk profile of HIV/AIDS patients receiving HAART at a health facility in Northern part of Nigeria. Twenty-one percent of their patients on HAART had MS compared with 9% of HAART-naïve patients. They had defined MS using the NCEP adult treatment panel III (ATP III) guidelines. From Ogbomoso, Southwest Nigeria, Ayodele *et al.*^[6] looked at the prevalence and clinical correlates of MS among an HIV-infected outpatient population using the NCEP-ATP III, the IDF, and the joint interim statement (JIS) definitions. The prevalence rates of MS according to the ATP III, IDF, and JIS criteria were 12.7%, 17.2%, and 21.0%, respectively. In their study, MS was significantly associated with female gender (all definitions), body mass index (BMI) (all definitions), increasing age, and CD4 count (IDF definition). There was no significant association between MS and HAART. They conclude that the prevalence of MS in HIV/AIDS varied with the criteria used and that MS correlates with traditional cardiovascular risk factors rather than HAART-related factors.

METHODOLOGY

We set out to determine the prevalence of MS in our HAART-treated and HAART-naïve patients, and to determine any association of MS with the different drug combinations, duration of treatment, and other clinical variables such as age, gender, occupation, alcohol consumption, level of education, social class, and physical activity. Our study design was cross-sectional.

The location of the study was the ART clinic, of the Federal Medical Centre (FMC), Umuahia, Nigeria.

The sample size was determined using Fisher's formula^[9] $n = z^2pq/d^2$, where n = minimum sample size, z = 95% confidence level, i.e., 1.96, d = level of precision (0.05), P = the proportion in the target population estimated to have a particular characteristic, i.e., maximum prevalence reported in a study of a similar population (22.1%), and q = the proportion in the target population estimated to lack a particular characteristic, i.e., $(1.0 - p)$.^[9] The prevalence of MS in black Africans with HIV/AIDS was reported as 22.1%.^[8] Therefore, the calculated minimum sample size was 118. Patients were recruited from the ART clinic of FMC, Umuahia, during the period of the study. All eligible patients were recruited if they gave consent. The study was reviewed and approved by the FMC, Umuahia, Health Research Ethics Committee.

The inclusion criteria were (1) patients of both sexes aged 18 years and above as at their last birthday, with confirmed HIV positive serology, were eligible. The lower limit of 18 years was used to reflect the age limit for classification of an adult in Nigeria in accordance with the child rights Act adopted by the Federal Government in May 2003.^[10] (2) Regular attendance to the ART clinic, of FMC, Umuahia, i.e., using their appointment cards as a check. (3) For the subgroup on HAART, regular treatment for at least 1 year. (4) Obtained informed consent. Patients below 18 years of age as at the time of the study using their last birthday or estimated birthday, patients on chronic corticosteroids use, pregnant females based on their last menstrual period, patients who withdrew from combination HAART, patients with any active opportunistic infection or neoplasia and those with type 1 diabetes mellitus (DM), liver, or heart failure, patients with a history of abuse of tobacco, and other psychoactive agent, for example, cocaine, and patients who were unwilling to give their consent were all excluded from the study. About 140 patients of similar age and sex distributions were recruited from the ART clinic. One-hundred and five patients were HAART-treated, whereas 60 were HAART-naïve.

The clinical evaluation and collection of samples were carried out at the ART clinic of the FMC, Umuahia, between October 2011 and April 2012. The patients were invited to participate in this cross-sectional study. Those who responded were interviewed with a questionnaire by the investigator using a standard pro forma to obtain demographic data and clinical history. The evaluation included asking for a history of hypertension, DM, tobacco and alcohol use, and medication history including use and duration of ART. Three categories of social class (high, middle, and low) were defined based on the public service classification of occupations (respective civil servants categories: Upper, middle, and lower).^[11]

