# ASSESSMENT OF RISK FACTORS FOR CARDIOVASCULAR DISEASES AMONG HIV INFECTED PATIENTS ATTENDING MUHIMBILI NATIONAL HOSPITAL CARE AND TREATMENT CLINIC

**Amina Shabani Mgunya**

MMED (Internal Medicine) Disssertation

Muhimbili University of Health and allied Sciences

November 2012

# ASSESSMENT OF RISK FACTORS FOR CARDIOVASCULAR DISEASES AMONG HIV INFECTED PATIENTS ATTENDING MUHIMBILI NATIONAL HOSPITAL CARE AND TREATMENT CLINIC

**By**

**Dr Amina Shaban Mgunya**

**A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences**

**Muhimbili University of Health and Allied Sciences**

**November 2012**

## CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance of dissertation entitled **Assessment of risk factors for cardiovascular diseases among HIV infected patients attending Muhimbili National Hospital Care and Treatment Clinic**

in (Partial) fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences.

_____

**Dr. J.M Lwakatare**

(Supervisor)

Date: _____

## DECLARATION

## AND

## COPYRIGHT

**I,** Amina Mgunya **I declare that this** dissertation **is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.**

Signature ..... Date ……

## ACKNOWLEDMENT

With humility and gratitude I aknowledge all those who made this dissertation into being**.**

My sincere thanks goes to my supervisor Dr J.M Lwakatare for his tiredless supervision of my work from the proposal stage to its completion.

Special thanks goes to Prof Mugusi Principal Investigator of ICORTA for funding this study and also for his valuable comments.

My gratitudes also goes to Prof J Lutale the head of department internal medicine, for her support throught this dissertation work . My thanks are also directed to Dr Nagu my mentor and Dr Shayo for their useful inputs on this work.Special thanks to all the members of department Internal Medicine for their inputs in my dissertation.

Special thanks to Sr Ana Gaspar who assisted me in measurements of fasting blood glucose.

I thank Dr Mpembeni and Dr Moshiro for their assistance in statistical analysis.

My special thanks to my beloved son Jesse for his patience as I had to leave him when he was only six weeks of age for the data collection.Thanks to my husband Mr Robert for his constant support and patience.

## DEDICATION

To Jesse and Jethro our beloved sons,

To Robert Mussa my dear husband for his enduarance and patience.

## ABSTRACT

### Background

Mortality due to cardiovascular disease among HIV patients is a concern in both developed and developing countries. The increased cardiovascular events is suspected to be due to the metabolic complications atributed by HIV virus itself and antiretroviral drugs. The CVD risk factors noted to be increased among HIV patients include dyslipidemia, obesity, hypertension, diabetes,excessive alcohol intake and cigarette smoking. But the data is sparse on the magnitude and distribution of these risk factors among HIV patients in Tanzania.

### Objective

This study was aimed at assesing the risk factors for cardiovascular diseases among HIV infected patients attending Muhimbili National Hospital Care and Treatment Clinic.

### Methods

A hospital based cross - sectional study was conducted among HIV patients aged 30 years and above attending MNH Care and Treatment Clinic.The study was conducted between August and December 2011.Interviews were done using a structured questionaire followed by a clinical assessment. Fasting blood samples were collected for determination of fasting blood glucose and lipids parameters. Quantitative CVD risk was calculated using Q risk 2011 mathematical model.

### Results

A total of 370 patients were analysed, with 69% being females. The mean age of the study subjets was 40years ( $\pm$ 8.13) with range of 30-65 years. Seventy four percent of the patients were on HAART. The overall prevalence of dyslipidemia was 82% . The prevalence of hypertriglyceridemia, hypercholesterolemia, incresed LDL and low HDL were 36% ,42%, 53% and 50% respectively.The prevalence of dysglycermia was 16% with prevalence of impared fasting blood glucose and overt DM at 10% and 7% respectively. HAART use was

significantly associted with increased levels of total cholestrol, triglycerides, LDL, HTN, impared fasting blood glucose and DM .

Obesity and Low HDL were more prevalent among HIV patient who were not on HAART.Patients on PI containing regimes had higher prevalenc of CVD risk factors compared to patients on non PI containing regimen. Overal CVD risk of developing a cardiovascular event in 10years using 2011 mathematical model was in the low levels(<10%) with a median (IQR) of 1.2% (0.4-4).

**Conclusions**:

There is a high prevalence of risk factors for cardiovascular diseases among HIV patients at Muhimbili National Hospital Care and Treatment Clinic. HAART use was significantly associated with increased levels of total cholestrol, triglycerides, LDL, HTN, DM and impared fasting blood glucose. Using 2011 mathematical model risk for CVD is low in this study population.

**Recomendations**

Modification of these risk factors through intervention strategies including healthy education and proper management is recommended in order to reduce future cardiovascular events**.**

**TABLE OF CONTENTS**

**LIST OF TABLES**

**LIST OF FIGURES**

**LIST OF ABBREVIATIONS**

CVD Cardiovascular disease

CHD Coronary heart diseases

ARV Antiretroviral

HAART Highly Active Anti Retroviral Therapy

ART Antiretroviral therapy

CD4 Cluster of differentiation four

CTC Care and treatment clinic

DAD Data on Adverse effect of antiretroviral therapy

DM Diabetes Melitus.

HIV Human Immunodeficiency Virus

TC Total Cholesterol

HDL C High density lipoproteins cholesterol

LDL Low density lipoproteins

VLDL Very low density lipoprotein

MI Myocardial Infarction

NACP National AIDS Control Program

NNRTI Non nucleoside Reverse Transcriptase Inhibitors

PI Protease Inhibitors

HT Hypertension

# CHAPTER ONE

## 1. INTRODUCTION AND LITERATURE REVIEW

HIV infection continue to be a major health problem in both developed and developing countries. Worldwide around 33.3 million people are living with HIV, 30.8 million are adults.[1] In 2009, an estimated 2.6 million new HIV cases occurred. The estimated number of AIDS related deaths in 2009 was estimated to be 1.8 milion with adults being 1.6 milion.[1] WHO reported that as of December 2008, approximately 4 million people in low- and middle-income countries were receiving antiretroviral therapy. Between 2003 and 2008, access to antiretroviral drugs in low- and middle-income countries rose 10-fold. [1]

Sub-Saharan Africa remains the region most heavily affected with HIV. In 2009, sub-Saharan Africa accounted for 67.6 % of HIV infections worldwide. The region also accounted for 72.2% of the world's AIDS-related deaths in 2009.[1]

The prevalence of HIV in Tanzania estimated to be 5.7% , 5% for men and 7% for women.The prevalence varies between different regions with Dar es Salaam region having a prevalence of 9% [2] In Tanzania 1.2 million people are estimated to be living with HIV, and 20% or 240,000 are eligible for ART. Only 150,000 and 200,000 people are currently receiving ART, which represents between 63% and 83% of those in need in Tanzania. [2]

