
Metabolic Syndrome in HIV/AIDS Patients at the Tiko Central Clinic and Cottage Hospital in Cameroon: Influence on Cardiovascular Risk and Predictors

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Abstract: Highly active anti-retroviral therapy (HAART) use by HIV patients since the mid-1990's has led to a significant drop in HIV mortality. However, HAART and HIV related metabolic syndrome (hypertriglyceridaemia, reduced HDL-c, abdominal obesity, hypertension, and insulin resistance) is associated with increased cardiovascular risk in aging HIV sero-positive patients. This study was aimed at investigating the predictors of metabolic syndrome and influence of metabolic syndrome on cardiovascular (CV) risk amongst persons living with HIV on HAART. This is a hospital-based case-control study. The cases were HIV sero-positive individuals on HAART for at least 6 months and controls were HIV sero-negative individuals. Out of 135 participants, 74 (54.8%) were females amongst which 53/75 (70.7%) were in the cases group and 21/60 (35%) were in the control group. The mean age of the participants was 42.04 (± 9.61) years. HIV-infected participants at moderate CV risk based on the DAD risk calculator were more frequently diagnosed with metabolic syndrome based on the International Diabetes Federation (IDF) criteria with high statistical significance than those at low CV risk (5/19 – 26.3% vs. 12/55 – 21.8%, $P < 0.001$). Bivariate analysis of metabolic syndrome predictors in the study population revealed that gender is associated with increased odds of metabolic syndrome (OR: 5.376, 95% CI: 1.907-15.153; $P = 0.001$). Gender was the only predictor associated with metabolic syndrome (OR: 6.958, CI: 2.317-20.896; $P = 0.001$) following multivariate analysis of gender, vegetables or fruits intake, vigorous physical activity and family history of CVD and females were 7 times more likely to develop metabolic syndrome than males. More HAART-treated HIV patients at moderate CVD risk develop metabolic syndrome than those at low CVD risk. Female HIV patients on HAART have higher chances of developing metabolic syndrome compared to their male counterparts. HIV patients particularly females should be screened early for metabolic syndrome following HAART initiation.

Keywords: Metabolic Syndrome, HIV, HAART, Cardiovascular Risk, Predictors

1. Introduction

Highly active anti-retroviral therapy (HAART) use by HIV (human immunodeficiency virus) patients since the mid-1990's has led to a significant drop in HIV related mortality [1]. Nevertheless, metabolic disorders (hypertriglyceridaemia, reduced HDL-c, abdominal obesity, hypertension, and insulin

resistance) jointly termed metabolic syndrome is linked to HIV and HAART and associated with elevated cardiovascular disease risk in these patients as they age [2].

A recent study demonstrated that an association exists between HAART and metabolic syndrome and, between metabolic syndrome and increased cardiovascular risk in HAART experienced HIV individuals [3]. Studies conducted in Mexico and Australia reported that more HIV patients on HAART at high

CV (cardiovascular) risk are diagnosed with metabolic syndrome and incident metabolic syndrome is significantly associated with increased CVD risk respectively [4, 5]. Magdalena *et al* in 2008 revealed that HIV infection is independently associated with metabolic syndrome in adult female subjects [6]. Predictors of metabolic syndrome among HIV-infected individuals under ART from current reports include age, low physical activity, smoking, and gender amongst others [7, 8].

The prevalence of metabolic syndrome is significantly much higher in HIV sero-positive patients on HAART compared to HAART naïve patients and nearly similar (and insignificant) between HIV-infected and HIV-uninfected individuals [9, 10]. In Cameroon, HAART coverage has drastically risen from 26% in 2013 to 55% in 2018 [11, 12]. However, little is known about the predictors of metabolic syndrome and its influence on cardiovascular risk in HIV patients on HAART. In this light, therapeutic and lifestyle interventions geared towards metabolic syndrome and its predictors with a view of preventing cardiovascular events have been limited. This study was therefore aimed at investigating the predictors of metabolic syndrome and influence of metabolic syndrome on cardiovascular risk in HIV sero-positive subjects on HAART attending the Tiko Central Clinic and Cottage hospital in Cameroon.

