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Research Article

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Lipid Profiles, Cardiovascular Disease Risk and Dyslipidemia in HIV Positive Patients on HAART at Machakos Level Five Hospital, Machakos County

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Abstract

This study determined the lipid profiles, dyslipidemia and cardiovascular disease risk as well as their associated risk factors in patients who are positive for the human immunodeficiency virus on antiretrovirals. The study adopted a cross-sectional design. Blood samples were analyzed to determine lipid profiles and dyslipidemia. Framingham Risk Score was used to determine cardiovascular disease risk. Descriptive statistics, Pearson's Chi- Square test, bivariate and multivariable logistic regression analyses were performed. A p -value of ≤0.05 with corresponding 95% confidence interval was considered statistically significant. Participants using Protease Inhibitors were four times more likely to have a high Total Cholesterol to High Density Lipoprotein cholesterol ratio compared to those using Non- Nucleoside Reverse Transcriptase Inhibitors (OR =4.19, 95% CI: 1.03 - 17.02) p<0.05. Based on the Framingham risk score, 71.2%, 18.5%, 9.8% and 0.5% participants had low, moderate, moderately high and high cardiovascular disease risk respectively. Age, high-density lipoprotein, smoking and systolic pressure were significantly associated with a high Framingham Risk Score (p<0.001). Gender and duration on antiretrovirals were also significantly associated with high cardiovascular risk (p= 0.001). The overall prevalence of dyslipidemia was 74.5%. Age, systolic blood pressure and hypertension were significantly associated with dyslipidemia (p=0.005, p=0.049 and p<0.001) respectively. Gender, age, systolic pressure, hypertension, smoking and history of cardiovascular disease were significantly associated with cardiovascular disease risk (P= <0.001). The study offered information that will inform the policy makers on better approaches to employ in addressing the health outcomes for people living with the Human Immunodeficiency Virus under treatment with antiretrovirals.

Keywords: Dyslipidemia, Integrase Inhibitor, Lipodystrophy, Metabolic Syndrome, Non-Nucleoside Reverse Transcriptase Inhibitor, Nuceloside Reverse Transcriptase Inhibitor, Protease Inhibitor

1. Introduction

This study determined the lipid profiles, prevalence of dyslipidemia and the likelihood of developing cardiovascular disease (CVD) as well as the risk factors associated with dyslipidemia and CVD in patients who are positive for the human immunodeficiency virus (HIV) on antiretrovirals (ARVs).

The long-term use of HAART regimens has triggered concerns over dyslipidemia and CVD risk factors. Despite, the benefits of HAART for patients with HIV, the challenge of dyslipidemia and CVD risk factors can easily become a health care burden both in practice and economic-wise especially in developing countries such as Kenya. The mortality rate is high for HIV positive people suffering from CVD and related non-communicable conditions.

Studies have shown that one of the toxicities associated with Lopinavir/ritonavir (LPV/r) is dyslipidemia. Additionally, it is associated with risk factors to cardiovascular disease (CVD) such as diabetes and obesity, the same study shows that prolonged exposure to zidovudine (AZT) causes lipodystrophy, a severe form of dyslipidemia [1]. Patients with HIV who were taking the HAART drug combinations recommended by WHO showed a concerningly high proportion of abnormal lipid profiles [2]. The global occurrence of dyslipidemia among HIV-positive patients on HAART is estimated to be about 20 to 80% [3]. In China, a study of 64 HIV positive patients on HAART medication found an incidence rate of 92.2% with low HDL -c being associated with 54.7% of the HIV cases on HAART [4]. In one study, a large percentage of HIV-infected patients were diagnosed with metabolic syndrome (MetS) as a result of HAART regimens, particularly those that include

protease inhibitors, which may raise their possibility of cardiovascular disease [5].

In people living with HIV, the metabolic syndrome, a collection of risk factors for cardiovascular disease, is becoming more prevalent; however, there is a paucity of information on the incidence of MetS and the contribution of antiretroviral therapy (ART) as a risk factor in sub-Saharan Africa [6]. In Western Kenya, a study to determine the prevalence and risk factors for MetS in HIV-infected persons who were both on ART and ART-naïve who did not already have cardiometabolic problems, the prevalence of MetS was the same in both the ART-experienced (16.9%) and ART-naive (15.2%) groups [6]. However, patients who had received ART showed higher rates of raised fasting blood glucose and decreased rates of low high-density lipoprotein cholesterol [6]. In another study carried out in Kenya at Kenyatta National Hospital on prevalence of dyslipidemia and dysglycaemia in HIV positive people, the prevalence of dyslipidemia was 63.1% whereas risk factors to cardiovascular disease remained low [7].

In Machakos County, Kenya, high numbers of HIV infections have been reported. Most HIV positive patients at Machakos level V hospital are diagnosed with hypertension and diabetes after commencing HAART, both of which increase one's risk to CVD. Data on the prevalence of CVD and dyslipidemia at the county is still scarce. Also, data on the CVD risk factors associated with patients on HAART using Framingham risk score in Kenya remains limited. A study was done to investigate prevalence of dyslipidemia and dysglycaemia in HIV positive patients in 2008 at the Kenyatta National Hospital. Due to the increasing rates of HIV infections, more people have been enrolled on HAART. It is necessary to obtain the most recent data on dyslipidemia prevalence.

Thus, this study identified lipid profiles, dyslipidemia and cardiovascular risk in HIV positive people on HAART as well as risk factors associated with dyslipidemia and CVD. Data obtained from this study highlighted how the use of certain highly active antiretroviral therapy (HAART) regimens increases the occurrence of dyslipidemia and CVD risk. The study's findings also generated information on the potential risk factors for dyslipidemia and cardiovascular disease among people living with HIV on HAART. This will inform treatment guidelines and promote development of effective intervention strategies focused on better antiretrovirals combinations thus minimizing drug toxicity. Furthermore, it will aid in prevention, management and control of dyslipidemia and cardiovascular disease in HIV positive people on HAART.

2. Materials and Methods

2.1. Study Design

A cross-sectional study design was conducted to determine the lipid profiles, cardiovascular disease risk and dyslipidemia among HIV positive patients on HAART at Machakos Level V hospital from July to October 2022.

2.2. Study Site and Sample Collection

The study was carried out at Machakos Level 5 Hospital Kenya. The hospital is located at 1°31'25.6" S37°15'58.7" E in Machakos town in Machakos county, Kenya. According to Ministry of Health, the hospital is the county's referral facility, serves an average of 400 patients weekly in the comprehensive care clinic. It provides services to residents of Machakos County as well as the neighboring counties. The participants' socio-demographic information was collected using a structured questionnaire. Blood samples of 4 milliliters was collected from each participant after an overnight fast through the venipuncture technique and stored in the gold top vacutainer at (2-8) °c for transportation.

2.3. Sampling Technique

Systematic sampling technique was adopted among HIV-positive patients on HAART. The first patient was randomly selected on the first clinic within the study period. The study participants were HIV –positive patients aged 20 years and above who were on antiretrovirals for not less than 3 months. Participants who did not consent to the study, had been diagnosed with CVD and for females who were pregnant were excluded from the study.

2.4. Screening of Dyslipidemia and Cardiovascular Risk

Collected blood was centrifuged at 3000revolutions/minute for 4 minutes and serum obtained was used to assay for lipid profile. Lipid panel measurements were obtained using HumaStar 600 after running calibration and controls. This analyzer measured triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) levels and total cholesterol (TC) levels. The Friedewald formula was used to measure the low-density lipoprotein cholesterol (LDL-C) levels [8]. The Framingham risk score was used to determined cardiovascular risk according to six coronary risk factors: age, sex, total cholesterol, high density lipoprotein, smoking habits, and systolic blood pressure based on National Cholesterol Education Program – Adult Treatment Panel III guidelines.

Dyslipidemia was defined as TC≥200 mg/dl, TG≥150 mg/dl, LDL-C≥130 mg/dl, HDL-C<40 mg/dl, and TC/HDL-C ratio of ≥5 according to the United States National Cholesterol Education Program, Adult Treatment Panel (NCEP-ATP) III guidelines [9]. Total Cholesterol/HDL ratio of > 5.0 in men and >4.5 in women, LDL/HDL ratio of >3.5 in men and >3.0 in women were considered elevated [10]. Triglycerides to HDL -c ratio of <2 was considered normal [11].

2.5. Statistical Analysis

The data was analyzed using the statistical packages for social sciences version 28 and presented in tables. Descriptive statistics (percentages and frequencies), Pearson's Chi- Square, bivariate and multivariate logistic regression analysis were done. At 95% level of significance, observed difference was considered to be significant with a p-value of ≤ 0.05.

2.6. Quality Control

The questionnaire's validity and content were maintained under the supervision of the principal investigator and clinical officers working at the comprehensive care clinic. Prior to processing

samples for laboratory analysis, the chemistry analytical equipment underwent routine calibration and quality control in accordance with laboratory protocols. The controls for cholesterol, triglycerides and HDL -c were run daily. The calculated value was compared to the known value, and the Standard Deviation Index (SDI) was calculated. Only tests with values within ± 2 SDI were considered [12].

2.7. Ethical Approval

Ethical approval was obtained from Kenyatta University Ethical Review Committee (KU-ERC) ref no. P154/26876/2019. A research permit was obtained from National Commission for Science, Technology, and Innovation (NACOSTI) ref no. 741593. Permission to conduct this study and any other information from the participants were obtained from Machakos Level V Hospital ref no. MKS/DHES/RSCH/VOL1/155. All participants were only admitted to the study after offering informed consent. No medical services were denied from participants who do not consent to the study. All study participants received their results during subsequent CCC visits.

