

Metabolic Syndrome and Associated Factors among Adult HIV Positive People on Antiretroviral Therapy in Jugal Hospital, Harar, Eastern Ethiopia

Zerihun Ataro^{1*}, Wondimye Ashenafi²

¹Department of Medical Laboratory Sciences, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia

²School of Public Health, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia

Abstract

Background: Despite its significant importance in reducing the morbidity and mortality of HIV-positive people, antiretroviral therapy is associated with increased rate of metabolic syndrome. However, data on metabolic syndrome in HIV-infected people receiving antiretroviral therapy in Ethiopia is scarce. This study aimed to determine the prevalence and the associated factors of metabolic syndrome among adult HIV positive patients taking antiretroviral therapy.

Methods: A cross-sectional study was conducted from February to April, 2017 among adult 375 HIV positive patients taking antiretroviral therapy at Jugal Hospital, Harar, eastern Ethiopia. Demographic, clinical and anthropometric data were collected from each participant. Venous blood was collected and used for the measurement of glucose and lipid profile using Autolab 18 clinical chemistry analyzer. The International Diabetes Federation, National Cholesterol Education Program: Adult Treatment Panel III and Joint Interim Statement criteria were used to define metabolic syndrome. Data were analyzed using STATA Version 13. Bivariate and multivariable logistic regression was used to identify factors associated with the outcome variable. A p-value of <0.05 was considered statistically significant.

Results: The prevalence of metabolic syndrome was 22.1 % (95% CI: 18.2, 26.6) by National Cholesterol Education Program: Adult Treatment Panel III criteria, 26.7% (95% CI: 22.4, 31.4) by International Diabetes Federation criteria, and 29.9% (95% CI: 25.4, 34.7) by Joint Interim Statement criteria. Age over 40 years (AOR=2.3; 95% CI: 1.4-3.8); lack of formal education (AOR=2.4; 95% CI: 1.12-5.4); and using tenofovir-lamivudine-lopinavir/ritonavir regimens (AOR=6.7; 95% CI: 1.4-32.1) were significantly associated with metabolic syndrome defined by Joint Interim Statement criteria.

Conclusion: Metabolic syndrome is high among HIV-infected people receiving antiretroviral therapy. Age, educational level and regimens were significantly associated with metabolic syndrome. Therefore, regular screening for components of metabolic syndrome and promotion of a healthy lifestyle is recommended.

Keywords: ART; Eastern Ethiopia; Harar; HIV; Metabolic Syndrome

How to cite: Ataro, Z. and Ashenafi, W. 2020. Metabolic syndrome and associated factors among adult HIV positive people on antiretroviral therapy in Jugal Hospital, Harar, eastern Ethiopia. *East African Journal of Health and Biomedical Sciences*, Volume 4 (1): 13-24

Introduction

Metabolic syndrome (MS) is an interaction of various factors such as abdominal obesity, dyslipidemia, the elevation of blood pressure and insulin resistance which can increase the risk of developing cardiovascular disease and Type 2 diabetes (Alberti *et al.*, 2006). It is a global challenge which has been playing a major role as a marker for metabolic disorders (Eckel *et al.*, 2010; Rosolova and Nussbaumerova, 2011). It increases cardiovascular risk more than each single component (Isomaa *et al.*, 2001). The MS is associated

with a 2-fold increase in risk of cardiovascular diseases, cardiovascular mortality, and stroke (Salvatore *et al.*, 2010).

The introduction of Antiretroviral Therapy (ART) modifies the course of HIV infection, improves quality of life and survival of patients with HIV. It has transformed formerly fatal HIV/AIDS to a chronic, manageable infectious disease that requires life-long treatment (Narayan *et al.*, 2014). In Ethiopia, an estimated 0.9% men and women aged 15-49 years have been infected with HIV and 71% of the eligible patients are currently on ART (FHAPCO, 2018).



HIV infection and the use of ART regimen further can increase the susceptibility of HIV infected patients to cardio-metabolic abnormalities, such as lipodystrophy, dyslipidemia, insulin resistance and body shape changes (Katoto *et al.*, 2018; Mittal *et al.*, 2013; Paula *et al.*, 2013; Sweet, 2005; Syed and Sani, 2013). Such relationship increases the chance of exposure to MS among HIV patients (Wand *et al.*, 2007). Furthermore, the long-term toxicities are emerging after prolonged exposure to ART, which are becoming challenges to the successful management of HIV infection (Narayan *et al.*, 2014).

The prevalence of MS has varied among studies and varies by the type of definition used. A meta-analysis conducted to estimate pooled prevalence of MS in the global HIV infected population has shown a prevalence of 18% based on International Diabetes Federation (IDF) criteria, 24.6% based on Adult Treatment Panel (ATP) and 29.6% based on Joint Interim Statement (JIS) (Nguyen *et al.*, 2016).