2. Materials and Methods

2.1. Study Duration, Setting, and Sampling Technique

This study was conducted over a four-month period, from March to June 2016, at the treatment center of people living with HIV/AIDS, at the Tiko Central Clinic and Cottage hospital. Over 1500 patients receive their treatment at this center. The patients attend the clinic once a month for clinical evaluation and refill of anti-retroviral therapy (ART). A consecutive sampling technique was employed to recruit eligible participants.

2.2. Ethical Considerations

The goals of the study, research procedure, risks and benefits of this research were explained to the study participants and only consenting individuals were included in the study. Ethical approval was obtained from the Faculty of Health Sciences Institutional Review Board (FHSIRB) of the University of Buea, Cameroon (reference number: 2014-02-0514). Administrative authorizations were obtained from the following authorities: regional delegate of public health in Buea, district medical officer in Tiko, director of human resource in Limbe, and from the chief medical officer in Tiko.

2.3. Inclusion and Exclusion Criteria

The study population included all adult HIV sero-positive and HIV sero-negative persons attending the Tiko Central Clinic and Cottage hospital for routine health assessment. We included all people living with HIV/AIDS (PLWHA) aged at least 25 years (because QRISK 2-2016 calculator estimates the risk of individuals developing a cardiovascular disease in the

age range, 25-84 years) and excluded patients on highly active anti-retroviral therapy (HAART) for less than 6 months including defaulters of treatment regimen, pregnant and lactating women, those with documented hypertension, diabetes and dyslipidemia before commencing HAART and those with any acute illness that required medical/surgical treatment or admission. HAART was defined as the use of ≥ 2 nucleoside reverse transcriptase inhibitors (NRTIs) and at least one non-nucleoside reverse transcriptase inhibitor (NNRTI); or ≥ 2 NRTIs and at least one protease inhibitor (PI).

2.4. Administration of Questionnaires

A structured questionnaire was used to collect socio-demographic data from the participants while their medical records were accessed to obtain clinical information such as their recent CD4+ T cell count, HIV status, and type and duration of HAART regimen. Following a 10 minute resting period, while a participant was seated, 2 blood pressure measurements (systolic and diastolic) were taken in the left arm with an interval of 3 minutes using a wrist digital blood pressure monitor. The average blood pressure reading was calculated and used as the participants' actual blood pressure. Waist circumference (WC) was measured to the nearest 0.1cm with patients wearing light clothing at the midpoint between the lowest rib and the iliac crest using an inelastic tape in light contact with but not compressing the skin. The weight of each participant was measured using a Kinlee calibrated weighing scale in light clothing, with shoes off. Height was measured using a stadiometer to the nearest 0.1cm.

2.5. Blood Collection and Analysis

Following this, 3ml of venous blood was obtained, under strict aseptic conditions, after an overnight fast (8-12 hours). Fasting blood glucose was measured using the Accu Chek® Compact Plus glucometer at the spot. Serum was then collected and stored in eppendorf tubes until analysis. Lipid profiles of the participants' sera were later measured in batches using a MINDARY spectrophotometer (BA-88A semi-auto chemistry analyser with touch-screen and pop-up keypad) according to the manufacturer's instruction. Triglycerides level was measured based on a Glycerol phosphate oxidase method. HDL-c level was measured based on the Chemical precipitation technique in the presence of phosphotungstic acid and Mg^{2+} ions.

2.6. Definition of Operational Terms

Metabolic syndrome was defined based on the International Diabetes Federation (IDF) criteria. According to IDF criteria, metabolic syndrome was defined as having abdominal obesity (waist circumference of 80 cm in women and 94 cm in men or $BMI \geq 30 \text{ kg/m}^2$) and at least two of the following components: I) Elevated fasting glucose: $\geq 100 \text{ mg/dl}$ or diabetes mellitus; II) Elevated triglycerides: $\geq 150 \text{ mg/dl}$ or treatment; III) Reduced HDL-c: $< 40 \text{ mg/dl}$ in men and $< 50 \text{ mg/dl}$ in women or treatment; IV) Elevated blood pressure (Hypertension): SBP $\geq 130 \text{ mmHg}$ or DBP $\geq 85 \text{ mmHg}$ or treatment [13].