3. Results

3.1. Socio – Demographic Characteristics of the Study Participants

A total of 406 HIV positive patients on HAART were included in the study. The demographic characteristics that were investigated include gender, age, education level, marital status and body mass index. Majority of patients, 290 (71.4%) were female while 116 (28.6%) were male. The median age of the respondents was 46 interquartile range (IQR: 38 – 55) years. More than half, 224 (55.2%) were aged between 41 to 59 years, 100 (24.6%) were aged between 25 to 40 years, 59 (14.5%) were aged ≥60 years while 23 (5.7%) of the patients were aged ≤24 years. The education level of the study population was also assessed in this study. The findings showed that 180 (44.3%) had primary or lower level of education, 167 (41.1%) had secondary level education while 59 (14.5%) of the study respondents had tertiary level education. Analysis of marital status revealed that 217 (53.4%) of the patients were single while 189 (46.6%) were married. The findings showed that the median body mass index score was 24.4 (IQR: 21.2 – 28.3). Almost half of the study population, 197 (48.5%) had normal BMI, 27 (6.7%) were underweight, 114 (28.1%) were overweight and 68 (16.7%) were obese as shown in Table 1.

DEMOGRAPHIC FACTORS	FREQUENCY (N)	PERCENT
GENDER		
MALE	116	28.6
FEMALE	290	71.4
AGE (MEDIAN, IQR) YEARS	46(38 - 55)	
<=24 YEARS	23	5.7
25 - 40 YEARS	100	24.6
41 - 59 YEARS	224	55.2
>=60 YEARS	59	14.5
MARITAL STATUS		
SINGLE	217	53.4
MARRIED	189	46.6
EDUCATION LEVEL		
PRIMARY OR LOWER LEVEL	180	44.3
SECONDARY	167	41.1
TERTIARY	59	14.5
OCCUPATION		
UNEMPLOYED	76	18.7
EMPLOYED	68	16.7
SELF EMPLOYED	262	64.5
BMI (MEDIAN, IQR)	24.4(21.2 - 28.3)	
NORMAL	197	48.5
UNDERWEIGHT	27	6.7
OVERWEIGHT	114	28.1
OBESE	68	16.7
CIGARETTE SMOKING		

YES	22	5.4
NO	384	94.6

IQR: Interquartile range, **BMI:** Body mass index

Table 1: Demographic Characteristics of HIV Positive Patients on HAART at Machakos Level V Hospital

3.1.1. Medical History and Clinical Characteristics of the Study Participants

The clinical characteristics that were investigated include history of hypertension, history of cardiovascular disease, systolic pressure, diastolic pressure, duration of ARV drug use and treatment regimens utilized. The study showed that 62 (15.3%) of the respondents had history of hypertension while 344 (84.7%) did not have history of hypertension whereas 28 (6.9%) of the study population had history of cardiovascular disease with 378 (93.1%) not having history of cardiovascular disease. Twenty-two, 22 (5.4%) patients had history of cigarette smoking while majority 384 (94.6%) did not have history of cigarette smoking. A majority of the study participants, 337 (83%) had normal blood pressure (BP) while 69 (17%) were hypertensive.

The duration on HAART of the study population ranged from 6months- 20 years. The results showed that the median ARV drug use was 9 (IQR: 5 – 13) years with the majority 299 (73.6%) of the participants having used HAART for more than 5 years.

According to the HAART regimens, 378 (93.1%) were on first line regimen while the least number of patients; 28 (6.9%) patients were on second line regimen. The findings revealed that majority of the study population, 364 (89.7%) were on TDF/3TC/DTG, 13 (3.2%) of the patients were on AZT/3TC/ATV/r, 6 (1.5%) were on TDF/3TC/EFV. Further, 3 (0.7%) of the patients were on ABC/3TC/DTG and 2 (0.5%) were on ABC/3TC/ATV/r as shown in Table 2.

MEDICAL HISTORY AND CLINICAL FACTORS	FREQUENCY (N)	PERCENT (%)
HISTORY OF HYPERTENSION		
YES	62	15.3
NO	344	84.7
HISTORY OF CARDIOVASCULAR		
YES	28	6.9
NO	378	93.1
SYSTOLIC BLOOD PRESSURE		
≥140 MMHG	69	17.0
<140 MMHG	337	83.0
DIASTOLIC BLOOD PRESSURE		
≥90 MMHG	69	17.0
<90 MMHG	337	83.0
DURATION OF ARV DRUG USE (MEDIAN, IQR)YEARS	9(5 -13)	
< 5 YEARS	90	22.2
5 – 10 YEARS	149	36.7
> 10 YEARS	167	41.1
HAART TREATMENT LINE		
FIRST LINE	377	92.9
SECOND LINE	29	7.1
HAART REGIMEN TYPE		
ABC/3TC/ATV/R	2	0.5
ABC/3TC/DTG	3	0.7
AZT/3TC/ATV/R	13	3.2
AZT/3TC/DTG	1	0.2
AZT/3TC/LPV/R	1	0.2
AZT/3TC/NVP	1	0.2

AZT3TC/LPV/R	1	0.2
D4T/3TC/NVP	1	0.2
TDF/3TC/ATV/R	12	3.0
TDF/3TC/DTG	364	89.7
TDF/3TC/EFV	6	1.5
TDF/3TC/NVP	1	0.2

ARV: Antiretroviral, **IQR:** Interquartile range, **HAART:** Highly active antiretroviral therapy, **ABC:** Abacavir, **3TC:** Lamivudine, **ATV/r:** Atazanavir/ritonavir, **DTG:** Dolutegavir, **AZT:** Azidothymidine, **LPV/r:** Lopinavir/ritonavir, **D4T:** Stavudine, **NVP:** Nevirapine, **TDF:** Tenofovir disoproxil fumarate, **EFV:** Efavirenz

Table 2: Medical History and Clinical Characteristics of HIV Positive Patients on HAART at Machakos Level V Hospital

3.2. Lipid Profiles According to HAART for HIV-Positive Patients on HAART at Machakos Level V Hospital

The findings showed that TC/HDL ratio was significantly associated with antiretroviral regimens. Those who were using PI- based regimen were four times more likely to have a high ratio compared to those using NNRTI- based regimen (OR =4.19), 95% CI:1.03 - 17.02 p<0.05 as shown in Table 3 below.

	HIGH N (%)	LOW N (%)	OR (95%CI)	P-VALUE
TC				
INSTI	108(91.5)	260(90.3)	0.30(0.04 - 2.44)	0.26
PI	9(7.6)	20(6.9)	0.28(0.03 - 2.57)	0.259
NNRTI	1(0.8)	8(2.8)	Ref	
TG				
INSTI	139(88.0)	229(92.3)	2.06(0.544 - 7.80)	0.288
PI	14(8.9)	15(6.0)	1.34(0.30 - 6.02)	0.703
NNRTI	5(3.2)	4(1.6)	Ref	
HDL				
INSTI	161(87.5)	207(93.2)	1.61(0.43 - 6.08)	0.485
PI	18(9.8)	11(5.0)	0.76(0,17 - 3.47)	0.271
NNRTI	5(2.7)	4(1.8)	Ref	
LDL				
INSTI	93(92.1)	275(90.2)	0.85(0.17 - 4.14)	0.835
PI	6(5.9)	23(7.5)	1.10(0.18 - 6.70)	0.922
NNRTI	2(2.0)	7(2.3)	Ref	
TC/HDL				
INSTI	119(86.9)	249(92.6)	2.83(0.59 - 13.63)	0.194
PI	12(8.8)	17(6.3)	4.19(1.03 - 17.02)	0.046
NNRTI	6(4.4)	3(1.1)	Ref	
TG/HDL				
INSTI	275(89.3)	93(94.9)	1.18(0.24 - 5.80)	0.835
PI	26(8.4)	3(3.1)	0.40(0.06 - 2.91)	0.368
NNRTI	7(2.3)	2(2.0)	Ref	
LDL/HDL				
INSTI	100)88.5)	268(91.5)	3.35(0.88 - 12.73)	0.076
PI	8(7.1)	21(7.2)	3.28(0.70 - 15.41)	0.132

NNRTI	5(4.4)	4(1.4)	Ref	

TC: Total cholesterol, **TG:** Triglycerides, **HDL:** High density lipoprotein, **LDL:** Low density lipoprotein, **PI:** Protease inhibitor, **INSTI:** Integrase inhibitor, **NNRTI:** Non- nucleoside reverse transcriptase inhibitor, **OR:** Odds ratio

Table 3: Lipid Profiles According to HAART for HIV-Positive Patients on HAART at Machakos Level V Hospital

3.3. The Framingham Risk Score Among HIV –Positive Patients on HAART at Machakos Level V Hospital

The study findings showed that based on the Framingham risk score, 289 (71.2%) had low cardiovascular risk, 75 (18.5%) had moderate risk, 40 (9.8%) of the respondents had moderately high cardiovascular risk while 2 (0.5%) had high cardiovascular risk as shown in Table 4.