Several reports on the prevalence of the MS are from developed nations. The reported prevalence of MS from a review using different studies conducted on people living with HIV (PLWH) in high-income countries ranges from 11.2% to 45.4% (Paula *et al.*, 2013) and in developing regions, the MS prevalence ranges from 8.4% to 47% (Naidu *et al.*, 2017). Studies conducted in several African countries report a prevalence of MS up to 60.6% among HIV positive patients (Berhane *et al.*, 2012; Dimodi *et al.*, 2014; Kagaruki *et al.*, 2015). In Ethiopia, MS was diagnosed in 25% of HIV positive patients receiving ART (Tesfaye *et al.*, 2014).

The prevalence of MS is higher in PLWH than HIV negative. A systematic review and meta-analysis conducted to estimate the pooled prevalence of MS in sub-Saharan Africa has shown a prevalence of 21.5% among people living with HIV and 12.0% among HIV uninfected groups (Todowedo *et al.*, 2019).

Early detection of MS can be crucial for decision making in health care regarding cardiovascular disease prevention and patient management. Despite the large number of studies conducted on MS in relation to HIV infection and ART in many parts of the world, there are few data on the burden of MS in HIV-infected patients in resource-limited settings, including Ethiopia.

Hence, the current study aimed to assess the prevalence and associated factors of MS among HIV patients taking ART in Jugal Hospital, Harar, eastern Ethiopia.

Materials and Methods

Study area, period and design

An institution-based cross-sectional study was conducted between February and April 2017 in Jugal Hospital. The hospital is found in Harar town, which is located in east of Ethiopia, 526 km away from Addis Ababa, the capital city of Ethiopia. According to the central statistical agency census report, the total projected population of the Harari Region for 2017 is 244,711 (CSA, 2013). During the study period, more than 1300 HIV positive patients were on ART at ART clinics of Jugal hospital.

Study Population

HIV positive patients who were 18 years or older and had been on ART for at least 6 months were the study population. Pregnant women, patients with hypothyroidism, diabetes mellitus, chronic renal failure and those using corticosteroids and critically ill were excluded.

Sample size and sampling techniques

The sample size was calculated by using a single population proportion formula with the following parameters: considering 50% prevalence of MS, 95% confidence interval ($Z=1.96$) and a margin of error of 5%. Based on this, the estimated sample size was 384. The HIV patients taking ART and who fulfilled the inclusion criteria were recruited consequently by convenient sampling technique.

Data Collection

Face to face interview: Data were collected using a structured questionnaire adapted from questionnaire developed by WHO stepwise approach to chronic disease risk factor surveillance (WHO, 2010). The questionnaire contains socio-demographic characteristics (age, sex, marital status, educational status, residence area, occupation, ethnicity, religion) and habit of smoking, *Khat* chewing, and alcohol intake.

Blood pressure measurements: Blood pressure (BP) was measured using an automated sphygmomanometer by a nurse trained on ART services. Three readings were taken with 5 minute interval and the average of

the three readings was recorded as the final BP of the participant.

Anthropometric measurement: The body weight and height were measured using a digital balance with height measurement attached to it. Weight was measured by placing the weighing balance on a flat hard surface and height was measured while a patient is facing directly ahead. Body Mass Index (BMI) was calculated by dividing weight in kilogram (kg) to height in meter squared (m^2). The BMI results were categorized as obesity (BMI is ≥ 30 kg/m^2), overweight (BMI is 25-29.99 kg/m^2), normal (BMI is 18.5-24.99 kg/m^2), and underweight (BMI is < 18.5 kg/m^2) (WHO, 2011). Waist circumference was taken at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest while subjects were standing and breathing normally and with the patient wearing light clothe.

Patient record review: CD₄⁺ cell count, WHO clinical stage, type and duration of ART were collected from the patient's health record.

Blood sample collection and examination: Five ml of fasting venous blood specimen was collected. If the patient had not or fasting was not observed, the blood sample collection was rescheduled on the next day. Sample collection time was recorded in the test requisition form. Serum was separated by centrifuging of clotted blood sample. Fasting glucose level and lipid profile were measured using automated clinical chemistry analyzer (Autolab 18, Boehringer-Mannheim Diagnostics, USA) using reagents from the HUMAN Company (Human Biological Diagnostic, Germany). The laboratory analysis was performed by experienced laboratory technologist in the laboratory of Jugal hospital.

Serum glucose level was measured by the glucose oxidase method (GOD-PAP). Enzymatic colorimetric assay method was used for the measurement of total cholesterol (CHOD-PAP method) and triglyceride (GPO-PAP method). Enzymatic precipitation method was used for the measurement of high density lipoprotein cholesterol (HDL-C). Low density lipoprotein cholesterol (LDL-C) was calculated by using Friedewald equation, $LDL = TC - HDL - (TG/5)$, where TC represents total cholesterol, and TG represents triglyceride (Friedewald *et al.*, 1972).

Data quality control

Data collectors were trained for three days before the data collection. The questionnaire was pre-tested at Hiwot Fana Specialized University Hospital and the necessary corrections were made. All the data collected using the structured questionnaire were checked for completeness. All reagents were labeled with date of opening and preparation, checked for expiration date and storage requirements. Standard Operating Procedures (SOPs) and manufacturer instruction were adhered strictly during blood glucose and lipid profile measurements. Both normal and pathological quality control were used to verify acceptability of blood glucose and lipid profile measurement. Supervision by the experienced laboratory staffs working in the laboratory was made to verify test results.

