Original Research Article

Prevalence of metabolic syndrome and associated factors among human immunodeficiency virus patients on highly active antiretroviral therapy in North central Nigeria

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ABSTRACT

Background: Metabolic syndrome (MS) is a complex disorder defined by cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus. The Use of Highly active antiretroviral therapy in HIV patients is associated with metabolic syndrome which increases the risk of cardiovascular disease (CVD). The aim of the study was to determine the prevalence of MS among HAART treated HIV patients and HAART naïve patients.
Methods: This was a cross-sectional study that evaluated 581 (396 females, 184 males) consenting HIV patents in the hospital. Clinical characteristics, anthropometry, blood pressure, lipid profile, fasting blood glucose, fasting plasma insulin, CD4 cell counts and viral load were determined using appropriate standard techniques. MS was defined using International Diabetes Federation (IDF) cut-off values.
Results: The overall prevalence of MS was 10.7%, with more females 52 (13.1%) than males 10 (5.4%), p=0.005. MS in patients on HAART was 58 (15.1%) and HAART naive 4 (2.0%). Overall, waist circumference, BMI, systolic blood pressure (BP), diastolic blood pressure (BP), triglycerides and fasting blood glucose were 82.7±11.5, 22.7±, 120.6±17.6, 77.5±10.6, 1.1±0.7 and 5.1±1.9 respectively. Patients with MS had significantly higher (p<0.05) waist circumference (94.1 vs 81.3 cm), BMI (24.8 vs 22.5 kg/m2), systolic BP (135.4 vs 118.8 mmHg), diastolic BP (86.2 vs 76.5 mmHg), triglycerides (1.3 vs 1.0 mmol/l) and fasting blood glucose (6.3 vs 4.9 mmol/l). Insulin resistance (IR) was higher in patients with MS 11.8(7.9) compared with patients without MS 5.5 (6.8) p=0.02.
Conclusions: Prevalence of metabolic syndrome in this study was lower than that reported in previous works, the prevalence is much higher in the HAART treated patients. The risk of MS were high triglycerides, hypertension and abnormal fasting blood glucose. There was significant association with the traditional risk factors, age, female gender and HIV duration.

Keywords: HIV, HAART, Metabolic syndrome, Cardiovascular disease, IDF

INTRODUCTION

Metabolic syndrome (MS) is a cluster of risk factors for cardiovascular disease (CVD) and type 2 diabetes mellitus (DM). Many definitions exists to identify those at risk but the most widely used are the definition in the third report of National Cholesterol education Program Expert Panel (NCEP) on detection, evaluation and treatment of high cholesterol (Adult Treatment Panel III (ATP III) and International Diabetes Foundation (IDF).[1,2] Patients with MS from the general population have higher risk of developing type 2 diabetes and increased risk of dying from cardiovascular disease.[3-5] Highly active antiretroviral therapy (HAART) has changed the clinical course of HIV

infection resulting in increased quality of life and prolonged survival in the patients. However, metabolic abnormalities and abnormal body fat distribution were observed following a similar pattern described for MS.[6,7] Previous studies have shown that patients with HIV infection receiving HAART had high prevalence rate of MS with prevalent CVD and are at increased risk of developing them, even higher than those reported from the general population in some settings.[8-12] The aim of the study was to determine the prevalence of and the associated risk factors for MS among HIV patients on HAART in North central Nigeria.

METHODS

The was a cross-sectional study carried out at an antiretroviral therapy centre at a teaching hospital in North Central Nigeria over 11 months period. After obtaining ethical approval from the Institutional Research Ethics Committee, three hundred and eight four consenting patients who satisfied the inclusion criteria (HIV sero-positive on HAART for >12 months) and one hundred and ninety seventy (HIV sero-positive HAART naive), aged 18-70 years were consecutively recruited. Patients less than 18 years of age and pregnant women were excluded from the study. Informed consent was obtained from all patients at the clinic and documented these in an interviewer-administered proforma.

MS was diagnosed using IDF criteria which states that MS is present if waist circumference is ≥80 cm in women and ≥94 cm in men in the presence of any two of the following: raised blood pressure: systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg, fasting blood glucose ≥5.6 mmol/l, triglycerides ≥1.7 mmol/l or HDL-cholesterol <1.29 mmol/l in women and < 1.03 mmol/l in men.[2] Detailed history and clinical examinations were carried out and an 8 hours fasting venous blood sample was collected for enzyme-linked immunosorbent assay for HIV, CD4 T-cell count, serum cholesterol, high-density lipoprotein (HDL) cholesterol, serum triglycerides, fasting blood glucose (FBS) and serum insulin in all the patients. Insulin resistance was calculated using homeostatic model assessment (HOMA) and 1.93 was taken as cut-off value.[13]

Data management and analysis

Data was managed and analyzed using SAS software version 9.4 (SAS Institute, Cary, NC). The normality status of all continuous variables was ascertained using Kolmogorov-Smirnov test. Mean and standard deviation were used as measures of central tendencies and dispersion for all continuous variables that exhibited normal distribution whereas median and interquartile range were used for non-normally distributed variables. Differences between the means or medians of independent binary groups were analysed using t-test or Wilcoxon test respectively. Categorical variables were expressed using numbers and percentages and differences between independent groups were analyzed using chi square.