FRAMINGHAM RISK SCORE	FREQUENCY	PERCENT
LOW	289	71.2
MODERATE	75	18.5
MODERATELY HIGH	40	9.8
HIGH	2	0.5

Table 4: The Framingham Risk Score Among HIV Positive Patients on HAART at Machakos Level V Hospital

3.3.1 Association Between Patient Characteristics and Risk of Cardiovascular Disease

The results established that those who were aged between 25 – 40 years (AOR =37.11, 95% CI:10.12 – 140.16), p<0.001, 41– 59 years, (AOR =31.01, 95% CI:9.04 – 140.16), p<0.001 and those aged ≥60 years (AOR=9.75, 95% CI:7.14 – 31.74), p<0.001 were more likely to have high FRS compared to those aged ≤24 years. Male patients were 3.4 times more likely to have high FRS risk compared to female patients, (AOR =3.44, 95% CI:1.67 – 8.09), p =0.001.Those who had high HDL were 8.2 times more likely to have high FRS risk, (AOR =8.23, 95% CI:3.92 – 17.260), p<0.001. Respondents who were cigarette smokers were six times more likely to have high FRS risk compared to those who non-cigarette smokers, (AOR= 6.80, 95% CI:1.53 – 31.25), p<0.001.

The findings also revealed that those who had less than five years of disease were five times more likely to have high FRS risk compared to those who had duration of disease for more than 10 years, AOR = 5.17, 95% CI:1.94 – 13.79, p =0.001. Patients who had systolic of ≤140 mmHg were 30 times more likely to have high risk compared to those who had <140 mmHg, AOR =30.16, 95% CI:12.43 – 73.18, p<0.001 as shown in Table 5.

FACTORS	FRS RISK		OR (95%CI)	P-VALUE	AOR (95%CI)	P-VALUE
	High risk n (%)	Low risk n (%)				
AGE						
≤4 YEARS	1(0.9)	22(7.6)	Ref		Ref	
25 - 40 YEARS	8(6.8)	92(31.8)	3.62(1.99 - 6.59)	<0.001	37.11(10.12 - 140.16)	<0.001
41 - 59 YEARS	71(60.7)	153(52.9)	19.34(7.91 - 47.32)	<0.001	31.01(9.04 - 106.34)	<0.001
≥60 YEARS	37(31.6)	22(7.6)	37.0(4.66 - 293.90)	0.001	9.75(4.08 – 23.30)	<0.001
GENDER				<0.001		
MALE	57(48.7)	59(20.4)	3.70(2.33 - 5.88)		3.44(1.67 - 7.09)	0.001
FEMALE	60(51.3)	230(79.6)	Ref		Ref	
TC						
YES	41(35.0)	77(26.6)	1.49(0.94 - 2.35)	0.093	1.43(0.72 - 2.85)	0.313
NO	76(65.0)	212(73.4)	Ref		Ref	
HDL						
HIGH	75(64.1)	109(37.7)	2.95(1.89 - 4.61)	<0.001	8.23(3.92 - 17.26)	<0.001
LOW	42(35.9)	180(62.3)	Ref		Ref	
CIGARETTE SMOKING						
YES	19(16.2)	3(1.0)	18.48(5.35 - 63.81)	<0.001	6.80(1.53 - 31.25)	<0.001
NO	98(83.8)	286(99.0)	Ref		Ref	
DURATION ON HAART						

LESS THAN 5 YEARS	19(16.2)	71(24.6)	2.15(1.19 - 3.90)	0.012	5.17(1.94 - 13.79)	0.001
5 - 10 YEARS	37(31.6)	112(38.8)	1.74(1.07 - 2.84)	0.026	1.78(0.87 - 3.64)	0.113
>10 YEARS	61(52.1)	106(36.7)	Ref		Ref	
SYSTOLIC PRESSURE						
≤140 MMHG	51(43.6)	19(6.6)	10.98(6.08 - 19.84)	<0.001	30.16(12.43 - 73.18)	<0.001
<140 MMHG	66(56.4)	270(93.4)	Ref		Ref	

Reference category (Ref) = category of the independent variable which each other category is compared.
Low risk = participants having low risk of CVD according to FRS analysis.
High risk = participants having moderate, moderately high and high risk of CVD according to FRS
FRS: Framingham risk score, **OR**: Odds ratio, **AOR**: Adjusted odds ratio, **TC**: Total cholesterol, **HDL**: High density lipoprotein cholesterol, **HAART**: Highly active antiretroviral therapy

Table 5 : Association Between Patient Characteristics and Risk of Cardiovascular Disease

3.4. The Prevalence of Dyslipidemia Among HIV Positive Patients on HAART at Machakos Level V Hospital

The prevalence of dyslipidemia among HIV positive patients on HAART at Machakos level V hospital was 74.5% (n =301), 95% CI: 69.6% – 78.8% as shown in Figure 1.

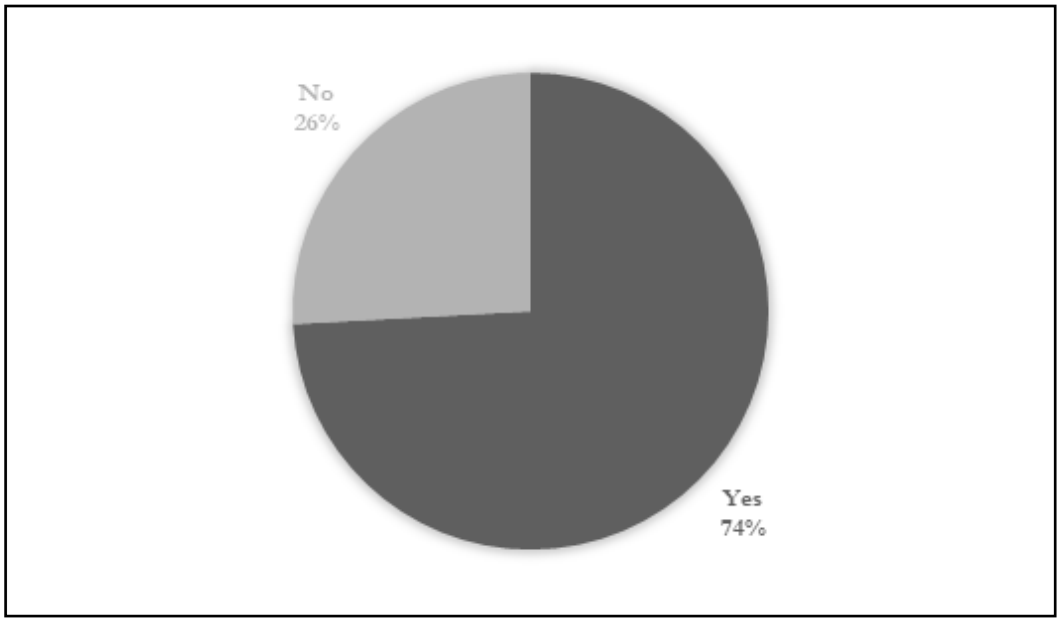

Figure 1: The Prevalence of Dyslipidemia Among HIV Positive Patients on HAART

The prevalence of dyslipidemia according to patient's characteristic was analyzed as shown in table 6. In investigating presence of hypertension, 84.6% of those who were hypertensive had dyslipidemia, with 55 out of 65 of hypertensive patients having dyslipidemia while the prevalence of dyslipidemia was 72.1% with 246 out of 341 participants who had normal BP. There was significant association between systolic pressure and dyslipidemia (x^2 = 9.19, df = 1, p =0.002) as well as diastolic pressure and dyslipidemia (x^2= 4.27, df = 1, p =0.049). Age, gender, BMI, family history of CVD, duration on HAART and antiretroviral regimen were not significantly associated with dyslipidemia.

FACTORS	DYSLIPIDEMIA		P-VALUE
	Yes n (%)	No n (%)	
AGE			
≤24 YEARS	13(56.5)	10(43.5)	
25 - 40 YEARS	78(78.0)	22(22.0)	0.262
41 - 59 YEARS	163(72.8)	61(27.2)	

≥60 YEARS	47(79.7)	12(20.3)	
GENDER			
MALE	88(75.9)	28(24.1)	0.707
FEMALE	213(73.4)	77(26.6)	
BMI			
NORMAL	145(73.6)	52(26.4)	
UNDERWEIGHT	17(63.0)	10(37.0)	0.408
OVERWEIGHT	85(74.6)	29(25.4)	
OBESE	54(79.4)	14(20.6)	
SYSTOLIC PRESSURE			
>=140 MMHG	62(88.6)	8(11.4)	0.002
<140 MMHG	239(71.1)	97(28.9)	
DIASTOLIC PRESSURE			
>=90 MMHG	58(84.1)	11(15.9)	0.049
<90 MMHG	243(72.1)	94(27.9)	
HYPERTENSION			
YES	55(84.6)	10(15.4)	0.044
NO	246(72.1)	95(27.9)	
CIGARETTE SMOKING			
YES	15(68.2)	7(31.8)	0.616
NO	286(74.5)	98(25.5)	
HISTORY OF CVD			
YES	20(71.4)	8(28.6)	0.823
NO	281(74.3)	97(25.7)	
DURATION OF ARV DRUG USE			
LESS THAN 5 YEARS	66(73.3)	24(26.7)	
5 – 10 YEARS	103(69.1)	46(30.9)	0.129
>10 YEARS	132(79.0)	35(21.0)	
TREATMENT LINE			
FIRST LINE	278(73.7)	99(26.3)	0.661
SECOND LINE	23(79.3)	6(20.7)	
HAART REGIMEN			
PI			
YES	23(79.3)	6(20.7)	0.661
NO	278(73.7)	99(26.3)	
INSTI			
YES	269(73.1)	99(26.9)	0.173
NO	32(84.2)	6(15.8)	
NNRTI			
YES	9(100)	0	1.00
NO	292(74.1)	105(25.9)	

CVD: Cardiovascular disease, **BMI:** Body mass index, **ARV:** Antiretrovirals, **HAART:** Highly active antiretroviral therapy, **PI:** Protease inhibitor, **INSTI:** Intergrase inhibitor, **NNRTI:** Non- nucleoside reverse transcriptase inhibitor

Table 6: Prevalence of Dyslipidemia According to Patient Characteristics

3.4.1. Frequency of Dyslipidemia in HIV Infected Patients

The findings established that there was major difference in TC between female (78%) and male (22%) with a difference of 56%. In assessing under mixed dyslipidemia, there was major difference in TC + LDL between female 78.5% and male 21.5% participants with 57% difference. In assessing three abnormalities, there was greater difference in TC + TG + LDL between female 78.7% and male patients 29.4% representing 57.4% difference. The findings also showed that there was higher rate of dyslipidemia in female patients (70.8%) compared to male patients (29.2%) with a difference of 41.6% as shown in Table 7.