**Atherosclerotic Heart diseases and HIV:**

After the introduction of ARVs morbidity and mortality due to HIV has decreased [3] . However, morbidity and mortality due to cardiovascular complications has become a concern due to metabolic complications attributed by long term use of HAART which inceases the risk for cardiovascular diseases.A study done by Crum et al showed that there was a change in a trend of cause of death among HIV patients from opportunistic infections to non infectious causes including cardiovascular diseases[3]. Death due to cardiovascular diseases attributed

22% of all deaths post HAART era compared to 8 % pre HAART era [3]. Clinical and subclinical atherosclerosis among HIV patients has been reported with a rate of up to 50% compared to HIV negative controls.[4]

### 1.1. 1 Cardiovascular Risk Factors.

A cardiovascular risk factor is a condition that is associated with an increased risk of developing cardiovascular disease[5]. It is a term coined by Dr William Kannel the first director of the Framingham study that was conducted between 1948 and 1970 that came out with the list of factors that were found to predispose an individual to the development of atherosclerotic heart diseases.the following are recognised as risk factors for cardiovascular diseases worldwide;

**a. <u>Non Modifiable risk factors</u>**

Age

Gender

Heredity

**b. <u>Modifiable risk factors</u>**

High blood pressure

Elevated serum cholesterol

Cigarette smoking

Obesity

Glucose intolerance

Diabetes mellitus

Rheumatoid arthritis

Behavioral factors (stress, type A)

**c. Protective factors**

HDL cholesterol

Exercise

Moderate alcohol intake

**Age**

Age is the most powerful unmodifiable independent risk factor for atherosclerosis. As the age increases above 45 years the risk of a cardiovascular event increases. This is because accumulated risk factos in an individual increases with age.[6]

**Sex**

Overall, men have a higher risk of heart attack than women because women have hormonal protective effect of estrogen which increases the HDL. But the difference narrows after women attain menopause. After the age of 65, the risk of heart disease is about the same between the sexes when other risk factors are similar [7]

**Family history.**

A positive family history is present when the first degree relative dies or suffer a coronary event at the age < 50 for men and < 55years for women Atherosclerotic vascular disease often runs in families. This may be due to a combination of shared genetic, environmental and lifestyle (e.g. smoking, exercise and diet) factors. The most common inherited risk characteristics (hypertension, hyperlipidemia, diabetes) runs in families [8, 9]

**Smoking.**

Smoking is probably the most important modifiable cause of atherosclerotic heart disease. Studies have shown that in absence of smoking there would be 1.62 million fewer cardiovascular deaths[10] Smoking induces inflammation and triggers atherosclerosis[11].Quarter of tobacco-related deaths are accounted for by ischemic heart disease (IHD)

**Hypertension**

Hypertension is an established modifiable risk factor for development of coronary heart disease and stroke .Hypertension almost doubles the risk of developing a cardiovascular event compared to people who are normotensive. The mechanism is that the continued shear stress associated with hypertension and the resulting endothelial dysfunction causes impairment in the synthesis and release of the potent vasodilator nitric oxide. A decreased nitric oxide level promotes the development and acceleration of arteriosclerosis and plaque formation. Antihypertensive therapy has been shown to reduce coronary mortality, stroke and heart failure.[12, 13]

**Hypercholesterolemia**

Elevated serum cholesterol above 5mmols /l is found to be associated with increased risk of developing a coronary event. [12] Studies have demonstrated that the risk of coronary heart disease and other forms of atherosclerotic vascular disease rises with plasma cholesterol concentration, and in particular the ratio of total cholesterol to high-density lipoprotein (HDL) cholesterol. Lowering total cholesterol concentrations reduces the risk of cardiovascular events including death, myocardial infarction and stroke. [14, 15]

**Diabetes mellitus.**

Diabetes mellitus increases the risk of coronary heart disease by two to four times compared to people without diabetes[16].In the population of diabetes cardiovascular diseases is the leading cause of mortality[16, 17]. Diabetes increases risk of coronary heart diseases by causing abnormal blood lipids and obesity, also hypertension occur more frequently in people with diabetes which predisposes these individuals to atherosclerosis.Good glycemic control can reduce a cardiovascular disease event by 42 % [18]

**Haemostatic disorders.**

Platelet activation and high levels of fibrinogen are associated with an increased risk of coronary thrombosis.[19] Anti-phospholipids antibodies are associated with recurrent arterial thromboses. And hence increases the risk of cardiovascular events [20]

**Physical inactivity**

Physical inactivity roughly doubles the risk of coronary heart disease and is a major risk factor for stroke.[12] Regular exercise (brisk walking, cycling or swimming for 20 minutes two or three times a week) will reduce risk of coronary heart disease by about 30%.[12] This is explained by increased HDL cholesterol, lower blood pressure, reduced blood clotting, and collateral vessel development. Physical activity is known to reduce the risk of developing Type 2 diabetes which is also a cardiovascular risk factor.[19]

**Obesity** .

Obesity, particularly if central or truncal, is an independent risk factor for cardiovascular diseases,[21] Obesity is contributed by genetic factors and lifestyle factors consisting of low levels of physical activity and consumption of excess calories. Central obesity is linked with hyperinsulinemia, insulin resistance, dyslipidemia, and proinflammatory and prothrombotic clinical states. This is because the adipose tissue synthesizes and secretes biologically active molecules include adiponectin, resistin, leptin, plasminogen activator inhibitor–1, tumor

necrosis factor–α, and interleukin-6. Weight loss may reduce release of these mediators and hence improving insulin sensitivity and dyslipidemia leading to reduction in risk factors for CVD and, consequently, the potential for cardiovascular events.[21]

**Alcohol.**

Alcohol consumption has been shown to be associated with all-cause mortality in a J- or U-shaped manner. A moderate intake of alcohol (2-4 units a day) appears to offer some protection from coronary disease[22] however, heavy drinking is associated with increased risk of atherosclerosis. This is partly explained by the fact that the moderate alcohol intake is associated with increased HDL and apolipoprotein A. Anti-inflammatory effects of moderate intake of alcohol have been considered as a possible explanation in prevention against atherosclerosis, as inflammation has a fundamental role in the initiation, progression and the thrombotic complications of atherosclerosis. The effect is reversed with excess alcohol intake [23].