Definition of metabolic syndrome

According to the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines, MS is defined as having three or more of the following criteria: waist circumference > 88 cm in women and > 102 cm in men; triglycerides ≥ 150 mg/dl, HDL < 50 mg/dL in women and < 40 mg/dL in men; fasting glucose ≥ 110 mg/dl, or blood pressure $\geq 130/85$ mmHg (Grundy, 2004). According to International Diabetes Federation (IDF) criteria, MS is defined as having waist circumference (adjusted for Africans) > 80 cm in women and > 94 cm in men plus two of the following: triglycerides ≥ 150 mg/dL, HDL < 40 mg/dl in males and < 50 mg/dl in females, fasting plasma glucose ≥ 100 mg/dL or hypertension (blood pressure $\geq 130/85$ mm Hg or current receipt of medication for hypertension) (Alberti *et al.*, 2006). Based on the Joint Interim Statement (JIS) criteria, MS is defined as the presence of three or more of the following criteria: waist circumference (adjusted for Africans) > 80 cm in women and > 94 cm in men; triglycerides ≥ 150 mg/dL; HDL < 40 mg/dl in males and < 50 mg/dl in females; fasting plasma glucose ≥ 100 mg/dL or hypertension (blood pressure $\geq 130/85$ mm Hg or current receipt of medication for hypertension) (Alberti *et al.*, 2009).

Data processing and analysis

All the collected data were double entered into Microsoft Excel spreadsheets. Cleaning and analysis of the data were done using STATA software Version-13

STATA Corp. College Station, Texas, USA). Descriptive statistics using frequency distribution were used to summarize the data. Binary logistic regression model was used to identify the independent variables associated with MS. All variables with P-value less than 0.25 in the bivariate logistic regression analysis were further entered into a multivariable logistic regression model in order to control the effect of confounding variables. Crude and adjusted odds ratios (OR) with 95% confidence intervals (CI) were reported. All statistical tests were two-sided. Kappa statistic was used to test the degree of agreement between the diagnostic criteria. A P-value of <0.05 was considered statistically significant.

Ethics approval

Ethical approval of this study was obtained from the Institutional Health Research Ethics Review Committee of the College of Health and Medical Sciences, Haramaya University. All the study participants were informed clearly about the purpose of the investigation and got their informed written and signed consent to take part in this study. Each study participant was informed of his/her physical assessment and biochemical test results. Abnormal findings were communicated to their clinician for better management of the study subjects.

Results

General characteristics of the study participants

A total of 375 study participants (97.4% response rate) were included in this study. Many of the respondents were female (70.1%). The mean age of the participants was 39.8 years (range 19-68 years) and some of them were between the ages of 31-40 years (45.3%). Of the 375 study subjects, 60.8% were Orthodox Christians, 93.9% were urban dwellers, and 56.0% Amhara by ethnicity. One hundred and fourteen (30.4%) of the study participants were daily laborers, and 47.2% were married. About one-third of the study participants (33.9%) had attained a primary level of education (Table 1).

Clinical characteristics

Almost all of the study participants were in World Health Organization (WHO) stage I (96.9%), and 47.4% were with CD4 > 500 cells/ul. The median (interquartile range (IQR)) of body mass index (BMI)

and CD4+ count of the participants were 22.9 (19.9-26.0) and 480 (341-676), respectively. The participant had received ART for a median duration of 70 months (range 6-156 months). The most commonly prescribed regimen was TDF-3TC-EFV (53.9%), followed by AZT-3TC-NVP (23.7%), AZT-3TC-EFV (12.0%), and TDF-3TC-NVP (7.7%) (Table 2).

Prevalence of Metabolic Syndrome

According to the NCEP-ATP III criteria, the overall prevalence of MS was 22.1% (95% CI: 18.2, 26.6). Whereas, MS was 26.7% (95% CI: 22.4, 31.4) in IDF criteria and 29.9% (95% CI: 25.4, 34.7) in JIS criteria. The JIS definition gave the highest overall prevalence compared to IDF and NCEP-ATP III.

A high level of agreement between the IDF and JIS criteria was observed (Kappa index=0.92), while there was a substantial level of agreement between the IDF and NCEP-ATP III criteria (Kappa index=0.70) and between JIS and NCEP-ATP III criteria (Kappa index=0.80) (Table 3).

Prevalence of MS components

The prevalence of MS components in this study participants was; low HDL-Cholesterol 64.5% (95% CI: 59.5, 69.2), high WC based on IDF and JIS criteria 59.2% (95% CI: 54.1, 64.1) and NCEP-ATP III criteria 37.3% (95% CI: 32.6, 42.3), hypertriglyceridemia 41.9% (95% CI: 36.9, 46.9), high glucose based on IDF and JIS criteria 25.1% (95% CI: 20.9, 29.7) and NCEP-ATP III criteria 18.4% (95% CI: 14.8, 22.7), high blood pressure 10.9% (95% CI: 8.1, 14.5) (Table 4).