LIPID ABNORMALITY	FEMALE N (%)	MALE N (%)	DIFFERENCE (%)	TOTAL N (%)
NO LIPID ABNORMALITY	77(73.3)	28(26.7)	46.6	105(25.9)
ISOLATED DYSLIPIDEMIAS				
ONE ABNORMALITY				
TC	92(78.0)	26(22.0)	56.0	118(29.1)
TG	114(72.2)	44(27.8)	44.4	158(38.9)
HDL	122(66.3)	62(33.7)	32.6	184(45.3)
LDL	78(77.2)	23(27.8)	44.4	101(24.9)
TC/HDL RATIO	84(70.6)	35(29.4)	41.2	119(29.3)
MIXED DYSLIPIDEMIA				
TWO ABNORMALITIES				
TG + LOW HDL	54(65.1)	29(34.9)	30.2	83(20.4)
LDL+ LOW HDL	32(74.4)	11(25.6)	48.8	43(10.6)
TC + TG	51(77.3)	15(22.7)	54.6	66(16.3)
TC + LDL	73(78.5)	20(21.5)	57.0	93(22.9)
THREE ABNORMALITIES				
TC + TG + HDL	21(67.7)	10(32.3)	35.4	31(7.6)
TC + TG + LDL	37(78.7)	10(21.3)	57.4	47(11.6)
FOUR ABNORMALITIES				
TC + TG + HDL +LDL	16(66.7)	8(33.3)	33.4	24(5.9)
TC + TG + HDL +LDL+TC/ HDL RATIO	16(66.7)	8(33.3)	33.4	24(5.9)
DYSLIPIDEMIA	213 (70.8)	88(29.2)	41.6	301(74.1)

TC: Total cholesterol, **TG:** Triglycerides, **HDL:** High density lipoprotein, **LDL:** Low density lipoprotein

Table 7: Frequency of Dyslipidemia in HIV Infected Patients

3.5. The risk factors associated with dyslipidemia and cardiovascular disease among HIV positive patients on HAART at Machakos level V hospital

3.5.1. The risk factors associated with dyslipidemia among HIV positive patients on HAART

The risk factors associated with dyslipidemia among HIV patients on HAART were analyzed as shown in Table 8. The findings revealed that those who were aged ≥60 years were 4 times likely to have dyslipidemia compared to those aged ≤24 years, with an adjusted odds ratio (AOR) of (AOR =3.61), 95% CI:1.21 – 9.00, p=0.005. Those who had high systolic pressure were two times more likely to have dyslipidemia compared to those with low systolic pressure (<140 mmHg), (AOR =2.41), 95% CI:1.21 – 5.78, p =0.049. Patients who had history of hypertension were three times more likely to have dyslipidemia compared to those without the history of hypertension, (AOR =3.11), 95% CI:1.22 – 7.81, p<0.001 as shown in Table 8.

RISK FACTORS	DYSLIPIDEMIA		OR(95%CI)	P-VALUE	AOR(95%CI)	P-VALUE
	Yes n(%)	No n(%)				
GENDER						
MALE	88(29.2)	28(26.7)	1.14(0.69 - 1.87)	0.616		
FEMALE	213(70.8)	77(73.3)	Ref			
AGE						
≤24 YEARS	13(4.3)	10(9.5)	Ref		Ref	
25 - 40 YEARS	78(25.9)	22(21.0)	1.47(0.73 - 2.95)	0.284	1.37(0.67 - 2.82)	0.387
41 - 59 YEARS	163(54.2)	61(58.1)	1.11(0.50 - 2.44)	0.805	0.97(0.43 - 2.21)	0.946
≥60 YEARS	47(15.6)	12(11.4)	3.01(1.07 - 8.52)	0.038	3.61(1.21 - 9.00)	0.005
BMI						
NORMAL	145(48.2)	52(49.5)	Ref			
UNDERWEIGHT	17(5.6)	10(9.5)	1.38(0.71 - 2.70)	0.341		
OVERWEIGHT	85(28.2)	29(27.6)	2.27(0.85 - 6.03)	0.211		
OBESE	54(17.9)	14(13.3)	1.32(0.64 - 2.71)	0.457		
SYSTOLIC						
≥140 MMHG	62(20.6)	8(7.6)	3.15(1.45 - 6.82)	0.002	2.41(1.21 - 5.78)	0.049
<140 MMHG	239(79.4)	97(92.4)	Ref		Ref	
DIASTOLIC						
≥90 MMHG	58(19.3)	11(10.5)	2.04(1.03 - 4.06)	0.049	1.20(0.55 - 2.60)	0.645
<90 MMHG	243(80.7)	94(89.5)	Ref		Ref	
HYPERTENSION						
YES	55(18.3)	10(9.5)	2.1(1.04 - 4.34)	<0.001	3.11(1.22 - 7.81)	<0.001
NO	246(81.7)	95(90.5)	Ref			
CIGARETTE SMOKING						
YES	15(5.0)	7(6.7)	0.73(0.29 - 1.85)	0.616		
NO	286(95.0)	98(93.3)	Ref			
HISTORY OF CVD						
YES	20(6.6)	8(7.6)	0.86(0.37 - 2.02)	0.823		
NO	281(93.4)	97(92.4)	Ref			
TREATMENT LINE						
FIRST	278(92.4)	99(94.3)	0.73(0.29 – 1.85)	0.166		
SECOND	23(7.6)	6(5.7)	Ref			

Reference category (Ref) = category of the independent variable which each other category is compared.
OR: Odds ratio, **AOR:** Adjusted odds ratio, **BMI:** Body mass index, **CVD:** Cardiovascular disease

Table 8: The Risk Factors Associated with Dyslipidemia Among HIV Positive Patients on HAART

3.5.2 The Risk Factors Associated with Cardiovascular Disease Among HIV Positive Patients on HAART

The likelihood of male patients having CVD was five times higher compared to female patients, AOR =5.24, 95% CI: 2.43 – 11.28, p<0.001. Those who were aged 25 to 40 years, AOR =3.21, 95% CI: 1.11 – 8.31, p<0.001, 41 to 59 years, AOR =5.11, 95% CI: 3.22 – 11.54, p<0.001 and those aged ≥60 years, AOR =6.60, 95% CI: 2.95 – 14.76, p<0.001 had a high risk of CVD compared to those aged ≤24 years (Table 9). Those who had high systolic pressure were 9 times more likely to have CVD compared to those with low systolic pressure, AOR =8.55, 95% CI: 3.49 – 20.96, p<0.001. There was a higher risk of CVD among patients with history of hypertension, AOR =9.73, 95% CI: 3.45 -27.41, p<0.001, cigarette smoking, AOR =28.13, 95% CI: 5.90 – 56.11, p<0.001 and history of CVD, AOR =20.28, 95% CI:6.07 – 67.76, p<0.001 as shown in Table 9.

	RISK					
	High risk n(%)	Low risk n(%)	COR(95%CI)	P-value	AOR(95%CI)	P-value
GENDER						
MALE	57(48.7)	59(20.4)	3.71(2.33 - 5.88)	<0.001	5.24(2.43 - 11.28)	<0.001
FEMALE	60(51.3)	230(79.6)	Ref		Ref	
AGE						
<=24 YEARS	1(0.9)	22(7.6)	Ref		Ref	
25 - 40 YEARS	8(6.8)	92(31.8)	3.62(2.0 - 6.60)	<0.001	3.21(1.11 - 8.31	<0.001
41 - 59 YEARS	71(60.7)	153(52.9)	19.34(7.91 - 47.32)	<0.001	5.11(3.22 - 11.54)	<0.001
>=60 YEARS	37(31.6)	22(7.6)	37.0(4.66 - 293.90)	0.001	6.60(2.95 - 14.76)	<0.001
BMI						
NORMAL	55(47.0)	142(49.1)	Ref			
UNDER-WEIGHT	7(6.0)	20(6.9)	1.24(0.68 - 2.24)	0.488		
OVERWEIGHT	33(28.2)	81(28.0)	1.37(0.50 - 3.71)	0.54		
OBESE	22(18.8)	46(15.9)	1.17(0.61 - 2.25)	0.629		
SYSTOLIC						
>=140 MMHG	51(43.6)	19(6.6)	10.98(6.08 - 19.84)	<0.001	8.55(3.49 - 20.96)	<0.001
<140 MMHG	66(56.4)	270(93.4)	Ref		Ref	
DIASTOLIC						
>=90 MMHG	39(33.3)	30(10.4)	4.32(2.52 - 7.40)	<0.001	1.09(0.41 -2.92)	0.861
<90 MMHG	78(66.7)	259(89.6)	Ref		Ref	
HISTORY OF HYPERTENSION						
YES	46(39.3)	19(6.6)	9.21(5.08 - 16.69)	<0.001	9.73(3.45 - 27.41)	<0.001
NO	71(60.7)	270(93.4)	Ref		Ref	
HISTORY OF CIGARETTE SMOKING						
YES	19(16.2)	3(1.0)	18.48(5.35 - 63.81)	<0.001	28.13(5.90 - 56.11)	<0.001
NO	98(83.8)	286(99.0)	Ref		Ref	
HISTORY OF CVD						
YES	18(15.4)	10(3.5)	5.07(2.27 - 11.36)	<0.001	20.28(6.07 - 67.76)	<0.001
NO	99(84.6)	279(96.5)	Ref		Ref	
HAART REGIMEN						
INSTI	108(92.3)	260(90.0)	Ref			
PI	7(6.0)	22(7.6)	0.69(0.14 - 3.36)	0.644		
NNRTI	2(1.7)	7(2.4)	0.90(0.15 - 5.36)	0.906		
TC/HDL RATIO						
HIGH	58(49.6)	79(27.3)	2.61(1.67 - 4.08)	<0.001	3.14(1.41 - 9.90)	
NORMAL	59(50.4)	210(72.7)	Ref		Ref	
TG/HDL						