Patients working for private firms or for themselves were allocated to these categories based on their profession. Homemakers were attributed the occupation category of their husbands.^[11] Alcohol consumption data were collected during the clinic interviews by asking whether the person "ever consumed alcoholic beverages" or "presently drinks alcoholic beverages at all;" if the latter, subjects were asked specifically about the number of drinks per week

of each type of beverage (beer, wine, and spirits).^[12] For purposes of the study, a “drink” was defined as a bottle of beer (12.6 g of alcohol), a glass of wine (13.2 g of alcohol), or a shot of spirits (15 g of alcohol). Mild, moderate, or high intake was defined as <5, 5–30, and >30 g/day, respectively.^[11] Patients were classified as nonsmoker (has never smoked), previous smokers, and current smokers. Subjects were considered current smokers if they smoked cigarettes at the time of the interview, previous smokers if they were not current smokers but had smoked 100 cigarettes in their entire life, and nonsmokers if they smoked less than this amount.^[13] Physical activity was graded as none (<4 times/month), low (4–10 times/month), moderate (11–19 times/month), or high (>19 times/month) based on the monthly frequency of engaging in leisure time physical activities such as walking for ≥1.6 km, jogging, swimming, cycling, aerobics, sports, gardening, and weight training.^[13]

The height and weight were measured, and the BMI (kg/m²) was calculated as the ratio of measured weight to the square of the measured height. Waist circumference (WC), hip circumference, and blood pressure were measured according to standard recommendations.^[11] HIV screening was by enzyme immunoassay and confirmatory test by Western-Blot electrophoresis. The CD4 cell counts were obtained using the flow cytometry method. Venous samples were collected to estimate plasma glucose, triglyceride (TG), total cholesterol (TC), and high-density lipoprotein-cholesterol (HDL-C) fraction after an overnight fast of 6–12 h. TG, TC, and HDL-C levels were measured enzymatically. HDL-C was determined after the precipitation of the low-density lipoprotein (LDL) fraction, whereas LDL-cholesterol LDL-C was calculated using Friedewald formula^[14] $LDL = (TC - HDL-C) - TG/2$. Fasting plasma glucose (FPG) was estimated using the glucose oxidase method. The samples were analyzed at the central laboratory of the hospital by the same medical laboratory scientist.

MS was defined according to the NCEP-ATP III definition^[15] based on three or more of the following: TG ≥1.7 mmol/l (150 mg/dL), FPG ≥6.1 mmol/l (110 mg/dL), WC >94 cm in men or >80 cm in women, systolic blood pressure ≥130 or diastolic blood pressure ≥85 mmHg or treatment for hypertension and HDL-C <40 mg/dL (1.03 mmol/L) in males <50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality. For data collection and analysis,

SPSS version 17.0 (SPSS Inc, Chicago Illinois, USA) was used. Descriptive statistics were computed with standard methods and are presented as mean and standard deviations. Chi-square test was used to compare the association between categorical variables, and independent *t*-test was used to compare the mean value of some laboratory parameters and sociodemographic variables. A *P* < 0.05 was considered to be statistically significant.

RESULTS

A total of 165 adults were enrolled into the study. They comprised 105 patients HAART-treated and 60 HAART-naïve patients. The patients included artisans (21.8%), traders (36.4%), students (1.9%), civil servants (21.8%), unemployed (2.4%), farmers (11.7%), and others which included missing data (3.9%). Demographic, clinical, and biochemical characteristics are as shown in Table 1. The prevalence of MS and its various components are as recorded in Table 2. Of the variables correlated with MS, (CD4 count, gender, age, occupation, level of education, social class, duration of illness, consumption alcohol, smoking, physical activity, and class of antiretroviral) only the correlation of MS with CD4 count ($r = -0.265$, $P = 0.024$) and gender ($r = -0.306$, $P = 0.002$) were statistically significant. When WC was controlled, the correlation between MS and CD4 count was no longer significant ($r = 0.217$, $P = 0.071$). The variables of age, CD4 counts, and gender were also compared between those with and without MS [Table 3].