### 1.1.2 Cardiovascular risk factors in HIV populations

HIV virus itself, adverse effects of HAART and life style changes such as cigarette smoking post diagnosis predispose HIV patients to increased risk of atherosclerotic heart diseases.[23, 24].The prevalence of traditional cardiovascular disease risk factors such as dyslipidemia, hypertension, diabetes and cigarette smoking is generally higher compared with the general population.Results from the Data Collection on Adverse Events of Anti-HIV Drugs study showed that HAART therapy is associated with a 26% relative risk increase in the rate of myocardial infarction per year of HAART exposure[25]

The cardiovascular risk factors attributed to HIV virus and/or HAART include:

**1:Hypercholesterolemia**

Total cholesterol, LDL and VLDL cholesterol are elevated in HIV population and is attributed by both HIV virus and the use of HAART. Results from the major trial on adverse effects of ARV demonstrated that there was a higher prevalence of hypercholesterolemia among patients treated with PI and/or NRTI containing regimens[26] However there were observed individual variability among PIs in causation of Hypercholesterolemia. Ritonavir was found to increase the risk of hypercholesterolemia 20-fold, nelfinavir 9-fold and indinavir 4-fold. NRTI are also associated with Hypercholesterolemia and among the NRTIs stavudine had a greater dyslipidemic effect than it was observed for zidovudine[27]. In a study which was done in Kenya at Jommo Kenyatta hospital to asses cardiovascular risk among HIV patient on ARV and ARV naives showed that hypercholesteremia occurred in 39.2% of HAART compared to 10.0% HAART naïve patients[24]

**2: Hypertriglyceridemia**

Hypertriglyceridemia has been observed among HIV patients as a part of HIV associated dyslipidermic lipodystrophy (HADL). This was especialy observed among patients treated with regimens containing PI and/or NRTI.[27] Biochemical studies shown that HADL patients have a severe, and probably 'primary', abnormality in triglyceride lipolysis with an increased rate of hydrolysis of free fatty acids (FFAs)In Tanzania a study which was done by Armstrong et al among HIV naive patient showed higher prevalence of hypertriglycidermia of 28%[28].

**3: Low HDL**

HDL cholesterol is also referred as good cholesterol because of its protective effect ,as it increases the delivery of cholesterol from blood to the liver. Its decrease is associated with increased risk of a coronary event. Decreased concentrations of HDL cholesterol were reported among HIV patients before the advent of HAART [29] Some studies have also demonstrated a decrease of HDL on different patients on HAART although the association of this abnormality with specific HAART agents is less clear [30]. Armstrong was able to

demostrate the high prevalence of decreased HDL in ART naive patient of 67% in a study which was conducted in Tanzania[28]

**Pathogenesis of dyslipidemia in HIV patients**

Pathogenesis of dyslipidemia in HIV patients include:

Hypertriglyceridemia thought to be related to poor virological control which leads to increased levels of TNF-$\alpha$. TNF-$\alpha$ interferes with Free fatty acid (FFA) metabolism and lipid oxidation and attenuates insulin-mediated suppression of lipolysis [31].

ARV through complex interaction also causes dyslipiadermia. Human studies have suggested that ARV particularly PI induces an increased hepatic synthesis of VLDL and VLDL-triglycerides[32] . It seems also that protease inhibitors affect apolipoprotein B degradation with increased levels of small and dense LDL [33, 34]

**4. Truncal obesity**

Different body fat abnormalities has been observed among HIV patients with a prevalence of up to 50% in both on HAART and ART naïve[35].Different anthropometric phenotypes has also been observed. They include a mixed 'centripetal' pattern of fat accumulation with increased fat deposition in the abdomen, chest or breast area, neck and upper back in the dorsocervical region ('buffalo hump'), together with fat loss in the face, arms, thighs and buttocks [36] ARV implicated include PIs which inhibit lipogenesis and impair the activity of adipocytes regulatory proteins **[37, 38]** and NRTI, especially stavudine which induce mitochondrial toxicity in subcutaneous fat tissues [39, 40]

**5.Type 2 DM**

Insulin resistance and risk of type 2 diabetes is high among HIV patients on HAART. The prevalence of diabetes mellitus, among HIV on HAART was reported by DAD study to be 2.5% [26] PI and NRTI therapy are implicated in causation of insulin resistance and DM

among HIV patients. Mechanism suggested include PIs directly inhibit the uptake of glucose by insulin-sensitive tissues, such as fat and skeletal muscle, and by selective Inhibition of the glucose transporter Glut4. [41] NRTI drugs, especially the thymidine analogs, also have a role in promoting insulin resistance in muscle and liver due to their mitochondrial toxicity induced toxicity. Manuthu et al demostrated a prevalence of DM to be 2.2% among HIVpatients on ART in Kenya[24]

**6.Cigarette smoking**

The prevalence of smoking among HIV patients is higher in HIV positive than in HIV negative. In a study whic was done by Burk Halter et al had shown the prevalence rates of smoking to range from 50% to 70% compared to 21% for the general population [42]In a study which was done in Nigeria HIV patients were shown to have a prevalence of 22%[43] Studies on smoking cessation among PLHIV identifies a number of positive factors that contribute to a high prevalence of smoking among this population, including, pleasure, assisting and sustaining social engagement, high levels of depression, social isolation, stress, and having a stigmatised disease[44]

**7.Hypertension**

Studies have demonstrated the prevalence of hypertension to be higher among HIV patients than among HIV negative individuals. A study which was done in India revealed the prevalence of hypertension to be as high as 33% in HIV patients who were on HAART compared to 19% among HIV negative[45] This higher prevalence is explained by HAART induced dyslipidemia, insulin resistance, and increased hip/waist circumference ratio which are risk factors for hypertension[46, 47].

### 1.1.3 Pathophysiology of coronary heart diseases.

Atherosclerosis in the coronary vessels is the key pathological changes that result into coronary heart disease. Insults to the coronary vessels such as infections or injury disrupt integrity of the endothelium leading to impaired function and initiate formation of atherosclerotic lesions known as fatty streaks which consist of macrophages and T cells embedded in a thin layer of lipids on the arterial walls.[48, 49]The macrophages will then engulf the LDL C and become activated foam cell that release an array of chemo attractant molecules, cytokines, and growth factors. More lymphocytes are attracted to the lesion that perpetuate the inflammatory response. As this cycle is repeated, the plaque develops a fatty core covered by a fibrous matrix that stabilizes the structure.[48]

As the plaque becomes thicker, the arterial wall responds by "remodeling," that is, gradually dilating to maintain the diameter of the vessel lumen. Eventually macrophages may be stimulated to release metalloproteinase that degrade the fibrous cap and render the plaque vulnerable to rupture.[50, 51] Although several types of plaque can result in serious coronary events, retrospective analyses have demonstrated that 70% of all fatal acute myocardial infarctions and sudden coronary deaths are attributable to plaque rupture or plaque erosion[52]

### 1.1.4 Coronary heart diseases in HIV patients

Prevalence of coronary heart diseases among HIV patients was reported to be as high as 50% [4]. Several mechanisms can explain these high prevalence

**A. HIV infection endothelial dysfunction**

HIV-1 sequences have been detected by in situ hybridization in the coronary vessels of an HIV-infected patient who died from acute myocardial infarction [53] Mechanism postulated is that in which HIV can cause inflammatory reaction that can initiate endothelial dysfunctions leading to acceleration of atherosclerosis by activation of cytokines and cell adhesion molecules and alteration of major histocompatibility complex class I molecules on the surface of smooth-muscle cells. It is also possible that HIV-1-associated protein gp 120 may induce

smooth-muscle cell apoptosis through a mitochondrion-controlled pathway by activation of inflammatory cytokines 21. **V**asculitis and coronary spasms have been noted in hiv pts as cause of vascular events even in the abscence of atherosclerosis similar phenomenon has been the cause of increased stroke in hiv pts

**B: Increased in cardiovascular risk factors among HIV patients.**

The increase in coronary events among HIV patients can also be explained by an increased risk factor profile among this group attributed by either the virus or ART which include hypercholesterolemia hypertriglyceridemia, insulin resistance ,truncal obesity, diabetes,and cigarette smoking. [26, 27],

### 1.1.5 Cardiovascular risk predictor models

Studies done in developed and in developing countries has shown an increased risk for cardiovascular events among people living with HIV [26, 54].UK guidelines recommends that the risk of cardiovascular diseases should be estimated by combination of different risk factors into a numeric estimate of risk. Epidemiologist have done population based studies and come up with equations that can be used to predict numeric estimate of risk after a certain period of time (1,2,3,5 and 10years risk.)