HIGH	100(85.5)	208(72.0)	2.29(1.29 - 4.07)	0.005	1.76(0.71 - 4.36)	0.221
NORMAL	17(14.5)	81(28.0)	Ref		Ref	
LDL/HDL RATIO						
HIGH	46(39.3)	67(23.2)	2.15(1.35 - 3.40)	0.001	1.25(0.39 - 4.07)	0.221
NORMAL	71(60.7)	222(76.8)	Ref		Ref	

Reference category (Ref) = category of the independent variable which each other category is compared.
Low risk = participants having low risk of CVD according to FRS analysis.
High risk = participants having moderate, moderately high and high risk of CVD according to FRS
CVD: Cardiovascular disease, **BMI:** Body mass index, **HAART:** Highly active antiretroviral therapy, **PI:** Protease inhibitor, **INSTI:** Intergrase inhibitor, **NNRTI:** Non- nucleoside reverse transcriptase inhibitor, **COR:** Crudes odds ratio, **AOR:** Adjusted odds ratio, **TC:** Total cholesterol, **TG:** Triglycerides, **HDL:** High density lipoprotein, **LDL:** Low density lipoprotein

Table 9: The Risk Factors Associated with Cardiovascular Disease Among HIV Positive Patients on HAART

4. Discussion

The long-term use of HAART regimens has triggered concerns over dyslipidemia and CVD risk factors. Despite, the benefits of HAART for patients with HIV, the challenge of dyslipidemia and CVD risk factors can easily become a health care burden both in practice and economic-wise especially in developing countries such as Kenya. In this study determined the lipid profiles, prevalence of dyslipidemia and the likelihood of developing cardiovascular disease as well as the risk factors associated with dyslipidemia and CVD in patients who are positive for the human immunodeficiency virus on antiretrovirals.

4.1. Lipid Profiles According to HAAART Regimens

The findings showed that TC/HDL ratio was significantly associated with protease inhibitors. Those who were using PIs were four times more likely to have high ratio compared to those with NNRTIs. It could because the prolonged use of some protease inhibitors has been associated with dyslipidemia and the risk of cardiovascular disease. A similar study reported that participants who switched from PI- based regimens observed a significant decrease in mean TC/HDL ratio however the FRS did not change significantly [13]. These results indicate that the most favourable lipid effect among the investigated antiretroviral switches is achieved by switching from PI/rand EFV to RPV, but there are also significant benefits to switching from PI/r to once-daily INSTI regimens [13]. It may be due to the neutral effect on INSTIs on lipids. In contrast to our finding, in another study participants who adhered to ABC-containing regimens had higher percentages of patients diagnosed with elevated TG levels (61.1%) and TC/HDL ratios (66.7%) [2]. This could be a result of all patients in this study taking first- line regimen antiretrovirals. Furthermore, in another study there were no significant variations in the prevalence of lipid abnormalities between patients on TDF-containing regimens and those on other NRTI-based regimens. The prevalence of lipid abnormalities was not different in individuals receiving NVP versus those receiving an EFV-based regimen [14]. This could be because none of the participants were on PI- based regimen. Moreover, majority of the participants had a normal BMI < 25, were non- smokers and non-alcoholic. Therefore, all these factors reduced the risk of dyslipidemia. The findings in our study also reported that high levels of TC, TG, HDL -c, LDL -c, TG/HDL ratio and LDL/HDL ratio were not significantly associated to HAART regimens but even so, their levels were higher in participants on PI- based regimen as compared to NNRTI- based regimen. This finding was similar to that of a study in China which found that in the group of patients receiving the LPV/r-based treatment, LDL levels were higher than in EFV- based regimen [15]. This could be because most patients were enrolled to LPV/r- based regimen due to its efficient viral suppression. Majority (93.8%) of participants who received initial LPV/r-based regimens experienced virological suppression within the first six months [15]. Atazanavir and darunavir should be the most frequently used protease inhibitors because they have fewer toxic lipid effects and are more tolerable [16]. Low density lipoprotein cholesterol/HDL-C and total cholesterol/HDL-C ratios are key risk factors for cardiovascular disease.

4.2. Framingham Risk Score

The findings revealed that based on the Framingham risk score, majority of the participants 289 (71.2%) had low cardiovascular risk, 75 (18.5%) had moderate risk, 40 (9.8%) of the respondents had moderately high cardiovascular risk while only 2(0.5%) had high cardiovascular risk. This could be because most of the study participants were non-smokers and normotensive. Smoking and high systolic pressure were among factors that were significantly associated with high CVD risk in the current study. In a similar study, the Framingham risk score showed that 8.7 % of participants showed high CVD risk, 23.3 % moderate CVD risk, and 68.0% low CVD risk [17]. These findings could be explained by the young study population. Another study comparing CVD risk among patient HIV positive and HIV negative patients found that 8.7% of the participants had high risk of CVD compared to 2.2% of HIV negative patients [18]. This could be because people living with HIV have a higher prevalence of undetected cardiovascular risk factors, such as hypertension and elevated total cholesterol levels which are associated with antiretrovirals. High total cholesterol and nucleoside reverse transcriptase inhibitor (NRTI)-based ART regimens were associated [19]. The focus on patients with pre-existing conditions such as HIV-positive patients and use of antiretrovirals enabled much of the similarities. In contrast to our findings, a study conducted in Ghana reported that the low, medi-

um, and high risk of CVD as per the Framingham risk score were 41.5%, 28.1% and 30.4% respectively [20]. The high CVD risk in this study could be explained by the fact that CVD risk increased with age and majority of the patients were aged 45 years with a mean age of 54.35 (sd±12.9) years. Studies such as the one conducted in Ghana focused on using hospital records to conduct the study, thus the difference in study designs which could have contributed to contrasting results. These findings have an implication on the need to use alternative tests for CVD risk and make comparisons with the Framingham risk score to make accurate predictions and prescribe appropriate interventions for patients with HIV on HAART.

In our study age, gender, HDL levels, cigarette smoking, duration of ARVs use and systolic blood pressure were significantly associated to high CVD risk. Based on gender, male patients were 3.4 times more likely to have high FRS risk as compared to female patients. This could be explained by the high prevalence of dyslipidemia among male patients, 88 (75.9%) compared to 213 (73.4%) female in the study population. Men were 1.14 times more likely to develop dyslipidemia as compared to women. Similar results were reported in a study carried out in Ethiopia where male gender was the best indicator of the 10-year FRS. Male participants were 96.3% more likely than females to acquire CVD [21]. This could be because men had higher levels compared to women of TC, LDL -c, TG, fasting blood sugar and systolic blood pressure. In contrast to our findings, another study using the Data Collection on Adverse Effects of Anti-HIV Drugs Cohort (DAD) risk equation, metabolic syndrome was linked to an increased risk of cardiovascular disease in HIV-infected patients and females were seven times more likely than males to acquire metabolic syndrome thus a higher risk to CVD [22]. It could be because women satisfy the waist requirements than men, or by biological, hormonal, and environmental factors that are believed to contribute to the occurrence of metabolic syndrome in women. The discrepancies in results could be explained by the difference in sample size which was higher in our study and the type of study. Njongang Vigny et al., carried out a case control study instead of a cross sectional study [22].

The results established that those who were aged between 25 – 40 years, 41– 59 years and those aged ≥60 years were more likely to have high FRS compared to those aged ≤24 years. This could be because age is a major factor in the decline of cardiovascular functionality, which leads to a higher risk of cardiovascular disease (CVD) in the elderly. Functional changes in the hearts of aging people have been identified, including reports of diastolic as well as systolic dysfunction, along with electrical dysfunction, such as the occurrence of arrhythmias [23]. Also, it could be explained by the fact that longer duration on antiretrovirals has been linked to CVD risk factors such as dyslipidemia and hypertension whose prevalence also increases with age. This finding was similar to that of a study done in Cameroon whereby with age the 10-year high CVD risk increased, with 38.80% of those between 56 and 60 years at risk [24]. This could be attributed to the fact that all study participants were 50 years and above. Moreover, the patients had a good adherence of 98.20% to antiretrovirals. Similarly, another study reported that participants over the age of 45 were three times more likely to develop CVD than those under the age of 45 [25]. It could be due to the increased prevalence of hypertriglyceridemia (a form of dyslipidemia) with age.