The distribution of the HAART-treated patients to various combinations was as follows: Combivir-efavirenz 1 (0.6%), Combivir-nevirapine 97 (58.8%), truvada-nevirapine 5 (3.0%), truvada-efavirenz 1 (0.6%), and kaletra -truvada 1 (0.6%). Combivir contained lamivudine and zidovudine, truvada contained emtricitabine and tenofovir, and kaletra contained lopinavir and ritonavir. The vast majority of the patients were on one of the antiretroviral drug combinations, so no significant associations could be pursued.

DISCUSSION

The prevalence of MS was 24.3% in the population studied. A study on apparently healthy adults from our center had reported the MS prevalence of 24.7%.^[16] This suggests HIV-infection in our center is

Table 1: Demographic, clinical, and biochemical features of the study population

Features	All patients n=165	HAART-treated n=105	HAART-Naïve n=60	T	P
Age (years)	41.35±10.41	42.09±11.15	40.07±8.90	1.200	0.232
Weight (kg)	64.72±13.83	67.77±14.04	59.58±11.89	3.782	0.000
Height (m)	1.65±0.093	1.66±0.10	1.65±0.09	0.593	0.554
BMI (kg/m ²)	24.27±7.56	25.97±8.90	22.01±4.46	2.763	0.007
Pulse rate	82.90±12.08	80.73±10.83	86.75±13.27	-3.061	0.003
SBP (mmHg)	124.90±23.64	129.69±22.59	117.12±23.42	3.316	0.001
DBP (mmHg)	78.51±15.27	81.76±15.54	73.22±13.32	3.503	0.001
WC (cm)	84.55±10.54	87.25±10.38	79.80±9.11	4.634	0.000
FPG (mmol/l)	84.45±19.80	86.25±23.24	82.09±13.98	1.064	0.290
TG (mmol/l)	127.00±64.75	121.73±69.11	134.07±58.43	-0.956	0.341
TC (mmol/l)	161.82±55.48	180.42±58.53	136.05±38.65	4.384	0.000
HDL-C (mmol/l)	49.14±18.49	56.27±16.62	39.41±16.49	5.130	0.000
LDL-C (mmol/l)	46.76±51.67	59.56±51.83	29.60±46.72	3.025	0.003
CD4 (cell/μl)	233.29±159.16	216.17±216.17	286.37±190.43	-2.131	0.035
Males (n)	75	48 (64%)	27 (36%)	$\chi^2=0.008$	0.929
Females (n)	90	57 (63.3%)	33 (36.7%)		

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WC: Waist circumference, FPG: Fasting plasma glucose, TC: Triglyceride, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein-cholesterol, HAART: Highly active antiretroviral therapy

Table 2: Prevalence (percentage) of Metabolic syndrome and its various components

Characteristic	All patients	HAART-treated	HAART-naïve	χ^2	P
MS	24.3	28.8	16.2	1.550	0.213
Hypertension	49.7	61.1	31.0	12.98	0.000
IFG	9.62	13.56	4.4	2.440	0.118
Hypertriglyceridemia	32.0	32.2	31.8	0.002	0.967
Low HDL-C	44.2	23.3	72.7	25.10	0.000
Central obesity	22.1	26.9	13.56	3.907	0.048

MS: Metabolic syndrome, IFG: Impaired fasting glucose, HDL-C: High-density lipoprotein-cholesterol

Table 3: Comparing metabolic syndrome by age, CD4 counts, and gender

Features	Mean±SD		T	P
	MS	No MS		
Age (years)	45.56±10.85	42.28±11.52	1.255	0.212
CD4 cell/μl	303.78±174.11	201.01±164.30	2.303	0.024
Gender (%)				
Males	9.09	90.9	$\chi^2=9.631$	0.002
Females	35.59	64.4		