From the five components used to define MS, based on ATP criteria, 62 (16.5%) of the study participants had three abnormal components, 18 (4.8%) of them had four abnormal components, and 3 (0.8%) of them had 5 abnormal components. Based on IDF criteria, 66(17.6%) had three abnormal components, 29 (7.7%) had 4 abnormal components, and 4 (1.1%) had 5 abnormal components. Based on JIS criteria, 75 (20.0%), 33 (8.8%) and 4 (1.1%) of the study participants had three, four and five abnormal components, respectively.

Table 1: General characteristic of the study participants at Jugal Hospital, Harar, eastern Ethiopia, 2017.

Variables	Variable Category	n=375 (%)
Age Group	18-30	64 (17.1)
	31-40	170 (45.3)
	41-50	96 (25.6)
	>50	45 (12.0)
Sex	Male	112 (29.9)
	Female	263 (70.1)
Residence	Urban	352 (93.9)
	Rural	23 (6.1)
Ethnicity	Amhara	210 (56.0)
	Oromo	108 (28.8)
	Gurage	20 (5.3)
	Harari	16 (4.3)
	Tigray	11 (2.3)
	Other	10 (2.7)
Educational status	No formal education	117 (31.2)
	Primary education	127 (33.9)
	Secondary education	80 (21.3)
	College/university	51 (13.6)
Marital status	Single	30 (8.0)
	Married	177 (47.2)
	Divorced/Separated	106 (28.3)
	Widowed	62 (16.5)
Occupation	Government employee	75 (20.0)
	Private work	92 (24.5)
	Labor work	114 (30.4)
	House wife	43 (11.5)
	Retired/dependent /no work	35 (9.3)
	Others*	16 (4.3)
Religion	Muslim	94 (25.1)
	Orthodox	228 (60.8)
	Protestant	47 (12.5)
	Others (Catholic and no religion)	6 (1.6)

*Others were farmer, prostitute and beggar

Factors associated with metabolic syndrome

In the bivariate logistic regression analysis, age, educational level, fruit consumption, WHO stage (baseline), ART duration, and ART regimen were considered as a candidate for multivariable logistic regression analysis. In the multivariable logistic regression analysis, age, educational level, and ART regimen remained independent predictors of MS (defined by JIS criteria). Those participants with age ≥ 40 years were

2.3 times more likely to develop MS compared to those < 40 years of age (AOR=2.3; 95% CI: 1.4, 3.8). Those study participants who had no formal education were 2.4 times more likely to develop MS compared to those with tertiary educational level (AOR=2.4; 95% CI: 1.12-5.4). Those taking TDF-3TC-LPV/r were 6.7 times more likely to develop MS compared to those taking TDF-3TC-EFV (AOR=6.7; 95% CI: 1.4-32.1) (Table 5).

Table 2: Clinical characteristics of the study participants at Jugal Hospital, Harar, eastern Ethiopia, 2017. (n=375)

Variables	Variable Category	n (%)
BMI Median (IQR)		22.9 (19.9-26.0)
BMI category (kg/m ²)	Underweight	63 (16.8)
	Normal	195 (52.0)
	Overweight	88 (23.5)
	Obese	29 (7.7)
WHO stage	Stage I	365 (97.3)
	Stage II	1 (0.27)
	Stage III	8 (2.13)
	Stage IV	1 (0.27)
CD4 (cells/ul)	Median (IQR)	480 (341-676)
CD4 (cells/ul)	>500	177 (47.2)
	200-499	170 (45.3)
	<200	28 (7.5)
Regimen	AZT-3TC-NVP	89 (23.7)
	AZT-3TC-EFV	45 (12.0)
	TDF-3TC-EFV	202 (53.9)
	TDF-3TC-NVP	29 (7.7)
	TDF-3TC-LPV/r	10 (2.7)
ART duration (month) Median (IQR)		70 (41-97)
ART duration	< 5 years	154 (41.1)
	>= 5 years	221 (58.9)

Abbreviations: n=number; BMI=body mass index; IQR=inter quartile range; ART=antiretroviral therapy; AZT= zidovudine; 3TC= lamivudine; EFV=efavirenz; TDF=Tenofovir; NVP=nevirapine; LPV/r=lopinavir/ritonavir

Table 3: Agreement between criteria used for the definition of the MS (estimated by the kappa statistics)

Criteria	JIS	IDF	NCEP-ATP III
JIS	1	0.92	0.80
IDF		1	0.70
NCEP-ATP III			1

Abbreviations: NCEP-ATP III=National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III); IDF=International Diabetes Federation; JIS=Joint Interim Statement

Table 4: Prevalence of MS components in HIV patients receiving ART at Jugal Hospital, Harar, eastern Ethiopia, 2017.

Parameters/variables	n=375 (%)
WC (NCEP-ATP III criteria): > 102 cm in men and >88 cm in women	140 (37.3)
WC (IDF criteria and JIS criteria): ≥ 94 cm in men and ≥ 80 cm in women	222 (59.2)
Glucose (NCEP-ATP III criteria): ≥110 mg/dl	69 (18.4)
Glucose (IDF criteria and JIS criteria): ≥100 mg/dl	94 (25.1)
Blood pressure: 130/85 mmHg	41 (10.9)
HDL cholesterol: < 40 mg/dl in men and <50 mg/dl in women	242 (64.5)
Triglyceride: ≥ 150 mg/dl	157 (41.9)

Abbreviations: NCEP-ATP III=National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III); IDF=International Diabetes Federation; JIS=Joint Interim Statement; HDL=High density lipoprotein

Table 5: Bivariate and multivariable analyses for factors associated with MS among HIV patients receiving ART at Jugal Hospital, Harar, eastern Ethiopia, 2017.