The famous equation is the American Framingham logarithm which was the equation derived from the large study known as American Framingham study. In this study the cardiovascular risk factors were identified and their contribution to an absolute risk was calculated.[55] The shortcomings of this model is that it did not incorporate DM and family history of cardiovascular disease in estimation of absolute risks. In Scotland a different mathematical model was developed and being used and is known as ASSIGN equation.[56]

**Q RISK 2011** .

A QRISK 2011 is a computarised tool which was developed in United Kingdom for quantitative research purposes .Whilst QRISK has been developed for use in the UK, it is being used internationally. It calculates a risk of having a heart attack or stroke over the next ten years by answering some simple questions as seen in Annex II . After answering the appropriate questions the computer calculates one's risk of of developing a cardiovascular event in the next ten years and gives the risk in parcentage. The results were stratified in levels.In which a risk from 0-10% were considered as low risk levels,11%-20% intermediate risk levels and >20% high risk levels. Q RISK2- 2011 has an advantage that it was adjusted for ethnicity and so can be uses in black Africans, additional estimations for patients who have family history of hypertension and Diabetes and those who are on medication for hypertension.[57].

These predictor models have also been applied in HIV populations in Latin America and Africa in which studies have shown increased 10years risk coronary diseases especially with HIV patients who are on ARV particularly Pis [58, 59]

## 1.2 PROBLEM STATEMENT

HIV is known to be associated with increased risk factors for cardiovascular diseases among infected individuals.[60] Management of HIV patients with ARVS has been associated with exacerbation of cardio-metabolic complications. Therefore there is an increased morbidity and mortality due to cardiovascular diseases among patients treated with anti retro viral therapy (ARV) [26]

The increased morbidity and mortality due to cardiovascular disease among HIV/AIDS patients on ART poses a new challenge in HIV/AIDS management. Despite present awareness on the rising cardiovascular events among HIV patients on ART, little is known on the extent of cardiovascular risks among HIV patients and their contribution to the overall risk

in the development of a cardiovascular disease in our setting. Cardiovascular risk factors attributed by HIV disease and its treatment are modifiable. Inadequate knowledge on the magnitude of the cardiovascular risk factors among HIV patients in Tanzania is among the limiting factor for intervention.

## 1.3 **RATIONALE**

An increase in cardiovascular attributable morbidity and mortality among HIV patients, justifies the compelling need to understand cardiovascular risks attached with HIV management options. This study was conducted in the light of paucity of information on the magnitude of cardiovascular disease risk factors among HIV patients in Tanzania.

The results of this study will provide knowledge on the magnitude and distribution of the cardiovascular risks factors in relation to HIV disease and its management. This knowledge is expected to improve care of HIV infected patients, particularly those with increased risk of cardiovascular morbidity, bearing in mind that most of cardiovascular risk factors are modifiable. This study will also form a baseline for further intervention studies aimed at modifying cardiovascular risk factors among HIV patients.

## 1.4 OBJECTIVES

### 1.4.1 Broad objectives

To assess risk factors for cardiovascular diseases among HIV patients attending Muhimbili National Hospital Care and Treatment Clinic

### 1.4.2 Specific objectives

1. To determine prevalence of cardiovascular risk factors among HIV infected patients attending MNH Care and Treatment Clinic.
2. To assess association between cardiovascular risk factors and highly active antiretroviral therapy among HIV infected patients attending MNH Care and Treatment Clinic
3. To assess the association between cardiovascular risk factors and WHO clinical stages of HIV disease
4. Determine cardiovascular risk levels using a Q risk 2011 mathematical model among HIV infected patients attending MNH Care and Treatment Clinic.

# CHAPTER TWO

## 2.1 METHODOLOGY

### a. Study design

This was a hospital based descriptive cross - sectional study. The study was designed to ascertain the prevalence of risk factors for atherosclerotic cardiovascular diseases among HIV patient and estimate numeric risk of patients developing cardiovascular event in 10 years using a Qrisk 2011mathematical model .

### b. Study Area

This study was done at Muhimbili National Hospital (MNH) HIV clinic. MNH is Tanzania's largest public and tertiary level referral hospital. It receives referred patients from district hospitals and from neighboring regions. It is located in the city of Dar es salaam which is also the largest commercial city in the country with a population of about 2.48 million. MNH HIV clinic has a total of 6,300 regular patients. The clinic receives patients referred from district hospital HIV clinics and those referred from the inpatient department of MNH.The MNH refferals are mainly those patients who are diagnosed to have HIV while admitted in the wards. The patients attend the clinic once in a month for clinical evaluation and refill of ARV.

### c. Study duration

The study was conducted between August and December 2011

### d. Study participants

**Inclusion criteria**

All HIV patients attending MNH HIV clinic at the time of study aged 30 years and above were eligible for inclusion to the study. This selection was based on the mathematical model

use to calculate the CVD risk,(QRISK 2011) the model can only compute risk in patients who are 30 years and above.

Both patients on HAART and HAART naive were included in the study.

Those who signed a written informed consent to participate in the study were recruited in the study.

**e. Sample size**

Sample size was calculated using the formula:

$$n = \frac{Z^2\, p(1-p)}{e^2}$$

n=Minimum sample size, Z=Standard normal deviate corresponding to two sided specified significant level. This is 1.96 (at 95%c confidence interval) e=Margin of error 5%. P =Prevalence of Hypercholesterolemia in HIV population on HAART at Jomo Kenyatta Hospital in Kenya 39.6% .

Sample size (N) = 368

**f. Sampling techniques and study procedure**

Study subjects were selected by systematic random sampling using daily attendance as sampling frame. About 10-15 patients were recruited on each clinic day if they met the inclusion criteria and signed a written consent to participate into the study. Every odd numbered patient starting from the third on the daily register was recruited upon their consent. In case a patient did not consent for the study then the next odd numbered patient in a row was recruited. Those who consented were requested to come next day in a fasting state for labaratory investigations.

### g. Data collection

**Patient interview**

A structured questionnaire was used to collect demographic data. Patient history including life style was collected to capture associated factors like smoking habits, family history of heart attack in first degree relative at age <60 years, alcohol consuption, drug history of lipid lowering drugs,antidiabic drugs and antihypertensive. Past medical history of hypertension and diabetes.