MS: Metabolic syndrome, SD: Standard deviation

not associated with a higher prevalence of MS. From Northeastern Nigeria, Muhammad *et al.*^[7] reported a prevalence of 15%, whereas Ayodele *et al.*^[6] in Southwestern Nigeria found 12.7%, both using ATP III guidelines. The mean age in our patients 41.4 ± 10.41 was higher than that of in the patients studied by Sanusi *et al.* (32.5 ± 7.55), which would contribute significantly to the lower prevalence reported by them. As in other locally reported studies,^[6,7] MS was strongly correlated with female gender. When the

sexes were compared, central obesity and low HDL were significantly more prevalent in females. Even in apparently healthy Nigerians,^[17] the prevalence of MS and obesity has been reported to be higher in female (20.9%; 31.0%) than male traders (6.5%; 7.1%), respectively. Elsewhere, higher rates of obesity have been reported among black women.^[18]

Environmental and sociocultural factors that contribute to increased obesity in Nigerian women will include engagement in occupations involving less physical activity,^[19] insecurity of life, and heavy traffic which discourage physical exercise and walking.^[20]

Sani *et al.* in their study of apparently healthy Nigerians also reported a higher prevalence of low HDL-C in females,^[21] with the prevalence to be 51.9% in males but 65% in females ($P < 0.05$). It will also be observed that central obesity and low HDL-C, the two conditions significantly elevated in females, were the ones defined in ATP-III by gender-specific criteria. The optimal cut-off value of WC has been noted to vary across different ethnicities, but as yet accepted criteria have not been locally developed.^[22,23] The same controversy trails are low-HDL. Ogbu and Ugwuja^[24] have suggested modifications in the ATP III criteria for the diagnosis of the MS in Nigerians including the use of ≤1.3 mmol as cutoff for HDL-C and ≥93 cm as cutoff for WC in both men and women.

MS also correlated with CD4 count level in our study. The CD4 level was lower in those without

MS. However, this difference was related to loss in the body weight as a result of chronic HIV infection (resulting in fewer numbers meeting the criteria). The correlation became insignificant when we controlled for WC. MS was not correlated with ART. This is expected since only 0.6% of the patients on HAART were on protease inhibitors.

Lipodystrophy must also be mentioned as another of the metabolic changes in HIV individuals, apart from dyslipidemia and insulin resistance.^[25] HAART regimens, especially those including protease inhibitors, have been implicated in the pathogenesis.^[26] The clinical lipodystrophy comprises both fat accumulation and fat wasting, with the fat wasting consisting of subcutaneous fat atrophy in the legs, buttocks, arms, and face. It is important because lipodystrophy on its own portends metabolic implications equivalent to those of MS.^[27] This will however be noted as a limitation in our methodology, which did not report peripheral fat distribution. This study had other limitations. The NCEP-ATP III criteria, which were derived in North America, may not correctly define MS in Africans. Only 0.6% of the patients studied were on protease inhibitors. The impact of wasting syndrome in HAART-naïve patients, which has been reported more in Sub-Saharan Africa, was not analyzed.^[28]

CONCLUSIONS

We report on the MS in HIV/AIDS patients seen in Umuahia, Southeast Nigeria. There was 24.3% overall prevalence of MS, with 28.8% in HAART-treated and 25% in HAART-naïve patients ($P = 0.554$). The prevalence of MS components was as follows: Hypertension (49.7%), impaired fasting glucose (9.62%), hypertriglyceridemia (32.0%), low HDL-C (44.2%), and central obesity (22.1%). Correlation of MS with female gender was highly significant ($r = -0.306$, $P = 0.002$).

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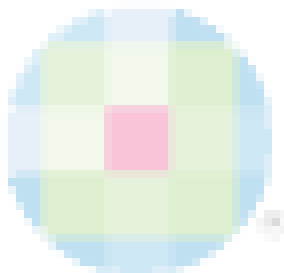
Conflicts of interest

There are no conflicts of interest.

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