Variables	Variable category	MS,	Normal,	COR (95% CI)	AOR (95% CI)
		n (%)	n (%)		
Age(years)	<40	42 (21.3)	155 (78.7)	1	1
	≥40	70 (39.3)	108 (60.7)	2.4 (1.5-3.8)	2.3 (1.4-3.8)*
Education	Tertiary	12 (23.5)	39 (76.5)	1	1
	Primary	26 (20.5)	101 (79.5)	0.8 (0.4-1.8)	0.8 (0.4-1.9)
	Secondary	22 (27.5)	58 (72.5)	1.2 (0.5-2.8)	1.3 (0.6-3.1)
	No formal education	52 (44.4)	65 (55.6)	2.6 (1.2-5.5)	2.4 (1.1-5.4)*
Fruit eat	No	23 (38.3)	37 (61.7)	1	1
	Yes	89 (28.2)	226 (71.8)	0.6 (0.4-1.1)	0.9 (0.5-1.7)
WHO stage (baseline)	Stage I	15 (22.1)	53 (77.9)	1	1
	Stage II	24 (42.1)	33 (57.9)	2.6 (1.2-5.6)	2.1 (0.9-4.8)
	Stage III	62 (29.9)	145 (70.1)	1.5 (0.7-2.9)	1.1 (0.5-2.1)
	Stage Iv	11 (25.6)	32 (74.4)	1.2 (0.5-2.9)	0.7 (0.3-1.9)
ART duration	<5 year	36 (23.4)	118 (76.6)	1	1
	≥5 year	76 (34.4)	145 (65.6)	1.7 (1.1-2.7)	1.2 (0.7-2.2)
ART type	TDF-3TC-EFV	48 (23.8)	154 (76.2)	1	1
	AZT-3TC-EFV	19 (42.2)	26 (57.8)	2.3 (1.2-4.6)	1.8 (0.8-3.9)
	AZT-3TC-NVP	30 (33.7)	59 (66.3)	1.6 (0.9-2.8)	1.7 (0.9-3.2)
	TDF-3TC-NVP	8 (27.6)	21 (72.4)	1.2 (0.5-2.9)	1.2 (0.4-3.2)
	TDF-3TC-LPV/r	7 (70.0)	3 (30.0)	7.5 (1.8-30.1)	6.7 (1.4-32.1)*

Abbreviations: *=statistical significant, n=number; MS=metabolic syndrome; JIS=Joint Interim Statement; COR=crude odds ratio; AOR=adjusted odds ratio; CI=confidence interval; ART=antiretroviral therapy; AZT=Zidovudine; 3TC=lamivudine; EFV=efavirenz; TDF=Tenofovir; NVP=nevirapine; LPV/r=lopinavir/ritonavir

Discussion

The overall prevalence of MS according to the NCEP-ATP III and IDF criteria was 22.1% and 26.7% respectively, while a relatively higher prevalence (29.9%) was found according to JIS definition. Age, educational level, and ART regimen remained independent predictors of MS.

The prevalence of MS in the present study is similar to the one found by a study from Jimma, southwest Ethiopia, which is 21.1% using ATP criteria (Berhane *et al.*, 2012), Thailand (22.2%) (Jantarapakde *et al.*, 2014), and Italy (20.8%) (Bonfanti *et al.*, 2007). But it is higher than the ones reported from Australia (14%) (Samaras *et al.*, 2007), Barcelona, Spain (17%) (Jericó *et al.*, 2005). However, our finding is slightly higher than the ones reported from Hawasa, southern Ethiopia, which are 18.1% and 17.8 using ATP criteria; and 25% and 24.3% using IDF criteria (Hirigo and Tesfaye, 2016; Tesfaye *et al.*, 2014), Australia (14%) (Samaras *et al.*, 2007), Barcelona, Spain (17%) (Jericó *et al.*, 2005). The prevalence of MS in our study is

lower than reported in Cameroon (32.8%) (Dimodi *et al.*, 2014), Taiwan (26.2%) (Wu *et al.*, 2012), Portugal (41.9%) (Santos and Barros, 2007), South Africa (60.6%) (Erasmus *et al.*, 2012), USA (33%) (Sobieszczyk *et al.*, 2008), and Ghana (61.1%) (Obirikorang *et al.*, 2016). The observed variation of prevalence of MS among different studies could be attributed to the use of different definition criteria, different exposure durations of ART among the study participants and different study populations. It could also be due to the difference in the guideline used for ART and difference in behavioral factors among the study subjects (Jericó *et al.*, 2005; Lutsey *et al.*, 2008; Onesi and Ignatius, 2014).