**Clinical examination**

WHO clinical staging was done after a thorough clinical examination according to standard clinical examination methods. WHO clinical staging of HIV for resource-constrained settings were developed by the WHO in 1990 and revised in 2007. This staging is based on clinical findings that guide the diagnosis, evaluation, and management of HIV/AIDS, and does not require a CD4 cell count. This staging system is used in many countries to determine eligibility for antiretroviral therapy. Clinical stages are categorized as 1 through 4, progressing from primary HIV infection to advanced HIV/AIDS. These stages are defined by specific clinical conditions or symptoms. (Annex V)

**Blood pressure measurements**

Blood pressure measurements were taken using mercury sphygnomomanometer in the left arm while seated. Two readings were taken at the interval of five minutes and the average reading was taken as patients blood pressure The 1st and the 5th Korotokoff's sounds were used to determine the systolic (SBP) and diastolic blood pressure (DBP) measurements respectively.

**Weight and height measurements**

Weight was measured using the calibrated weighing scale. Readings were measured to the nearest 0.5 kilograms

Height measuments was taken using a height measuring rod without shoes and recorded to the nearest 0.5 centimeters.

BMI for each respondent was calculated by dividing weight (kilograms) with height (meter) squared BMI of 30kg/$m^2$ and over was taken as obesity.

**Patient records**

Data on ARV types and duration was obtained from patients records.

**Laboratory investigations**

In a fasting state, 5mls of blood samlpes was drawn for determination of lipid profile, Blood Glucose levels and renal function tests. Lipid profile was measured using Vitros DT 6011 Chemistry Analyzer . Blood glucose measurements were done on the spot after collection using *HEMOCUE Glucose 201+*

**h. Numerical Risk calculations**

Estimated risk of CVD was calculated using a computerised mathematical model QRISK2 2011 calculator. A Q risk 2011 is a tool which was developed in United Kingdom for quantitative research purposes . Whilst QRISK has been developed for use in the UK, it is being used internationally. For non-UK use, the postcode field is left blank the score will be calculated using an average value. It calculates a risk of having a heart attack or stroke over the next ten years by answering some simple questions as seen in Annex II . After answering the appropriate question the computer calculates ones risk of of developing a cardiovascular event in the next ten years and gives the risk in parcentage. The results were stratified in levels.In which a risk from 0-10% were considered as low risk levels,11%-20% intermediate risk levels , and >20% high risk levels. Q RISK2- 2011 has an advantage that it was adjusted

for ethnicity and so can be used in black Africans.Most resent updates on the equation were made in April 2011.

## 2.2 DEFINITIONS FOR THE STUDY

**Cardiovascular risk factor in this study :** Cardiovascular risk factors that were assesed in this study included; eleveted total cholesterol, inceased LDL, increases VLDL, decreased HDL, hypertriglyceridemia, hypertension, DM, impared fasting blood glucose,obesity, cigarette smoking and excess alcohol intake.

**Dysglycaemia**- was defined as presence of either DM or impaired fasting blood glucose

**Diabetes mellitus –** was defined as a Fasting Blood Glucose of 7.1 mmol /L and above or those who will be in blood glucose lowering medicines.

**Impared fasting blood glucose** was taken as fasting blood sugar between 6.1mmol/L to 7.0mmol/L

**Dyslipidemia;**was defined as the presence of any of the following lpid abnomalities: hypercholestrolemia,hypretriglyceridermia,decreasesd HDL, increased LDL, or increased VLDL

**Hypercholesterolemia** was defined as total serum cholesterol of more than 5.2mmo/l and those who were in lipid lowering drugs,

**Hypertrigyceridemia** was defined as serum triglyceride of more than 1.7 mmo/l

**Decreased HDL** was take as levels <1.04mmol/l

**Increased LDL** was taken as levels>3.3mmol/l

**Hypertension:** systolic pressure equal or above 140mmHg and diastolic pressure of equal or above 90mmHg and those on treatment for high blood pressure.

Overall CVD risk levels using 2011 mathematical model was categorized into 3 levels as follows; <10% was considered low risk levels, 10-20- intermediate risk levels, and >20% were considered as high risk level.

Excessive alcohol intake was defined as use of more than 14 units per week for females and more than 21 units per weeks for males.

A smoker was defined as anyone who was actively smoking at the time of the study regadless of the number of cigarette smoked.

## 2.3 STATISTICAL ANALYSIS

Statistical analysis was done using a computer program SPSS version 15.0. Subgroups were compared using Chi square or Fishers exact test where the number in a cell was less than five for categorical data. Linear and multiple regression were done to determine the independent predictors of different CVD risk factors. Differences were considered significant if p-value were less than 0.05

## 2.4 ETHICAL CONSIDERATION

Ethical clearance to conduct the study was sought from Muhimbili University and Allied Sciences Ethical Review Board. Permission to do the study was obtained from MNH director of clinical services. Detailed Information about the study was given to the patients and informed written consent was required from the individuals who accepted to participate in the study. For the patients who were found to have diabetes mellitus and hypertension were referred to the appropriate physician for treatment .Those with dyslipidemia were given dietary advices, and those with hypercholesterolemia and hypertriglyceridemia on top of dietary advises were refered to attending doctor for a decision on prescription of a lipid lowering drugs. Patients with impaired fasting blood glucose, excessive alcohol intake and

cigarette smokers were referred to a counselor for life style modification counseling. All information collected on questionnaires was entered into computer with identification number. The questionnaires were handled with greater secrecy in order to maintain confidentiality.

# CHAPTER THREE

## RESULTS

A total of 370 HIV infected patients were recruited, out of them females were 69%. The overall mean (SD) age was 40 years (± 8.13), ranging from 30-65 years. The majority of study subjects were young, with (51%) aged between 30-40 years. Only 15% of the participants were above 51years .The socio demographic characteristics of the study population are summarised in table 1

Majority of the participants (63%) had attained a primary education or no formal education, whereas only 10% of the patients had attained a post secondary education

Married and cohabiting people contributed the large proportion of the study subjects (58%), whereas the participants who were divorced contributed the minority, (10%). (Table 1)

### HIV related characteristics

Mean time since diagnosis of HIV was 5years (± 3.7), with a range of 1-17 years. More than half of the study participants(50.5%) were in WHO clinical stage III, whereas (22.4%) were in WHO clinical stage II .WHO clinical stage I and stage IV had almost the same propotion of patients, 13.3%and 13.8% respectively(table 1)

Ninety six patients (25.9%) were HAART naïve whereas 274 (74.1%) patients were on HAART. Propotion of patients on different ART regime are summarised in table 1. Patients on Protease inhibitors constituted 18% and Tenofovir containing regimen constituted the minority 3%. Median duration of ART use was 5years IQR of (3-7) years