The following parameters were defined as follows: Physical inactivity (failure to engage in physical activities, recreation or work that lasted < 30 mins per day for < 3 times in a week) and insufficient fruit or vegetable consumption (failure to consume fruit or vegetable daily).

2.7. Data Analysis

Data analysis was performed on SPSS version 22.0 using Chi-square (χ^2) test, bivariate and multivariate logistic regression. QRISK®2-2016 risk calculator was used to determine the 10- year risk of developing a coronary heart disease [14]. The 10-year CVD risk was calculated using QRISK2-2016 risk equation for each participant by entering the following variables: age, gender, ethnicity, smoking status, diabetes status, Agina or heart attack in a first degree relative < 60 years, chronic kidney disease (stage 4 or 5), atrial fibrillation, rheumatoid arthritis, SBP, cholesterol/HDL ratio, weight, height and current treatment for high blood pressure. Participants were regarded as low risk, moderate risk, or high risk when the risk score for developing CVD in 10 years was <10%, 10–20% or >20% respectively.

D. A. D (Data collection on Adverse events of anti-HIV Drugs) risk calculator was used to determine the 5-year risk of myocardial infarction, coronary heart disease and CVDs [15]. Variables included in the 5-year DAD risk estimation

tool were: age, sex, height, weight, SBP, TC, HDL-C, diabetes mellitus, smoking status, family history of CVD, current use of abacavir, indinavir, or lopinavir and duration on indinavir and lopinavir. The risk of developing coronary heart disease in the next 5-years was regarded as low (<1%), moderate (1–5%), high (5–10%), or very high (>10%).

QRISK2-2016 risk calculator was developed from a prospective cohort study conducted within a large UK primary care population in which the probability of an individual developing a cardiovascular disease in 10 years was calculated [29]. In contrast, DAD risk equation was developed from the DAD cohort study in which HIV patients on HAART were followed for 4.8 years and their risk of developing a coronary heart disease in 5 years (follow-up time) was calculated [31].

3. Results

A total of 135 participants were recruited, 75 (55.6%) were HIV sero-positive amongst which 53 (70.7%) were females and 60 (44.4%) were HIV sero-negative amongst which 39 (65%) were males. The mean age was 42.04 (\pm 9.61) years in the HIV sero-positive group and 39.00 (\pm 11.3) years in the control group. The median duration on HAART was 42.0 (18 – 82) months (Table 1).

Table 1. Demographic Characteristics of Study Population.

Parameter	HIV seropositive group (n=75)	HIV seronegative group (n=60)	Total (n=135)	
Gender	Male	22 (29.3)	39 (65.0)	61 (45.2)
	Female	53 (70.7)	21 (35.0)	74 (54.8)
Age (years)	< 40 years	34 (45.3)	39 (65.0)	73 (54.1)
	\geq 40 years	41 (54.7)	21 (35.0)	62 (45.9)
Occupation	Salary employed	43 (57.3)	45 (75.0)	88 (65.2)
	Self employed	22 (29.3)	12 (20.0)	34 (25.2)
	Unemployed	8 (10.7)	2 (3.3)	10 (7.4)
Marital status	Retired	2 (2.7)	1 (1.7)	3 (2.2)
	Married/Cohabitation	38 (50.7)	33 (55.0)	71 (52.6)
	Single	32 (42.7)	23 (38.3)	55 (40.7)
Level of education	Divorced	5 (6.7)	4 (6.7)	9 (6.7)
	No formal education	4 (5.3)	5 (8.3)	9 (6.7)
	Primary	39 (52.0)	28 (46.7)	67 (49.6)
CD4+ T cell count* (cells/ μ L)	Secondary	28 (37.4)	18 (30.0)	46 (34.1)
	Tertiary	4 (5.3)	9 (15.0)	13 (9.6)
Duration of HIV infection (months)	< 250	17 (23.6)	-	-
	250-500	27 (37.5)	-	-
Duration of HAART (months)	>500	28 (38.9)	-	-
	Median (IQR)	63 (28-67)	-	-
Type of HAART regimen	Median (IQR)	42 (18-82)	-	-
	TDF+3TC+EFV	47 (62.7)	-	-
	AZT+3TC+NVP	23 (30.6)	-	-
	AZT+3TC+EFV	2 (2.7)	-	-
	TDF+3TC+LPV+RTV	2 (2.7)	-	-
Number of participants by HAART agent	TDF+3TC+NVP	1 (1.3)	-	-
	3TC	75 (100.0)	-	-
	TDF	50 (66.7)	-	-
	EFV	49 (65.3)	-	-
	AZT	25 (33.3)	-	-
	NVP	24 (32.0)	-	-
	LPV+RTV	2 (2.7)	-	-