Univariate logistic regression models were used to assess the association between the various factors and metabolic syndrome. Independent associations were further assessed using different multivariable logistic regression models that were adjusted for confounders including age, sex, BMI and duration of HIV. Statistical significance was set at a significance level of p<0.05.

RESULTS

Characteristics of study participants

A total of 581 patients were recruited; comprising of 396 (68.3%) females and 184 (31.7%) males. The mean age was 36.0±8.7 years. More than 60% of the patients were on HAART and 197 were HAART naive. There were more patients who lived in the urban (58.6%) than in suburban 105 (18.1%) or rural 135 (23.3%) areas with majority (67.4%) being diagnosed with HIV within 12-24 months.

Prevalence of MS

The overall prevalence of MS was 10.7% as shown in Table 1, which has higher in females 52 (13.1%) than males 10 (5.4%), p=0.005. MS in Patients on HAART was 58 (15.1%) and HAART naive 4 (2.0%). Table 2 shows the anthropometric, hemodynamic and biochemical characteristics of the subjects. Patients with MS had significantly higher waist circumference (94.1 vs 86.3 cm, p<0.05), BMI (24.8 vs 22.5 kg/m^2, p<0.05), systolic BP (135.4 vs 118.8 mmHg, p<0.05), diastolic BP (86.2 vs 76.5 mmHg, p<0.05), triglycerides (1.3 vs 1.0 mmol/l, p<0.05) and fasting blood glucose (6.3 vs 4.9 mmol/l, p<0.05). IR was higher in patients with MS 11.8 (7.9) compared with patients without MS 5.5 (6.8), p=0.02.

Factors associated with MS

Table 3 shows the association of various factors with MS determined using univariate logistic regression models. Compared to patients diagnosed of HIV within 12-24 months, male patients and HAART naive patients respectively, the odds of MS doubled in patients diagnosed of HIV within 25-48 months [2.329 (1.203-4.511)], tripled in female patients [2.630 (1.305-5.301)], and non-upled in patients on HAART [8.581 (3.068-24.000)]. Also, the odds of MS increased with increasing age [1.038 (1.009-1.069)], waist circumference [1.099 (1.069-1.130)], hip circumference [1.096 (1.065-1.129)], BMI [1.142 (1.071-1.218)], systolic BP [1.045 (1.031-1.059)], diastolic BP [1.080 (1.054-1.107)], LDL-cholesterol [1.264 (1.001-1.596)], triglycerides [1.608 (1.188-2.176)], fasting blood glucose [1.626 (1.325-1.994)], 2 hours postprandial glucose [1.180 (1.058-1.316)], HOMA-IR [1.072 (1.007-1.140)] and CD4 cell count [1.004 (1.002-1.005)].

The results in Table 4 show the association of MS with various factors after adjusting for age, sex, BMI and duration of HIV. The odds of MS persistently increased with increasing age [1.040 (1.002-1.079)], waist

circumference [1.100 (1.054-1.148)], hip circumference [1.066 (1.020-1.114)], BMI [1.091 (1.011-1.176)], systolic BP [1.054 (1.032-1.075)], diastolic BP [1.091 (1.011-1.176)], fasting blood glucose [1.322 (1.051-1.66)] and 2hrs post-prandial glucose [1.177 (1.019-1.360)]; as well as in female patients [4.934 (2.125-11.456)] and patients diagnosed of HIV within 25-48 months [2.273 (1.142-4.524)].

Table 1: Sociodemographic characteristics of study subjects.