**Table 1:Social - demographic characteristics of study participants attending Muhimbili National Hospital Care and Treatment Clinic (N=370)**

| Characteristic | Number | Percentage (%) |
|---|---|---|
| ***Sex*** | | |
| Female | 255 | 68.9 |
| Male | 115 | 31.1 |
| ***Age groups*** | | |
| 30-35yr | 95 | 25.7 |
| 36-40yr | 96 | 25.9 |
| 41-45yr | 76 | 20.5 |
| 46-50yr | 49 | 13.3 |
| 51+ | 54 | 14.6 |
| ***Education*** | | |
| Primary education and below | 232 | 62.7 |
| secondary education | 101 | 27.3 |
| Post secondary education | 37 | 10 |
| ***Marital status*** | | |
| Single | 76 | 20.5 |
| Married/cohabiting | 216 | 58.4 |
| Divorced | 37 | 10 |
| Widowed | 41 | 11.1 |

**Table 1 continues.....**

| Characteristic | Number | Percentage (%) |
|---|---|---|
| ***WHO clinical stages*** | | |
| 1 | 49 | 13.2 |
| II | 83 | 22.4 |
| III | 187 | 50.5 |
| IV | 51 | 13.8 |
| ***ART subgroups*** | | |
| ART naive | 96 | 25.9 |
| Stavudine containing regime | 101 | 27.3 |
| Lopinavir/ritonavir containing regime | 66 | 17.8 |
| Tenofovir containing regime | 11 | 3.1 |
| Zidovudine containing regime | 96 | 25.9 |

**Prevalence of risk factors for cardiovascular diseases.**

Dyslipidemia was detected in 306/370 patients (82.7%) with no significant gender variation. Among the individual lipid abnomalities increased LDL was the most prevalent (53% ) with no significant difference between males and females p= 0.6

The prevalence of hypertriglyceridemia was significant higher among males(50.4%) as compared to females (29.8%)p =0.000. Decreased HDL and increased VLDL were also more prevalent among males as compared to females (p=<0.0001 and 0.002 respectively)

Dysglycaemia was prevalent in 16.2% of the patients, being more prevalent among females(17%) as compared to males(14%) p=0.5 Overt diabetes occurred in twenty five patients (6.8%) The prevalence of Diabetes mellitus was similar in males and females being 7%.

Obesity was present in 16% of the patients being significantly higher in females(19.2%) as compared to males(8.7%). p=0.006.

Hypertension was significant more prevalent among males (31.3%) as compared to females (19.2%)p= 0.01.

**Table 2: Prevalence of risk factors for CVD among patients attending MNH Care and Treatment Clinic (N=370)**

| Characteristic | Females (%) n= 225 | Males (%) n=115 | Overall | p-value |
|---|---|---|---|---|
| Dyslipidemia | 205(80.4) | 101(87.8) | 306(82.7) | 0.08 |
| Hypercholesterolemia | 108(43) | 49(43.3) | 157(42.2) | 0.9 |
| Hypertriglyceridemia | 76(29.8) | 58(50.4) | 134(36.4) | **<0.0001** |
| Increased LDL | 137(54) | 58(50.4) | 195(52.7) | **0.6** |
| Increased VLDL | 16(6.3) | 19(16.5) | 35(9.5) | **0.002** |
| Decreased HDL | 111(43.5) | 73(63.5) | 184(49.7) | **<0.0001** |
| Dysglycaemia | 44(17.3) | 16(13.9) | 60(16.2) | 0.4 |
| Impared FBG | 27(10.6) | 8(22.7) | 35(9.5) | 0.2 |
| Diabetes melitus | 17(6.7) | 8(7.0) | 25(6.8) | 0.5 |
| Obesity | 49(19.2) | 10(8.7) | 59(15.9) | **0.006** |
| Hypertension | 49(19.2) | 36(31.3) | 85(23.0) | **0.01** |
| Alcohol excess | 4(1.57) | 5(4.3)\| | 9(2.4) | 0.14* |
| Smoking | 3(1.2) | 4(3.5) | 7(1.9) | 0.133* |

*****p-value by Fisher's Exact Test

**CVD risk factors and socio demographic characteristics**

Table 3 Shows comparison between the prevalence of the CVD risk factors and age . Prevalence of diabets mellitus was significantly increasing with age with the lowest prevalence at the lowest age group (4.2%) and the highest prevalence (15%) among those aged more than 51years ($\chi^2$ trend=7 p =0.008.)

HDL cholesterol was also significantly increasing with age with the lowest prevalence(46%) at the lowest age group and the highest prevalence (63%) among those aged more than 51 years $\chi 2$ trend 5= p=0.03

The prevalence of hypertriglyceridemia was significantly decreasing with advanced age from (43%) at the lowest age group to (22% )in those who were above 51 years ($\chi 2$ trend=11: p=0.001.)Prevalence of hypercholesterolemia, increased LDL, HTN,increased VLDL were increasing with age but the difference in diferent age groups was not statisticaly significant.

**Table 3:Prevalence of CVD risk factors by age among study participants attending Muhimbili National Hospital HIV Care and Treatment Clinic (N=370)**

| **CVD risk factor** | **30-40 years** **n=191** | **41-50years** **n=125** | **>51years** **n=54** | **p-value *** |
|---|---|---|---|---|
| Hypercholesterolemia | 76(40) | 52(43) | 29(56) | 0.058 |
| Hypertriglyceridemia | 57(30) | 47(38) | 30(56) | **0.001** |
| Increased LDL | 101(53) | 61(48.8) | 33(61) | 0.5 |
| Increases VLDL | 18(9.4) | 11(8.8) | 6(31.4) | 0.814 |
| Decreased HDL | 87(46) | 63(50) | 34(63) | **0.030** |
| Obesity | 31(16) | 20(16) | 8(15) | 0.821 |
| Diabetes mellitus | 8(4.2) | 9(7.2) | 8(14.8) | **0.008** |
| Impaired fasting blood glucose | 21(11) | 8(6.4) | 6(11.1) | 0.6 |
| Hypertension | 39(20.4) | 28(22.4) | 18(33.3) | 0.074 |

***p-value for trend**

Association between the CVD risk factors and different levels of education were assesed and were not found to be statisticaly significant. Also there was no association between the different CVD risk factors and the marital status.

**CVD risk factors and HAART status**

The prevalence of diabetes mellitus and impaired fasting blood glucose were significantly higher among patients who were on HAART as compared to those who were not on HAART, with prevalence of 8% and 12% respectively for the patients on HAART as compared to 3% and 4% for the patients who were HAART naive with p-values of 0.003 an 0.001 respectively.

The individual components of dyslipidemia with exception of low HDL were found to be significantly higher among patients on HAART as compared to the HAART naïve patients . Hypertension was found to be significantly higher among patients on HAART as compared to patients who were HAART naive.

Decreased HDL and obesity were significant higher in HAART naive patients compared to patients on HAART p=0.004 and 0.02 respectively.