*CD4+ T cell count available only for 72 participants. *Number of participants by HAART agent (No).

Note: HAART - Highly Active Antiretroviral therapy.

Metabolic syndrome was associated with cardiovascular disease risk among HIV-uninfected persons using the QRISK risk equation (P=0.029). HIV-uninfected participants at moderate cardiovascular risk using the QRISK calculator

were more frequently diagnosed with metabolic syndrome based on IDF criteria than those at low cardiovascular risk with statistical significance (4/8 - 50.0% vs. 8/52 - 15.4%, p=0.029) Table 2.

Table 2. Prevalence of Cardiovascular risk based on Metabolic Syndrome status in HIV-uninfected participants.

Parameter		QRISK			Total (n=60)	X ²	P-value
		Low (n=52)	Moderate (n=8)	High (n=0)			
HIV uninfected (IDF Criteria)	Without MS	44 (84.6)	4 (50.0)	0 (0.0)	48 (80.0)	10.778	0.029
	With MS	8 (15.4)	4 (50.0)	0 (0.0)	12 (20.0)		

Note: MS - Metabolic syndrome, IDF - International Diabetes Federation, X² - Chi square.

Metabolic syndrome was associated with cardiovascular disease risk among HIV-infected patients using the DAD risk equation only (P<0.001). HIV-infected participants at moderate cardiovascular risk using the DAD risk calculator

were more frequently diagnosed with metabolic syndrome based on IDF criteria than those at low risk with very high statistical significance (5/19 - 26.3% vs. 12/55 - 21.8%, P<0.001) Table 3.

Table 3. Prevalence of Cardiovascular risk based on Metabolic Syndrome status in HIV-infected participants.

Parameter		QRISK			Total (n=75)	X ²	P-value
		Low (n=70)	Moderate (n=4)	High (n=1)			
HIV infected (IDF Criteria)	Without MS	53 (75.7)	4 (100)	1 (100)	58 (77.3)	4.703	0.319
	With MS	17 (24.3)	0 (0.0)	0 (0.0)	17 (22.7)		

Parameter		DAD RISK			Total (n=75)	X ²	P-value
		Low (n=55)	Moderate (n=19)	High (n=1)			
HIV infected (IDF Criteria)	Without MS	43 (78.2)	14 (73.7)	1 (100)	58 (76.0)	135.828	< 0.001
	With MS	12 (21.8)	5 (26.3)	0 (0.0)	17 (22.7)		

Note: MS - Metabolic syndrome, IDF - International Diabetes Federation, X² - Chi square.

Binary logistic regression analysis showed that only gender was an independent predictor of metabolic syndrome (OR: 5.376, 95% CI: 1.907-15.153; P=0.001). Furthermore, more participants aged < 60 years (100% vs. 91.5%, P=0.375), with formal education (100% vs. 92.5%, P=0.999), with insufficient fruits or vegetables intake (79.3% vs. 66%,

P=0.177), with no vigorous physical activity (34.5% vs. 19.8%, P=0.100) or with family history of CVD (27.6% vs. 17.0%, P=0.204) were frequently diagnosed with metabolic syndrome compared to those who did not develop metabolic syndrome but no association was observed between these predictors and metabolic syndrome (Table 4).