Characters	Overall	No MS	MS	P value
Number (%)	581	519 (89.3)	62 (10.7)	<0.0001
Age (years)	36.0±8.7	35.6±8.9	38.7±7.0	0.0103
Sex				
Males	184 (31.7)	174 (94.6)	10 (5.4)	0.0052
Females	396 (68.3)	344 (86.9)	52 (13.1)	
Educational status				
Informal	59 (10.2)	52 (88.1)	7 (11.9)	
Primary	161 (27.9)	143 (88.8)	18 (11.2)	
Secondary	135 (23.4)	121 (89.6)	14 (10.4)	0.9916
Tertiary	210 (36.3)	188 (89.5)	22 (10.5)	
Post graduate	13 (2.3)	12 (92.3)	1 (7.7)	
Marital status				
Single	106 (18.3)	97 (91.5)	9 (8.5)	
Married	264 (45.6)	229 (86.7)	35 (13.3)	0.1345
Divorced	72 (12.4)	69 (95.8)	3 (4.2)	
Widowed	137 (23.7)	122 (89.1)	15 (10.9)	
Occupational status				
Civil servants	142 (24.6)	126 (88.7)	16 (11.3)	
Business men	120 (20.8)	114 (95.0)	6 (5.0)	0.1023
Farmers	30 (5.2)	28 (93.3)	2 (6.7)	
Others	286 (49.5)	249 (87.1)	37 (12.9)	
Place of residence				
Rural	135 (23.3)	122 (90.4)	13 (9.6)	
Urban	340 (58.6)	294 (86.5)	46 (13.5)	0.0075
Suburban	105 (18.1)	102 (97.1)	3 (2.9)	
HIV duration (months)				
12-24	260 (67.4)	228 (87.7)	32 (12.3)	
25-48	69 (17.9)	52 (75.4)	17 (24.6)	0.0357
>48	57 (14.8)	47 (85.5)	10 (17.5)	
Use of HAART				
Yes	384 (66.1)	326 (84.9)	58 (15.1)	<0.0001
No	197 (33.9)	193 (98.0)	4 (2.0)	

Table 2: Anthropometric, hemodynamic and biochemical characteristics of subjects.

Mean±SD	Overall	No MS	MS	P value
Anthropometric				
Waist circumference (cm)	82.7±11.5	81.3±9.9	94.1±16.5	<0.0001
Hip circumference (cm)	93.3±9.5	92.4±9.2	100.9±8.5	<0.0001
Body mass index (kg/m^2)	22.7±4.2	22.5±4.2	24.8±3.7	<0.0001
Hemodynamic				
Systolic BP (mmHg)	120.6±17.6	118.8±16.8	135.4±17.6	<0.0001
Diastolic BP (mmHg)	77.5±10.6	76.5±10.1	86.2±11.1	<0.0001
Biochemical				
HDL-cholesterol (mmol/l)	1.6±1.2	1.6±1.2	1.6±1.0	0.9043
LDL-cholesterol (mmol/l)	2.3±1.1	2.2±1.1	2.5±1.0	0.0480
Triglycerides (mmol/l)	1.1±0.7	1.0±0.7	1.3±0.9	0.0016
Total cholesterol (mmol/l)	3.5±2.2	3.4±2.3	3.8±1.2	0.0402

Continued.

Mean±SD	Overall	No MS	MS	P value
Fasting blood glucose (mmol/l)	5.1±1.9	4.9±1.9	6.3±1.4	<0.0001
2 hours post-prandial glucose	7.0±2.0	7.0±2.0	7.8±1.5	0.0021
Median (interquartile range)				
Fasting plasma insulin	28.3 (32.9)	27.7 (32.2)	58.0 (28.1)	0.0137
HOMA-IR	5.8 (6.8)	5.5 (6.8)	11.8 (7.9)	0.0223
CD4 cell count (x10^6 cells/l)	221.0 (225.0)	205.0 (229.0)	341.0 (254.0)	<0.0001
Viral load	200.0 (8929.0)	200.0 (17906.0)	200.0 (0.0)	<0.0001

Table 3: Univariable association of sociodemographic, anthropometric, biochemical and hemodynamic characteristics with MS.

Number (%)	Odds ratio	95% CI	P value
Age (years)	1.038	1.009-1.069	0.0111
Sex			
Males	Ref		
Females	2.630	1.305-5.301	0.0068
Duration of HIV (months)			
12-24	Ref		
25-48	2.329	1.203-4.511	0.0121
>48	1.516	0.697-3.295	0.2936
Waist circumference (cm)	1.099	1.069-1.130	<0.0001
Hip circumference (cm)	1.096	1.065-1.129	<0.0001
Body mass index (kg/m^2)	1.142	1.071-1.218	<0.0001
Systolic BP (mmHg)	1.045	1.031-1.059	<0.0001
Diastolic BP (mmHg)	1.080	1.054-1.107	<0.0001
HDL-cholesterol (mmol/l)	1.011	0.815-1.255	0.9194
LDL-cholesterol (mmol/l)	1.264	1.001-1.596	0.0492
Triglycerides (mmol/l)	1.608	1.188-2.176	0.0021
Total cholesterol (mmol/l)	1.050	0.965-1.143	0.2567
Fasting blood glucose (mmol/l)	1.626	1.325-1.994	<0.0001
2 hours post prandial glucose	1.180	1.058-1.316	0.0030
Fasting plasma insulin	1.009	0.996-1.022	0.1601
HOMA-IR	1.072	1.007-1.140	0.0297
CD4 cell count (x10^6 cells/l)	1.004	1.002-1.005	<0.0001
Viral load	1.000	1.000-1.000	0.0123
Use of HAART	8.581	3.068-24.000	<0.0001

Table 4: Multivariable association of sociodemographic, anthropometric, biochemical and hemodynamic characteristics with MS.