**Table 4:Association between CVD risk factors and HAART status among HIV patients at Muhimbili National Hospital Care and Treatment Clinic(N=370)**

| CVD risk factor | HAART naive n(%)=96 | HAART Experienced n(%)= 274 | P-value |
|---|---|---|---|
| Hypercholesterolemia | 21(22) | 136(49) | **0.0001** |
| Hypertriglyceridemia | 23(24) | 111(41) | **0.001** |
| Increased LDL | 42(44) | 153(56) | **0.01** |
| Increases VLDL | 9(9) | 26(10) | 0.8 |
| Decreased HDL | 56(58) | 128(47) | **0.004** |
| Obesity | 23(24) | 36(13) | **0.02** |
| Diabetes mellitus | 3(3) | 22(8) | **0.01** |
| Impaired fasting blood glucose | 4(4) | 31(12) | **0.029** |
| Hyprtension | 12(13) | 73(27) | **0.002** |

**Prevalence of CVD risk factors and the type of ARV.**

Figure 2 shows the comparison between the prevalence of the CVD risk factors among patients treated with PI containing regime as compared to non PI containing regimen.All the CVD risk factors asseses were more prevalent among patients on PI containing regime as compared to non PI containing regime.The observed difference were statisticaly significant except for elevated LDL, obesity and hypertension.

**percentages**

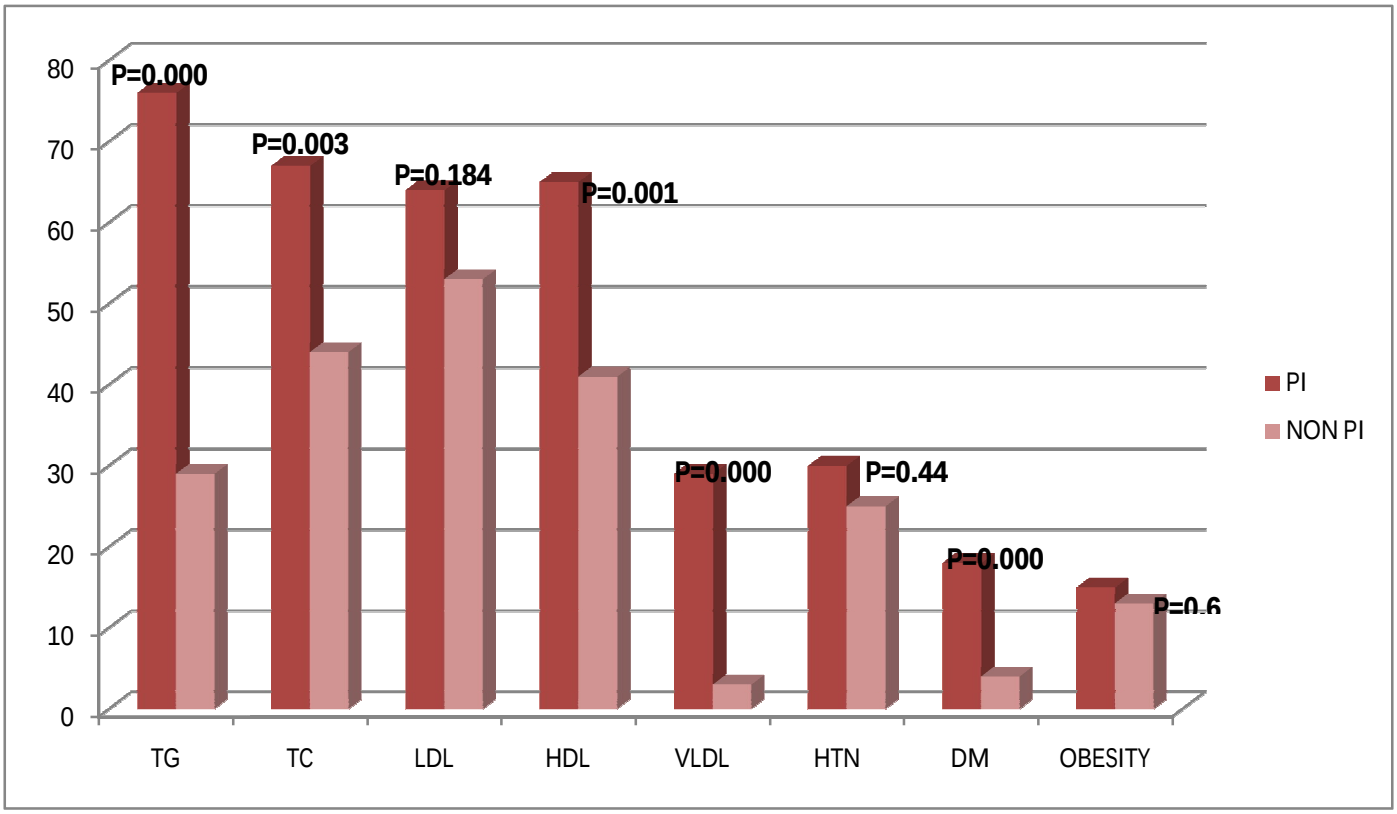


**Figure 1 :Prevalence of CVD risk factors in patients treated with PI containing regime compared to non PI containing regimen**

KEY: TG-elevated triglyceride,TC-elevated total cholesterol,HTN-hypertension,DM-diabetes melitus,LDL-elevated low density lipoprotein, HDL-decreased high density lipoprotein,VLDL-increases very low density lipoproteion

Prevalence of CVD risk factors among patients on stavudine containing regime as compared to non stavudine containg regime was also assesed .

There was no significant difference between the prevalence of all of the CVD factors between patients who were on stavudine containg regime as compared to patients on non stavudine containing regime( zidovudine/tenofovir).

**Prevalence of CVD risk factors and WHO clinical stage**

Table 5, shows the association between CVD risk factors and WHO clinical stage of HIV disease There was a statistically significant difference between the prevalences of Hypercholesterolemia, hypertriglyceridemia, and increased LDL across the WHO clinical stage of HIV disease. The prevalences peaked at clinical stage III, The prevalences for the three risk factors dropped in clinical stage 1V. (Table 5).

The prevalence of hypertension and DM was also statisticaly significant different accross the different WHO clinical stages of HIV disease. P value 0.021 and 0.001 respectively.

Although the same trend is observed with other risk factors, the differences observed were not statistically significant

**Table 5:Association between CVD risk and WHO clinical stage of HIV disease among HIV patients at Muhimbili National Hospital Care and Treatment Clinic(N=370)**

| CVD Risk factor | WHO Stage 1 | WHO STAGE 2 | WHO STAGE 3 | WHO STAGE 4 | P value for trend |
|---|---|---|---|---|---|
| Hypercholesterolemia | 13(8.3) | 23(14.7) | 96(61.5) | 24(15.3) | **0.0001** |
| Hypertriglyceridemia | 16(11.9) | 16(11.9) | 73(54.5) | 29(21.6) | **0.001** |
| Increased LDL | 20(10.3) | 31(15.9) | 116(59.5) | 28(14.4) | **0.002** |
| Increases VLDL | 29(14.2) | 52(14.3) | 71(57.1) | 23(14.2) | 0.642 |
| Decreased HDL | 26(14.1) | 44(23.9) | 85(46.2) | 29(15.7) | 0.781 |
| Obesity | 9(15.2) | 15(25.4) | 29(49.1) | 6(10.1) | 0.310 |
| DM | 2(8) | 2(8) | 14(56) | 7(28) | **0.021** |
| HT | 5(5.9) | 18(21.2) | 41(48.2) | 21(24.7) | **0.001** |

**CVD risk factors and duration of ARV.**

Table 6 shows the association between the prevalence CVD risk factors and duration of ARV use. The prevalence of hypertriglyceridemia was significantly increasing with increased duration of ARV use. A trend test perfomed p= 0.027.The prevalence of the rest of the CVD risk factors assesed the prevalences were all increasing with duration of ARV use but the increment were not statisticaly significant.