Table 4. Bivariate Analysis of Predictors of Metabolic Syndrome in the Study Population.

Parameter		Study participants (MS based on IDF Criteria)		Total (n=135)	Crude OR (95% CI)	P-value
		Without MS (n=106)	With MS (n=29)			
Gender	Male	56 (52.8)	5 (17.2)	61 (45.2)	1.00 (-)	-
	Female	50 (47.2)	24 (82.8)	74 (54.8)	5.376 (1.907-15.153)	0.001
Age	≥ 60 years	9 (8.5)	0 (0.0)	9 (6.7)	1.00 (-)	-
	< 60 years	97 (91.5)	29 (100)	126 (93.3)	0.385 (0.47-3.170)	0.375
Education	Formal	98 (92.5)	29 (100)	127 (94.1)	1.00 (-)	-
	Informal	8 (7.5)	0 (0.0)	8 (5.9)	478048717.2 (0.000-no value)	0.999
Smoking	No	85 (80.2)	25 (86.2)	110 (81.5)	1.00 (-)	-
	Yes	21 (19.8)	4 (3.8)	25 (18.5)	0.648 (0.203-2.063)	0.462
Vegetables/fruits intake	Sufficient	36 (34.0)	6 (20.7)	42 (31.1)	1.00 (-)	-
	Insufficient	70 (66.0)	23 (79.3)	93 (68.9)	1.971 (0.737-5.275)	0.177
Vigorous physical activity	Yes	85 (80.2)	19 (65.5)	104 (77.0)	1.00 (-)	-
	No	21 (19.8)	10 (34.5)	31 (23.0)	0.469 (0.190-1.157)	0.100
Family history of CVD	No	88 (83.0)	21 (72.4)	109 (80.7)	1.00 (-)	-
	Yes	18 (17.0)	8 (27.6)	26 (19.3)	0.537 (0.206-1.401)	0.204

Note: MS - Metabolic syndrome, X² - Chi square, OR - Odds Ratio, CVD - Cardiovascular disease.

Following multivariate analysis of predictors of metabolic syndrome whose P values were < 0.25 (gender, vegetable or fruits intake, vigorous physical activity and family history of CVD) only gender was associated with metabolic syndrome and females were 7 times more likely to develop metabolic

syndrome than males (OR: 6.958, CI: 2.317-20.896; P=0.001). On the contrary, vegetable or fruits intake, vigorous physical activity and family history of CVD were not associated with metabolic syndrome (Table 5).

Table 5. Multivariate Analysis of Predictors of Metabolic Syndrome in the Study Population.

Parameter		Study participants (MS based on IDF Criteria)		Total (n=135)	Adjusted OR (95% CI)	P-value
		Without MS (n=106)	With MS (n=29)			
Gender	Male	56 (52.8)	5 (17.2)	61 (45.2)	1.00 (-)	-
	Female	50 (47.2)	24 (82.8)	74 (54.8)	6.958 (2.317-20.896)	0.001
Vegetables/fruits intake	Sufficient	36 (34.0)	6 (20.7)	42 (31.1)	1.00 (-)	-
	Insufficient	70 (66.0)	23 (79.3)	93 (68.9)	2.819 (0.973-8.172)	0.056
Vigorous physical activity	Yes	85 (80.2)	19 (65.5)	31 (23.0)	1.00 (-)	-
	No	21 (19.8)	10 (34.5)	104 (77.0)	2.597 (0.946-7.129)	0.064
Family history of CVD	No	88 (83.0)	21 (72.4)	109 (80.7)	1.00 (-)	-
	Yes	18 (17.0)	8 (27.6)	26 (19.3)	1.462 (0.510-4.193)	0.480

Note: MS - Metabolic syndrome, χ^2 - Chi square, OR - Odds Ratio, CVD - Cardiovascular disease.