Our study reported that those who had low HDL cholesterol levels were 8.8 times more likely to have high FRS risk. This could be because high levels of HDL -c which is the healthy cholesterol are known to reduce CVD risk while low levels of HDL are a known to increase CVD risk. Additionally, it could be because the study participants were on antiretrovirals and majority of them were on INSTI- based regimen which are known to lower HDL -c levels. In a similar study low HDL -c levels were common among HIV-positive young people in Sub Saharan Africa who were on dolutegravir based regimen [26]. However, in contrast to other studies, antiretrovirals were associated with a low prevalence for low HDL [27]. It could be because HAART has been associated with higher levels of HDL at first, which then decline over time.

The study found that respondents who were cigarette smokers were 15 times more likely to have high FRS risk compared to those who non-cigarette smokers. This could be explained be the fact that smoking causes vascular dysfunction by reducing nitric oxide (NO) bioavailability, followed by increased expression of adhesion molecules and consequent endothelial dysfunction [28]. Similar findings were reported in another study where dyslipidemia (39.5%), smoking (33.0%) and high blood pressure (19.8%), were among the most common concomitant cardiovascular risk factors [29]. In another study in Indonesia, smoking was one of the common CVD risk factors [17]. These similarities in results could be because smoking is one of the leading causes of cardiovascular disease globally and may be one of the most modifiable risk factors for CVD in HIV-positive patients.

The findings also revealed that patients who had systolic of ≥140 mmHg were 25.9 times more likely to have high risk compared to those who had <140 mmHg. This could be because hypertension is among known CVD risk factors. Also, it could be explained by the fact that majority of the study participants were on INSTI- based regimen. From previous studies INSTI- based regimens have been linked to higher blood pressure when compared to NNRTIs although the mechanism behind this association is unknown [30]. In a similar study, Wu et al., reported that higher systolic blood pressure was independently associated with an atherosclerotic CVD risk score of ≥7.5% in multiple logistic regression [31]. This could be explained by their older age (≥ 40) years and that most participants were current smokers both of which have been linked to high blood pressure. In another study, lower systolic blood pressure was among factors independently associated with low atherosclerotic CVD risk [21]. This could be because the study subjects were on antiretrovirals and they have been associated with high blood pressure.

According to duration on antiretrovirals, those who had used an-

tiretrovirals for less than five years were four times more likely to have high FRS risk compared to those who had used HAART for more than 10 years. This is in contrast to the expectation that longer duration on HAART increases CVD risk. It could be because majority of the study participants used INSTIs which are known to have low toxic effects on lipid levels thus reducing risk of dyslipidemia which is a CVD risk factor. However, these results were similar to other studies in that duration on HAART was not associated with increased CVD risk [29]. In contrast to our findings, in another study viral suppression with combination antiretroviral therapy and long-term treatment was linked to dyslipidemia and a higher risk of pulmonary artery disease [32]. This could be because the study participants were on antiretrovirals and majority were on lamivudine which is a NRTI. According to Juma et al., high total cholesterol and nucleoside reverse transcriptase inhibitor (NRTI)-based ART regimens are associated [19].

In our study, high total cholesterol levels were not significantly associated with a high risk of CVD. This could be explained by the fact that most of the study participants had normal total cholesterol levels as compared to those who had high TC levels. It is also probably because majority of the patients were on INSTI- based regimen. Integrase inhibitors and CCR5 antagonists appear to have low immediate CVD toxicity, in contrast to the related metabolic changes and increased risk of CVD with protease inhibitors (PI) and efavirenz Vos, A. G., & Venter, W. D. F. [33]. Similarly, in another study total cholesterol was associated with low ankle branchial index which is used to check for peripheral artery disease [32]. In contrast to our findings, another study reported that high levels of TC were associated with high CVD risk [34]. This difference in results could be because of the sample size which was large (9704 participants) and the study population which were not HIV positive patients on HAART.

4.3. Prevalence of Dyslipidemia

The study found a high (74.5%) prevalence of dyslipidemia among HIV positive patients on HAART at Machakos level V hospital with those with high cholesterol, triglycerides, LDL, TC/HDL ratio and low HDL at 29.1%, 38.9%, 24.9%, 29.3% and 45.3% respectively. This could be because majority of the study participants had been on HAART for a long duration (more than 5 years). Moreover, it could be attributed to the fact that dyslipidemia is one of the complications associated with antiretroviral drugs such as NNRTIs, NRTIs and PIs. Dyslipidemia in HIV-positive patients on HAART is caused by four mechanisms; inhibiting plasmatic lipoprotein lipase activity, ending the viral subdivision on lipid absorption receptors, LDL receptor-based protein (LRP) and cellular retinoic acid-binding protein 1 (CRABP-1) which increases the levels of liver Apolipoprotein B and prevents the activity of the glucose transporter known as type 4 (GLUT4) [35]. These findings are comparable to those of a study done in China where the prevalence of dyslipidemia was 75.4% with low HDL as the highest (54.4%) lipid abnormality [36]. This could be explained by the fact that long duration of HIV infection is associated with low HDL -c levels. In another study done in Ethiopia the prevalence of dyslipidemia was 74.8% [37]. Longer duration on antiretrovirals and PI-based regimens are significantly associated with dyslipidemia [37].

A similar study conducted at the Kenyatta National Hospital recorded a lower prevalence (63.1%) of dyslipidemia as compared to this study's findings [7]. The study illustrated that high TC was exhibited in 39.2% of patients on HAART, high LDL was noted in 40.8% of participants on HAART, high TG only occurred in 25.6% of participants on HAART, while HDL levels were lower at 14.6% of patients on HAART [7]. This could be attributed to the fact that majority (82%) of the study participants were on lamivudine which is a NRTI. According to Juma et al., high total cholesterol and nucleoside reverse transcriptase inhibitor (NRTI)-based ART regimens are associated [19]. However, in our study low HDL -c was the highest lipid abnormality instead of high total cholesterol. This could be because majority (73.1%) of the study participants were on INSTI- based regimen instead of a NRTI -based regimen.

Another study conducted in Eritrea found the frequency of dyslipidemia to be higher at 86.6% in a sample of 382 patients [2]. The study findings reported that the high TC, high TG, low HDL-cholesterol, and high LDL-cholesterol obtained were 29.1%, 33.2%, 44% and 55.8%, respectively [2]. In this study the highest lipid abnormality was high LDL levels (55.8%) whereas in our study prevalence of high LDL levels was 24.9%. This may be because zidovudine is associated with higher increase in TC and LDL levels as compared to tenofovir. All patients in the Achila et al., study was either using lamivudine (3TC), zidovudine (AZT), tenofovir (TDF), or abacavir (ABC)-based treatment combinations, all of which were first-line combination regimens whereas majority of the study participants in our study were using tenofovir based regimen [2]. Another study in Southern Ethiopia compared the prevalence of dyslipidemia in pre-HAART and HAART HIV- positive patients. The study found that HAART patient had a higher prevalence of 82% while pre-HAART had a frequency of 76.39%. Total cholesterol, HDL, LDL, and TG among HAART and pre-HAART participants were found to be 43.4%: 15.9%, 43.4%: 63.7%, 33.6%: 15%, and 55.8%: 31.0% respectively [38]. Evidently, HIV -positive patients on antiretrovirals have a higher risk to dyslipidemia as opposed to HAART naïve patients.

The similarities with other studies can also be explained by the focus on HIV-positive patients on HAART. Differences noted can also be explained by the study design used in each study. This study was a cross sectional study while Manuthu et al., focused on comparing HIV-positive populations on HAART and HAART-naïve which is a comparative study [7]. These comparisons varied also by the duration of participants on HAART. Also, some differences in our study occurred due to the inclusion of CVD risk factors that have not been included in other studies. As such, the current study prospectively predicted the prevalence of dyslipidemia and CVD concurrently helping to illustrate the risk factors and correlations.

Based on gender, the current study showed that there was higher

prevalence of dyslipidemia among male patients, 88 (75.9%) compared to 213 (73.4%) female. Probably because men were 1.14 times more likely to develop dyslipidemia as compared to women as well as the anatomical differences between male and female. This finding was in contrast to a study on gender heterogeneity in dyslipidemia prevalence where prevalence of dyslipidemia was significantly higher in females than in males [39]. This could be explained by the fact that the study participants in this study were neither HIV positive patients nor patients on antiretrovirals. However, in the current study females were more affected with 213 females having dyslipidemia as compared to only 88 males having dyslipidemia. This could be because majority of the study participants were female. Also, it could be because of the anatomical and hormonal differences between men and women.

Based on age, the study found that the prevalence rate for participants aged ≤24yrs was 56.5%, 25yrs – 40yrs was 78%, 41yrs-59yrs was 72.8% and was highest (79.7%) among those aged ≥60. This may be due to the fact that those who were aged ≥60 years were 4 times likely to have dyslipidemia compared to those aged ≤24 years, with an adjusted odds ratio of (AOR =3.61), 95% CI:1.21 – 9.00, p=0.005. Furthermore, it could be because the rate of metabolism decreases with age thus as one ages the slower it may take for the body to metabolize lipids therefore leading to abnormal levels of lipids in the body. Similar findings were reported in a study done in Western Kenya where adults 50 to 59 years of age, both HIV positive and negative, exhibited a 2-fold higher risk of dyslipidemia compared to those 30 to 39 years of age [40]. Age is highly associated with the high prevalence of participants aged over 60 years since lipid abnormalities increase by age [41]. There is need for regular lipid profile tests for patients above 60 years on HAART treatment to reduce the prevalence and enhance management of dyslipidemia.