In this study, the prevalence of MS was higher among those aged > 40 years. This has been reported in other similar studies conducted in Ethiopia, in which the prevalence of MS increased noticeably in the age group 45 years against the age group 24 years (Tsfaye *et al.*, 2014). Different studies reported that MS was more prevalent among old age patients than younger ones (Jericó *et al.*, 2005; Magny Bergersen *et al.*,

2006; Mangili *et al.*, 2007; Wand *et al.*, 2007). The increased risk of MS in older age-group is supported by the fact that aging has been shown to affect the cardio-metabolic activity (Alberti *et al.*, 2006).

Antiretroviral therapy has been proposed to induce MS in HIV-infected patients. Different types of metabolic abnormalities such as dyslipidemia, increased blood pressure, and insulin resistance were developed on HIV positive patients on ART (Wand *et al.*, 2007). It has also been reported that the risk of MS is higher in HIV patients who use a Protease inhibitor (PIs) based regimen (Samaras *et al.*, 2007). Evidence of hyperlipidemia dyslipidemia (both hypertriglyceridemia and hypercholesterolemia) were commonly observed during lopinavir/ritonavir (LPV/r) treatment (Muya and Kamuhabwa, 2019). These could be due to protease inhibitors interact with adipose tissue, altering lipid metabolism by generating oxidative stress which modifies the secretion, differentiation, and autophagic activities of adipocytokines that leads to metabolic abnormalities.

In our study, lack of formal education was associated with increased odds of MS. A similar finding has been reported from a study conducted in Kenya (Kiama *et al.*, 2018), but it is unlike the finding of a study done in Tanzania, where the prevalence of MS was significantly greater among study participants with higher level of education (Kagaruki *et al.*, 2015).

The finding of this study has clinical and public health implications. Screening of MS at ART clinics is not frequently performed in the management of metabolic disorders in settings with limited resources. The finding from this study implies the need for the importance of close monitoring of cardiovascular risk factors for early prevention and management of HIV patients.

The main strengths of this study include that it provides the opportunity of evaluating the prevalence of MS in HIV infected patients receiving ART. This contributes to improved assessment of the problem in the context of resource-constrained countries in which HIV comorbidities data are scarce and much needed. However, potential limitations of this study must be considered. Because of the convenient sampling technique was used, which cannot be considered representative of all HIV infected patients receiving ART

in the country. Our study design was cross-sectional and, as a result, it could only identify associated factors and not risk factors.

Conclusion

This study has indicated that MS is high among HIV-infected patients receiving ART in our set up. Age above 40 years old, lack of formal education, and using TDF-3TC-LPV/r regimen were found to be independent predictors of MS. Regular monitoring of MS among HIV/AIDS patients who are on ART is mandatory in the ART clinic. Therefore, patients with HIV infection on ART should be screened for components of MS and provide access to affordable CVD and metabolic care services in order to reduce the potential risk for morbidity and mortality related to long-term metabolic abnormalities. Regular follow up of old age patients and those taking TDF-3TC-LPV/r regimen is highly recommended. Further wide scale studies are recommended to evaluate the occurrence of metabolic syndrome using sample representative of all HIV infected patients receiving ART.

Acknowledgments

The authors greatly acknowledge Haramaya University for funding this research. Our special thanks go to our study participants for willing to participate in this study. We would like to express our sincere thanks to our data collectors for their proper collection of the required data.

Conflict of interest

The authors declared that there is no conflict of interests

Authors' contributions

ZA designed the study, participated in data collection, analysis, and drafted the manuscript. WA participated in study design, analysis, write-up, and critically revised the manuscript. All authors gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

References

- Alberti, K., Eckel, S.M., Grundy, P.Z., Zimmet, J.I., Cleeman, K.A., Donato, J.C.2009. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes

- federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. *Circulation*, 120 (16):1640-1645.
- Alberti, K.G.M.M., Zimmet, P., and Shaw, J. 2006. Metabolic syndrome-a new world-wide definition. A consensus statement from the international diabetes federation. *Diabetic Medicine*, 23 (12): 469-480.
- Berhane, T., Yami, A. F., Alemseged, T. Yemane, Hamza, L., Kassim, M. and Deribe, K. 2012. Prevalence of lipodystrophy and metabolic syndrome among HIV positive individuals on Highly Active Anti-Retroviral treatment in Jimma, South West Ethiopia. *Pan African Medical Journal*, 13 (43):1-14.
- Bonfanti, P., Giannattasio, C., Ricci, E., Facchetti, R., Rosella, E., Franzetti, M. 2007. HIV and metabolic syndrome: a comparison with the general population. *Journal of Acquired Immune Deficiency Syndrome*, 45 (4): 426-431.
- Central Statistical Agency. 2013. Population projection for Ethiopia 2007-2037, Addis Ababa, Ethiopia. [www.csa.gov.et/368-population-projection-2007-2037 PDF](http://www.csa.gov.et/368-population-projection-2007-2037-PDF)
- Dimodi, H.T., Etame, L.S. Nguimkeng, B.S. Mbappe, F.E. Ndoe, N.E., Tchinda, J.N. 2014. Prevalence of metabolic syndrome in HIV-infected Cameroonian patients. *World Journal of Acquired Immune Deficiency Syndrome*, 4 (1): 85-92.
- Eckel, R.H., Alberti, K., Grundy, S.M. and Zimmet, P.Z. 2010. The metabolic syndrome. *The Lancet*, 375 (9710):181-183.
- Erasmus, R.T., Soita, D.J., Hassan, M.S., Blanco-Blanco, E., Vergotine, Z., Kengne, A.P. and Matsha, T.E. 2012. High prevalence of diabetes mellitus and metabolic syndrome in a South African coloured population: Baseline data of a study in Bellville, Cape Town. *South African Medical Journal*, 102 (11): 841-844.
- FHAPCO. 2018. The federal HIV/AIDS Prevention and Control Office. HIV Prevention in Ethiopia National Road Map 2018–2020. ethiopia.unfpa.org
- Friedewald, W.T., Levy, R.I. and Fredrickson, D.S. 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry*, 18 (6): 499-502.
- Grundy, S. 2004. American Heart Association, National Heart, Lung, and Blood Institute. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*, 109 (10): 433-438.
- Hirigo, A.T. and Tesfaye, D.Y. 2016. Influences of gender in metabolic syndrome and its components among people living with HIV virus using antiretroviral treatment in Hawassa, southern Ethiopia. *BMC Research Notes*, 9 (145): 1-7.
- Isomaa, B., Almgren, P. Tuomi, T., Forsén, B., Lahti, K.M., Nissén, M., Taskinen, R. and Groop, L. 2001. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*, 24 (4): 683-689.
- Jantarapakde, J., Phanuphak, N., Chaturawit, C., Pengnonyang, S., Mathajittiphan, P., Takamtha, P., Dungjun, N., Pinyakorn, S., Pima, W. and Prasithsirikul, W. 2014. Prevalence of metabolic syndrome among antiretroviral-naive and antiretroviral-experienced HIV-1 infected Thai adults. *AIDS patient care and STDs*, 28 (7): 331-340.
- Jericó, C., Knobel, H., Montero, M., Ordoñez-Llanos, J., Guelar, A., Gimeno, J. L. 2005. Metabolic syndrome among HIV-infected patients: prevalence, characteristics, and related factors. *Diabetes Care*, 28 (1):132-137.
- Kagaruki, G.B., Kimaro, G.D., Mweya, C.N., Kilale, A.M., Mrisho, R.M., Shao, A.F., Kalinga, A.K., Ngadaya, E.S., Mfinanga, S.G. and Mayige, M.T. 2015. Prevalence and Risk Factors of Metabolic Syndrome among Individuals Living with HIV and Receiving Antiretroviral Treatment in Tanzania. *British Journal of Medicine and Medical Research*, 5 (10):1317-1327.
- Katoto, P.D., Thienemann, F., Bulabula, A.N., Esterhuizen, T.M., Murhula, A.B., Lunjwire, P.P., Bihehe, D.M. and Nachege, J.B. 2018. Prevalence and risk factors of metabolic syndrome in HIV-infected adults at three urban clinics in a post-