Number (%)	Odds ratio	95% CI	P value
Age (years)	1.040	1.002-1.079	0.0369
Sex			
Males	Ref		
Females	4.934	2.125-11.456	0.0002
Duration of HIV (months)			
12-24	Ref		
25-48	2.273	1.142-4.524	0.0194
>48	1.442	0.626-3.319	0.3898
Waist circumference (cm)	1.100	1.054-1.148	<0.0001
Hip circumference (cm)	1.066	1.020-1.114	0.0047
Body mass index (kg/m^2)	1.091	1.011-1.176	0.0251
Systolic BP (mmHg)	1.054	1.032-1.075	<0.0001
Diastolic BP (mmHg)	1.091	1.054-1.131	<0.0001

Continued.

Number (%)	Odds ratio	95% CI	P value
HDL-cholesterol (mmol/l)	0.683	0.492-0.948	0.0229
LDL-cholesterol (mmol/l)	0.960	0.726-1.269	0.7749
Triglycerides (mmol/l)	1.349	0.946-1.925	0.0987
Fasting blood glucose (mmol/l)	1.322	1.051-1.664	0.0173
2 hours post prandial glucose	1.177	1.019-1.360	0.0268
HOMA-IR	1.053	0.961-1.153	0.2698
CD4 cells count (x10^6 cells/l)	1.002	1.000-1.003	0.0707
Use of HAART	3.350	0.183-61.340	0.4151

Note: Adjusted for age, sex, BMI and duration of HIV.

DISCUSSION

The prevalence of MS using the 1DF definition showed a prevalence of 10.7% in this study, this is similar with other studies.[8,14] A recent review of metabolic syndrome among patients with HIV by Paula et al demonstrated that MS prevalence ranged from 11% in a Mediterranean multicentre lipodystrophy case definition cohort up to 45% in an Italian cohort.[15,16] Differences in characteristics among study participants may contribute to the variability observed in previously published MS prevalence estimates.[17] Ayodele et al in Nigeria found a prevalence rate of MS as 17.2%,12.7 % and 21.0% by IDF, ATP 111 and JIS criteria respectively.[18] A systemic review and meta-analysis done recently in South Africa by Olamide and colleagues revealed that the prevalence of metabolic syndrome in sub-Saharan Africa is 12% for HIV uninfected individuals and 21.5% for HIV infected persons, the study further revealed that most studies in Africa have reported hypertension and high triglycerides as common components of MS.[19] MS was much higher (p<0.05) in the HAART treated group 58 (15.1%) than the HAART naive group 4 (2.0%), and most prevalent in females 52 (13.1%) than males 10 (5.4%) which is also reported in other studies.[8,20,21]

High triglycerides, hypertension and elevated fasting blood glucose were the most prevalent individual components of MS in our study which agrees with other findings from Alfred et al in 2018 in Western Kenya who reported Central obesity, high triglycerides and high blood glucose; Girma and colleagues in 2020 in Southern Ethiopia found hypertension, high blood glucose and central obesity.[22,23] Conversely other studies, observed high blood glucose being the least fulfilled among all the 5 criteria, as they reported high triglycerides, low HLD cholesterol and hypertension. There was no significant difference in HDL-c level in our patient with MS and those without MS (p>0.05).[8,24] IR based on HOMA was 11.8 (7.9) in patients with MS while those without MS was 5.5 (6.8), thereby reiterating its important role in the pathogenesis of this condition with the attendant metabolic sequel.[25] Expectedly, patients with MS have 2-fold increase in the risk of fatal and non-fatal CVD compared to patients without MS.[26] Our study showed several independent risk factors for MS through multivariable analysis. Among them; age, sex, HIV duration, and the traditional risk factors, are well recognised risk factors for MS. It is also important to note that other factors or conditions not considered in this study may also be implicated in the odds of acquiring MS among HIV patients on HAART. Lack of controls from the general population and relatively small sample size were some of the limitations of the study but this does not affect the quality of our work.

CONCLUSION

Metabolic syndrome prevalence in HIV patients in this study was lower than that reported in other findings, the prevalence is much higher in the HAART treated patients. MS was driven by high triglycerides, HBP and elevated fasting blood glucose. There was significant association with the traditional risk factors, age, female gender and HIV duration, use of HAART. This study also highlights the need for regular screening and monitoring of metabolic syndrome with the view to offer treatment early to reduce the risk of cardiovascular disease in HIV patients on HAART.

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