The study established a high (79.4%) prevalence of dyslipidemia among participants who were obese. However, there was no statistical significance between BMI and dyslipidemia. The high prevalence of dyslipidemia in obese patients could be because obesity is one of the risk factors of dyslipidemia. Also, it could be due to the fact that the study participants were on antiretrovirals which have been associated with weight gain leading to obesity and dyslipidemia. In a similar study in comparison to normal and underweight patients, the probabilities of dyslipidemia were 2.5 and 15.5 times greater in overweight and obese subjects, respectively [41]. This could have been influenced by physical activity like walking as individuals who walked for less than 150 minutes a week were 1.7 times more likely to have dyslipidemia than their counterparts [41]. The Ministry of Health lists obesity, poor diet, and sedentary life as key risk factors of dyslipidemia, explaining the high rate of the condition in obese and overweight patients [42]. A similar study illustrated that high BMI was associated with hypertriglyceridemia [43]. This could be because hypertriglyceridemia is an indicator of dyslipidemia in obesity.

There was a significant association between hypertension (systolic blood pressure ≥ 140mmHg and diastolic pressure ≥ 90mmHg) and dyslipidemia. A high prevalence of dyslipidemia (84.6%) was recorded in participants with a history of hypertension while 72.1% had normal BP had dyslipidemia. This could probably be due to the fact that hypertension is associated with HIV infection and increase in blood lipid levels. This finding confirms that individuals taking HAART may develop hypertension. This finding is supported by a study in developed nations where use of protease inhibitors increased likelihood of obesity and hypertension, which was measured through BMI and waist circumference [44]. The Ministry of Health guidelines require that HIV patients be subject to hypertension tests before recommending use of HAART since it is a known risk factor alongside dyslipidemia [42]. Similar findings were documented in the Achila et al., study, it was found that those with a prior history of CVD and hypertension had considerably higher total cholesterol levels [2]. One possible explanation for this finding could be because hypertension is one of the risk factors of dyslipidemia.

Moreover, the current results have been supported in Opoku et al., study that reported patients who had history of hypertension were three times more likely to have dyslipidaemia compared to those without the history of hypertension [45]. In another study done in Cameroon after controlling for family history of hypertension, smoking, body mass index (BMI), gender, and alcohol use, HAART was linked to hypertension [46]. This could be because the study population which had the highest prevalence of hypertension were on HAART. However, Angassa, Solomon & Seid, study found no association between dyslipidemia and hypertension [47]. This variation might be due to difference in the study population. For example, the study population in the current study included only HIV- positive patients on antiretrovirals whereas in the Angassa, Solomon & Seid, study the participants were chosen randomly among employees in a wine factory [47].

Based on family history of CVD, prevalence of dyslipidemia was high (74.3%) among those with no family history of CVD as compared to 71.4% among with history of cardiovascular disease. However, there was no statistical significance between the two groups. These findings are in contrast to those of a study done in Eritrea which found that those with a prior history of CVD and hypertension had considerably higher total cholesterol levels [2]. This could be attributed to the fact the current study did not target study participants who had history of CVD but instead it targeted HIV- positive patients on HAART thus the low numbers of those with a prior history of CVD. In another study findings' a positive family history of CVD was related with an increased lipid profile [48]. The variations in these findings could be explained by the clinical characteristics of the study participants which included other CVD risk factors such as type 2 diabetes, cerebrovascular accident and premature coronary artery disease. There is limited data on the association between family history of CVD and dyslipidemia. This warrants for more research to determine a scientific reason behind this finding.

In investigating the line of treatment, the HAART regimen was not statistically associated with dyslipidemia. Nonetheless, the prevalence of dyslipidemia was high (79.3%) among patients on second line treatment as compared to participants on first line treatment (73.7%). This could be due to the fact that PI-based regimens which are second line regimens are significantly associated with dyslipidemia. The primary protein component of triglyceride and cholesterol-rich plasma lipoproteins, nascent apolipoprotein B, is inhibited by protease inhibitor therapy from being degraded by proteasomal enzymes [49]. This finding was similar to that a study which found that compared to those using PI -based regimen, INSTI participants had a lower prevalence of dyslipidemia [35]. Among patients on NNRTIs in the present study, the prevalence of dyslipidemia was 100% with all nine patients on NNRTI having dyslipidemia. This could be in view of the fact that our participants had been on antiretrovirals for a long time (9 years). Also, the presence of both nucleoside and non-nucleoside reverse transcriptase inhibitors; arterial stiffness in HIV-1 patients with metabolic syndrome is worse [50]. A similar study reported that 72% of the participants on pre-HAART treatment had dyslipidemia while those on post-HAART treatment were about 65% [38]. This could be due to the fact that highly active antiretroviral therapy is associated with numerous metabolic side effects in HIV-positive populations. The use of HAART regimens among patients with HIV is associated to dyslipidemia [51].

Based on duration on HAART, there was no significant association between duration on HAART and dyslipidemia. Nevertheless, a high (79%) prevalence of dyslipidemia was among those who had HAART for more than 10 years as compared to those who had use HAART for 5 - 10 years which was 69.1%. This may be due to the prolonged use of antiretrovirals among the study participants as the median ARV drug use was 9 (IQR: 5 – 13) years with the majority 299 (73.6%) of the participants having used HAART for more than 5 years. In a similar study, it was noted that patients with over 10 years on HAART illustrated a prevalence of dyslipidemia at 72% while those on HAART for less than 5 years had a lower occurrence of dyslipidemia at 55% [52]. In another study, patient on HAART between 5 and 10 years illustrated a 27% occurrence of dyslipidemia compared to less than 5 years at 18% [38]. In all the three studies, this current one included there has been an increase in prevalence of dyslipidemia with duration on HAART. These findings affirm that prolonged use of antiretrovirals increases chances of developing dyslipidemia.

Smoking was not statistically significant when associated to dyslipidemia. The prevalence of dyslipidemia was higher in participants who were non-smokers as compared to smokers. The number of non-smokers in this study was more than smokers because the study was not targeting smokers and this could be the reason why prevalence of dyslipidemia was higher in non-smokers. This study' findings were similar to a study where, patients with no smoking habit illustrated a higher occurrence of dyslipidemia at 76% compared to 74.2% on smokers [45]. In the current study participants who were smokers had a high prevalence, 68.2% of dyslipidemia, with 15 out of 22 of participants who were smokers having dyslipidemia while prevalence of dyslipidemia was highest (74.5%) among participants who were non-smokers. This is because marital status, gender, smoking history, HAART duration, and history of CVD were not seen to have huge associations with dyslipidemia.

4.4. Risk Factors Associated with Dyslipidemia and Cardiovascular Disease

Our findings revealed that age, systolic blood pressure and history of hypertension were significantly associated with dyslipidemia. Those who were aged ≥60 years were 4 times likely to have dyslipidemia compared to those aged ≤24 years. This could be attributed to the fact that the rate of metabolism decreases with age thus as one ages the slower it may take for the body to metabolize lipids therefore leading to abnormal levels of lipids in the body. Additionally, it might be because those who were aged ≥60 years had been on antiretrovirals for a longer duration as compared to those aged ≤24 years. This finding was in line with that of another study where 69.4% of people aged 40 and older had at least one form of dyslipidemia and older people >60 years displayed a higher prevalence of metabolic syndrome (which includes dyslipidemia) among the 82.6% of subjects investigated for it [53]. The likelihood of having dyslipidemia increased by 3.61 times, in the older age group (≥40) years [53]. This could have been influenced by the HAART regimen the study participants were on which included TDF, lamivudine and nevirapine. From this study using these drugs increased the odds of obesity and in turn dyslipidemia. Therefore, longer duration on this antiretrovirals could be the reason prevalence of dyslipidemia increased with age. However, previous studies in Iran illustrated that while prevalence of dyslipidemia continued to increase among women as they aged, it increased in men by the fifth decade before decreasing as they aged [54]. These differences could be explained by the geographical locations and the fact that the study participants were not HIV positive patients on antiretrovirals. As such, age is a key determinant of dyslipidemia in HIV positive patients on antiretrovirals.

Those who had high systolic pressure were two times more likely to have dyslipidemia compared to those with low systolic pressure (<140 mmHg). Systolic pressure was significantly associated with dyslipidemia. Patients who had history of hypertension were three times more likely to have dyslipidemia compared to those without the history of hypertension. This could be because of antiretrovirals use which is associated to risk factors of dyslipidemia such as hypertension. Moreover, the link between dyslipidemia and an increased risk of hypertension in this cohort may be caused by a number of pathophysiological mechanisms such as dyslipidemia impairing the endothelial function, reducing baroreflex sensitivity and lowering the distensibility of large elastic arteries. A cohort study of Japanese males of working age discovered that participants who were subjects in the highest quintiles of TC, LDL- C, and non-HDL- C had a considerably higher chance of developing hypertension [55]. This could be explained by the fact that a high-fat diet and insufficient exercise encourage obesity and dyslipid-

emia. In contrast to our finding, a study in Nigeria found that none of the associated risk factors, such as hypertension, HAART usage, or HIV duration, were significantly correlated with the study's high (40.2%) prevalence of dyslipidemia [56]. This could be as a result of the sample's insufficient power to detect these relationships. In HIV patients in the study, none of the factors that were examined predicted dyslipidemia.