4. Discussion

In this study, a significantly higher proportion (26.3%) of HIV sero-positive patients at moderate cardiovascular risk had metabolic syndrome compared to the proportion (21.8%) of patients at low risk for cardiovascular disease. Among the predictors (gender, vegetable or fruits intake, vigorous physical activity and family history of CVD) of metabolic syndrome in this research, gender was the only predictor associated with metabolic syndrome in both the HIV infected and uninfected individuals among whom females were 7 times more likely to develop metabolic syndrome than males.

This study revealed a higher proportion (26.3%) of HIV sero-positive patients at moderate cardiovascular risk (DAD risk: 1-5%) had metabolic syndrome compared to the proportion (21.8%) of patients at low risk (DAD risk: < 1%) for cardiovascular disease ($P < 0.001$). Similarly, Elizabete et al reported that metabolic syndrome is associated with a higher cardiovascular disease risk in HIV patients [16]. This similarity could be owing to the fact that both studies studied HAART experienced participants. A study conducted in Poland reported similar findings where a higher percentage (73%) of HIV-infected patients with metabolic syndrome had intermediate CV risk compared to the percentage (10%) of patients at low cardiovascular risk ($P = 0.006$) [30]. Moreover, Latin American and American investigators estimated that HIV-infected individuals with metabolic syndrome were at a higher 10-year risk of developing cardiovascular disease using the Framingham 10-year risk calculator compared to those without [17, 18]. Conversely, Mariana and colleagues reported that more HIV patients at low risk had metabolic syndrome compared to those at moderate and high risk (80% vs. 20%, $p = 0.22$) [19]. This difference is likely because Mariana and colleagues studied only HAART naïve HIV patients who were significantly younger whereas HAART drastically increases metabolic syndrome prevalence in HIV sero-positive patients and hence cardiovascular risk.

We highlighted in this study that gender was the only predictor of metabolic syndrome in both the HIV infected and uninfected individuals among whom females were 7 times more likely to develop metabolic syndrome than males (OR: 6.958, CI: 2.317-20.896; $P = 0.001$). Among the study participants with metabolic syndrome, more than three-quarters (82.8%) of them were females. Cultural factors like

different diets in males compared to females may be a possible contributor. It could as well be explained by more women meeting the waist criteria compared to men or biological, hormonal and environmental factors that are thought to be contributing to the occurrence of metabolic syndrome in women. Our result is not in conformity with those of studies conducted in (Adjusted OR: 1.28, 95% CI: 0.68–2.59; $P = 0.44$) Congo [8], (Crude OR: 1.38, 95% CI: 0.77–2.46; $P = 0.278$) Kenya, (Univariate analysis: $P = 0.80$) Barcelona, and (Crude OR: 0.837, 95% CI: 0.411–1.703; $P = 0.623$) Ethiopia [20-22]. The contradictory findings reported by Patrick et al in Congo, Dula et al in Ethiopia and Carlos and colleagues in Barcelona might have stemmed from the fact that investigators from these three studies used the NCEP ATP III criteria to diagnose metabolic syndrome among HAART experienced HIV patients. Furthermore, the use of the harmonized Joint Scientific Statement criteria by Catherine et al in Kenya might account for the discrepancy in finding indicated in her study. However, our result is consistent with results revealed by studies conducted in the United States [1], Tanzania, Burkina Faso, Kenya, Nigeria, Ethiopia, and South Africa [23-28].

The sample size of HIV patients on HAART in this study was small due to a short study duration and small number of these patients who visited the HIV/AIDS treatment center daily. Despite these limitations, this study is the first in Cameroon (to the best of our knowledge) which shows that HAART experienced HIV patients diagnosed with metabolic syndrome have an increased cardiovascular risk and HIV infected and uninfected females are 7 times more likely to develop metabolic syndrome than their male counterparts.

5. Conclusion

A significantly higher proportion of HAART-treated HIV patients at moderate CVD risk are diagnosed with metabolic syndrome compared to those at low CVD risk. Gender is associated with metabolic syndrome in both HAART-experienced HIV patients and HIV-uninfected individuals. HIV sero-positive females have higher chances of developing metabolic syndrome than their male counterparts. Early screening of HIV patients on HAART particularly females for metabolic syndrome after initiating them on HAART is recommended.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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