- conflict setting, eastern Democratic Republic of the Congo. *Tropical Medicine and International Health*, 23 (7):795-805.
- Kiama, C.N., Wamicwe, J.N., Oyugi, E.O., Obonyo, M.O., Mungai, J.G., Roka, Z.G. and Sum, A.M. 2018. Prevalence and factors associated with metabolic syndrome in an urban population of adults living with HIV in Nairobi, Kenya. *Pan African Medical Journal*. 29 (90):128-33.
- Lutsey, P.L., Steffen, L.M. and Stevens, J. 2008. Dietary intake and the development of the metabolic syndrome. *Circulation*, 117 (6): 754-761.
- Magny Bergersen, B., A. Schumacher, L. Sandvik, J.N. Bruun, and K. Birkeland. 2006. Important differences in components of the metabolic syndrome between HIV-patients with and without highly active antiretroviral therapy and healthy controls. *Scandinavian Journal of Infectious Diseases*, 38 (8): 682-689.
- Mangili, A., Jacobson, D.L., Gerrior, J., Polak, J.F., Gorbach, S.L. and Wanke, C.A. 2007. Metabolic syndrome and subclinical atherosclerosis in patients infected with HIV. *Clinical Infectious Diseases*, 44 (10): 1368-1374.
- Mittal, A., B. AchAppA, D., MADi, M.N., Chowta, J.T., Ramapuram, S., Rao, Unnikrishnan, B. and Mahalingam, S. 2013. The development of metabolic risk factors after the initiation of the second line anti-retroviral therapy. *Journal of Clinical and Diagnostic Research*, 7 (2): 265-68.
- Muya, E. and Kamuhabwa, A.A. 2019. Comparative Assessment of the Magnitude of Hyperlipidemia in HIV-Infected Patients Receiving Lopinavir/rand Atazanavir/r-Based Antiretroviral Drugs. *Journal of the International Association of Providers of AIDS Care*, 18 (3): 1-10
- Naidu, S., Ponnampalvanar, S., Kamaruzzaman, S.B. and Kamarulzaman, A. 2017. Prevalence of metabolic syndrome among people living with HIV in developing countries: a systematic review. *AIDS patient care and STDs*, 31 (1):1-13.
- Narayan, K.V., Miotti, P.G., Anand, N.P., Kline, L.M., Harmston, C., Gulakowski III, R. and Vermund, S.H. 2014. HIV and noncommunicable disease comorbidities in the era of antiretroviral therapy: a vital agenda for research in low-and middle-income country settings. *Journal of Acquired Immune Deficiency Syndrome*, 67 (S3): S2-S7.
- Nguyen, K.A., Peer, N., Mills, E.J. and Kengne, A.P. 2016. A meta-analysis of the metabolic syndrome prevalence in the global HIV-infected population. *PloS one*, 11 (3): e0150970.
- Obirikorang, C., Quaye, L., Osei-Yeboah, J., Odame, E.A. and Asare, I. 2016. Prevalence of metabolic syndrome among HIV-infected patients in Ghana: A cross-sectional study. *Nigerian Medical Journal*, 57 (2): 86-90.
- Onesi, S.O. and Ignatius, U.E. 2014. Metabolic syndrome: Performance of five different diagnostic criterias. *Indian journal of endocrinology and metabolism*, 18 (4): 496-501.
- Paula, A.A., Falcão, M.C. and Pacheco, A.G. 2013. Metabolic syndrome in HIV-infected individuals: underlying mechanisms and epidemiological aspects. *AIDS Research and Therapy*, 10 (32):1-8.
- Rosolova, H., and Nussbaumerova, B. 2011. Cardio-metabolic risk prediction should be superior to cardiovascular risk assessment in primary prevention of cardiovascular diseases. *EPMA Journal*, 2 (2011):15-26.
- Salvatore, M., Kristian, B.F., Jacques, G., Lawrence, J. P. Louise, P. Paul, R. Stéphane, L.S. Ernesto, and J.E. Mark. 2010. The Metabolic Syndrome and Cardiovascular Risk A Systematic Review and Meta-Analysis. *Journal of American College of Cardiology*, 56 (14): 1113-1132.
- Samaras, K., H., Wand, M., Law, S., Emery, D. Cooper, and Carr, A. 2007. Prevalence of metabolic syndrome in HIV-infected patients receiving highly active antiretroviral therapy using International Diabetes Foundation and Adult Treatment Panel III criteria: associations with insulin resistance, disturbed body fat compartmentalization, elevated C-reactive protein, and hypoadiponectinemia. *Diabetes Care*, 30 (1): 113-119.
- Santos, A.C., and Barros, H. 2007. Impact of metabolic syndrome definitions on prevalence estimates: a study in a Portuguese community. *Diabetes and Vascular Disease Research*, 4 (4): 320-327.
- Sobieszczyk, M.E., Hoover, D.R., Anastos, K., Mulligan, K., Tan, T., Shi, Q., Gao, W. 2008. Prevalence and predictors of metabolic syndrome among

- HIV-infected and HIV-uninfected women in the Women's Interagency HIV Study. *Journal of Acquired Immune Deficiency Syndrome*, 48 (3): 272-280.
- Sweet, D.E. 2005. Metabolic complications of antiretroviral therapy. *Topics in HIV Medicine*, 13 (2): 70-74.
- Syed, F.F., and Sani, M.U. 2013. Recent advances in HIV-associated cardiovascular diseases in Africa. *Heart*, 99 (16): 1146-1153.
- Tesfaye, D.Y., Kinde, S., Medhin, G., Megerssa, Y.C., Tadewos, A., Tadesse, E. and Shimelis, T. 2014. Burden of metabolic syndrome among HIV-infected patients in Southern Ethiopia. *Diabetes and Metabolic Syndrome: Clinical Research and Reviews*, 8 (2): 102-107.
- Todowede, O.O., Mianda, S.Z. and Sartorius, B. 2019. Prevalence of metabolic syndrome among HIV-positive and HIV-negative populations in sub-Saharan Africa: a systematic review and meta-analysis. *Systematic reviews*, 8 (4): 1-17.
- Wand, H., Calmy, A. Carey, D.L. Samaras, K. Carr, A., Law, M.G. Cooper, D.A. Emery, S. and Committee, I.T.I.C. 2007. Metabolic syndrome, cardiovascular disease and type 2 diabetes mellitus after initiation of antiretroviral therapy in HIV infection. *Acquired Immune Deficiency Syndrome*, 21 (18): 2445-2453.
- World Health Organization. 2010. Chronic diseases and health promotion: stepwise approach to surveillance (STEPS). *Geneva, Switzerland*. <https://www.who.int/ncds/surveillance/steps/en/>
- World Health Organization. 2011. Global database on body mass index. *PrFont34Bin0BinSub0Frac0Def1Margin0Margin0Jc1Indent1440Lim0Lim1* <http://apps.who.int/bmi/index.jsp>.
- Wu, P.Y., Hung, C.C., Liu, W.C., Hsieh, C.Y., Sun, H.Y., Lu, C.L. 2012. Metabolic syndrome among HIV-infected Taiwanese patients in the era of highly active antiretroviral therapy: prevalence and associated factors. *Journal of Antimicrobial Chemotherapy*, 67 (4): 1001-1009.