This study found no association between gender, BMI, cigarette smoking, history of CVD and HAART regimen with dyslipidemia. This could be due to the sociodemographic and clinical characteristics of the study participants. For instance, majority of the study participant had normal BMI, were non- smokers and had no family history of CVD. Additionally, majority of the study participants were on first line antiretrovirals regimen which included an integrase inhibitor (DTG) instead of second line regimen which included protease inhibitors. This is probably because integrase inhibitors and CCR5 antagonists appear to have low immediate CVD toxicity, in contrast to the related metabolic changes and increased risk of CVD with protease inhibitors (PI) and efavirenz. These findings were in line with those of Kemal et al., study, the same observation was made as marital status, gender, smoking history, HAART duration, and history of CVD were not seen to have huge associations with dyslipidemia [37]. In another study done in Western Kenya both abdominal obesity and overweight status were associated with a higher risk of dyslipidemia: the risk was 2.5 times higher for abdominal obesity than for none, and it was 1.9 times higher for overweight than for normal BMI [40]. This could be explained by other modifiable variables such as vegetable intake, fruit intake and physical active which are known to have an effect on BMI. In contrast to our findings, sex, BMI, waist-to-hip ratio, smoking, the type of HAART regimen used, and duration on antiretrovirals were all associated with dyslipidemia [2]. These variations could be explained by different factors such as abdominal obesity was observed in a high percentage of study's research participants, the understanding that users of tobacco have worse lipid profiles than non-smokers, both in HIV patients and also in the general population and also because there has been an increase in prevalence of dyslipidemia with duration on HAART.

This study found that gender, age, systolic blood pressure, hypertension, smoking and family history of CVD were significantly associated with CVD risk. Based on gender, the likelihood of male patients having CVD was five times higher compared to female patients. One of the reasons for this finding could be because men had a higher prevalence of dyslipidemia (which is a CVD risk factor) as compared to women. Additionally, all smokers in the current study were male and smoking was also one of the CVD risk factors. Also, it could have been due to hormonal differences between men and women. Women in the reproductive age can be protected against atherosclerosis due to estrogen's beneficial effects on the cardiovascular system. By stimulating angiogenesis and vasodilation while reducing reactive oxygen species, oxidative stress, and fibrosis, estrogen mediates its cardioprotective activities [57]. The result is in line a previous study where out of 57 participants 4 had cardiac disorders and all 4 were male [58]. This could have been attributed to the fact that majority of the patients in this study had good adherence to antiretroviral drugs.

In reference to age, those who were aged 25 to 40 years, 41 to 59 years and those aged ≥60 years, had a high risk of CVD compared to those aged ≤24 years. Those who were aged ≥60 years were 6.6 times more likely to get CVD as compared to those who were aged ≤24 years. The increase in CVD risk in relation to age could be explained by the fact that prevalence of dyslipidemia increases with age maybe due to a decrease in the rate of metabolism. According to the previous studies, dyslipidemia is believed to be the most common risk factor for CVD [59]. Furthermore, longer duration on HAART could account for this observation. Human Immunodeficiency Virus infected patients receiving anti-retroviral therapy experience a range of metabolic side effects, including subcutaneous fat loss, visceral fat accumulation, lipodystrophy and dyslipidemia with elevated low-density lipoprotein (LDL) cholesterol and triglycerides which have been linked to early atherosclerosis [60]. Finally, it could be because cardiovascular disease is one of the comorbidities in HIV positive patients as they age and this explains why from the FRS in this study the 2 patients with high CVD risk were more than 60 years old. These findings are in consistent with another study that noted that those over the age of 45 were approximately 9.5 times more likely than those under the age of 45 to experience a CVD incident (medium and high risk) for both HAART naïve and HAART experienced group [25]. This could be because the number of participants who were hypertensive and had high TG levels was higher among participants aged >45 years. Similarly, in another among HIV- positive people aged 40 to 79 years using the FRS, only younger age (40 to 59), female gender, and lower systolic blood pressure were linked to decreased risk for CVD [21]. This could be explained by the fact that majority of the participants were on NNRTI- based regimen which was associated with high CVD risk. In contrast to our findings, another study shows that CVD risk is high between 40- 65 years but tends to decrease above 65 years [61]. The discrepancies could be because participants in this study were not HIV patients on antiretrovirals.

Those who had high systolic pressure were 9 times more likely to have CVD compared to those with low systolic pressure. History of hypertension was also significantly associated with cardiovascular disease. There was a higher risk of CVD among patients with history of hypertension. This could be because of the high prevalence of dyslipidemia recorded in the current study. Those who had high systolic pressure were two times more likely to have dyslipidemia compared to those with low systolic pressure (<140 mmHg). These findings are in line with those of another study where 72% of the patients had hypertension, 153 (61.2%) of the patients had dyslipidemia [62]. Although these patients were not on antiretrovirals, there were other factors which were not considered in the current study such as diabetes mellitus, physical inactivity and unhealthy diet that could have contributed to dyslipidemia and in turn hypertension. Also, the use antiretrovirals could be another reason why some participants in our study had high systolic pressure and

hypertension. Most study participants were on INSTIs. Therefore, this could be explained by the fact INSTIs when compared to NNRTIs have been associated with hypertension. Despite being extremely effective for viral suppression, INSTI-based regimens appear to cause more weight gain and treatment-emergent obesity than non-INSTI-based regimens and may raise the risk of hypertension and other weight-related co-morbidities [63]. In another study participants who received INSTIs had a higher prevalence of hypertension as compared to those who received NNRTIs, but there was no difference in those who received PIs [30]. This could be because majority (3164) of the study participants were on INSTI based regimen. Highly active antiretroviral therapy is associated with numerous metabolic side effects in HIV-positive populations. The use of HAART regimens among patients with HIV is associated to dyslipidemia [51]. In contrast to our findings, another study reported that compared to individuals with optimum blood pressure, young adults with normal blood pressure had a higher risk of cardiovascular events [64]. The differences in the findings could be attributed to the different study design, study population and sample size.

History of cardiovascular disease was significantly associated with cardiovascular disease risk. It is probably because of genetics, someone with family history of CVD is likely to develop cardiovascular disease as compared to someone without family history of CVD. Moreover, it could be because participants who had family history of CVD were on antiretrovirals as well. While antiretrovirals decrease systemic inflammation, which is important for cardiovascular development, they may also be proatherogenic by causing dyslipidemia, body fat redistribution, and insulin resistance [65]. Previous studies have also identified the above factors as risk factors for CVD. Secondary research in the Asian- pacific region reported similar results in that dyslipidemia and a family history of CVD were among factors which elevated the risk of CVD among HIV -positive people by over 20 times [66]. There is limited data on association between family history of CVD and high CVD risk. This observation warrants for more research in this area.

Smoking was significantly associated with cardiovascular disease. There was a higher risk of CVD among patients who were smokers. This could be explained by the fact that the development of atherosclerotic alterations with narrowing of the arterial lumen and production of a hypercoagulable state, which increases the risk of acute thrombosis, are some of the general processes by which smoking causes cardiovascular events [67]. Smoking was also found to be a high predictor of CVD occurrence among participants in previous studies, thus confirming our results. For instance, Grand et al., (2020) reported that dyslipidemia, smoking and high blood pressure were the most common concomitant cardiovascular risk factors. This finding could be because 1 in every 5 of the study participants in the study had a moderate- high CVD risk thus an association between CVD risk factors such as smoking and CVD risk were expected. In a similar study done in Brazil using the FRS, smoking among other factors such as male sex, older age, diabetes, hypertension and metabolic syndrome were related as predictive factors for a higher cardiovascular risk [68]. Due to the association between smoking and increased CVD risk in the current study and previous studies, methods such as smoking cessation should be adopted to manage this risk. Jeong et al., reported that smoking cessation was linked to a lower incidence of fatal stroke and myocardial infarction [69].

In multivariate logistics, the current study found no association between BMI, HAART regimen, lipid profile ratios (TC/HDL, TG/HDL and LDL/HDL) and diastolic blood pressure even though in univariate logistics lipid profile ratios and diastolic blood pressure were significantly associated to CVD risk. This could be due to the clinical characteristics of the study participants. For instance, majority of the study participant had normal BMI and were on first line antiretrovirals regimen which included an intergrase inhibitor (DTG) instead of second line regimen which included protease inhibitors. This is probably because integrase inhibitors and CCR5 antagonists appear to have low immediate CVD toxicity, in contrast to the related metabolic changes and increased risk of CVD with protease inhibitors (PI) and efavirenz. In contrast to our findings Bune et al., found that patients subjected to HAART had a slightly increased incidence of metabolic syndrome which is a risk factor for CVD [70]. Antiretrovirals lead to cardiometabolic toxicity by inducing new cardiovascular risk factors (such as dyslipidemia, weight gain, and insulin resistance) or by worsening existing ones [71].

5. Conclusions

Our findings showed that the TG/HDL ratio was significantly associated with HAART regimen. The study also showed that cardiovascular risk using Framingham risk score is significantly associated with age, gender, low HDL -c levels, high systolic blood pressure, smoking and duration on ARVs but it is not significantly associated with high TC values. Also, the study recorded a high prevalence of dyslipidemia. Out of all HIV -positive patients on HAART at Machakos level V hospital who participated in the study, 74.5% among them had dyslipidemia. This shows that there is need to introduce the lipid profile test as one of the routine tests in HIV positive patients who are on HAART. Dyslipidemia was significantly associated with gender, age, high systolic blood pressure and history of hypertension. Cardiovascular disease was significantly associated with gender, age, high systolic blood pressure, history of hypertension, history of cardiovascular disease and smoking. Body mass index, HAART regimen and diastolic blood pressure did not have any significant association with both dyslipidemia and cardiovascular disease. Further research is recommended on other associated risk factors to dyslipidemia and cardiovascular disease including; how to prevent, treat and manage these risk factors.

6. Limitations

i. The findings in this study may not represent the countrywide health situation as this was a single hospital-based study with a small sample size.

ii. We were not able to exhaust all risk factors to CVD and dyslipidemia such as diabetes.

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