**Table 6:Association between the prevalence of CVD risk factors and duration of HAART use.(n=274)**

| RISK FACTOR | <2years | 3-5years | >5years | p-value * |
|---|---|---|---|---|
| Hypercholesterolemia | 32(42%) | 53(53.5) | 51(54) | 0.111 |
| Hypertriglyceridemia | 28(36) | 37(37) | 50(52.1) | **0.027** |
| Increased LDL | 43(55%) | 55(56) | 57(59) | 0.562 |
| Increases VLDL | 6(7.7) | 8(8.1) | 12(12.5) | 0.268 |
| Decreased HDL | 35(44.9) | 43(43.4) | 53(55.2) | 0.155 |
| Obesity | 67(86) | 87(88) | 82(85) | 0.901 |
| DM | 6(7.7) | 7(7.1) | 9(9.4) | 0.666 |
| Impaired fasting blood glucose | 6(7.7) | 12(12.1) | 13(14) | 0.236 |
| HT | 21(27) | 31(31) | 21(22) | 0.4 |

***p-value for trend**

**CVD risk levels using 2011 mathematical model**

In this study it has been found that vast majority (322/370) 87% of the study participants were in the low risk levels of developing a cardiovascular event in 10 years measured by QRISK 2011mathematical model, whereas only 1% were in the high risk level (figure 3) Median risk(IQR) was 1.2 (0.4-4).

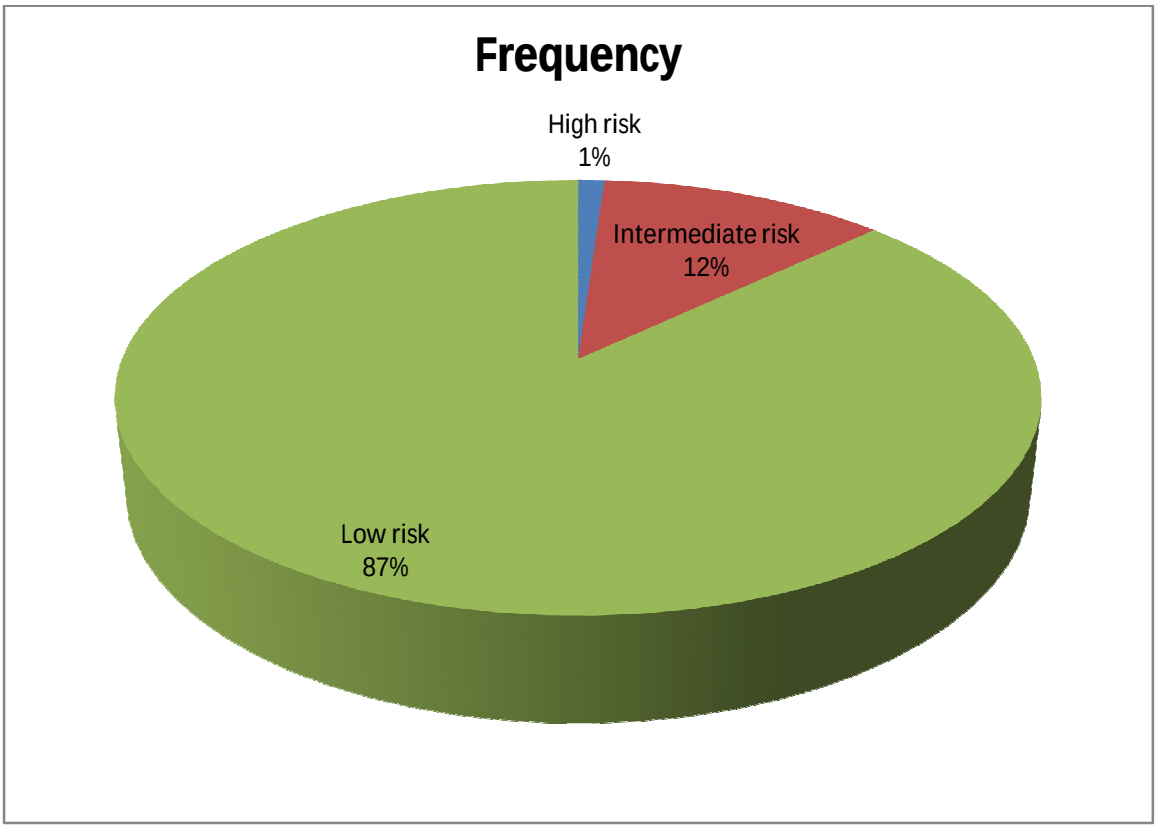


**Figure 2:CVD risk levels using 2011 mathematical model.**

**Independent predictors of CVD risk factors**

Table 7 shows the independent predictors of different CVD risk factors among HIV patients attending MNH care and treatment Clinic.After adjusting for age and sex use of ARV was an independent predictor for hypercholesterolemia,hypertriglyceridemia and hypertension.Other independent predictors are of different CVD risk factors are summarised in table 7.

**Table 7:Predictors of CVD risk factors among study subjects attending Care and Treatment Clinic at MNH(N=370)**

| | univariate | | | | multivariate | |
|---|---|---|---|---|---|---|
| **CVD** | **predictor** | **OR** | **CI** | **P value** | **OR** | **CI** |
| ***TG*** | Male sex | 2.4 | 1.52 - 3.7 | 0.000 | 3.23 | **1.82 - 5.72** |
| | ARV use | 2.9 | 1.68 - 5.11 | 0.000 | 2.67 | **2.67 - 4.21** |
| | age >51 | 2.939 | 1.15-5.462 | 0.001 | 2.204 | **1.153-4.211** |
| | stage IV | 2.719 | 1.204-6.140 | 0.016 | 0.97 | 0.354-2.697 |
| TC | ARV use | 3.81 | 2.20-6.6 | 0.000 | 2.6 | **1.46-5.59** |
| | Age>51 | 1.908 | 1.02-3.54 | 0.000 | 1.56 | 0.82-2.97 |
| | Stage III | 3.09 | 1.538-6.21 | 0.002 | 0.42 | 0.61-3.3 |
| | Stage IV | 2.66 | 1.15-6.16 | 0.022 | 0.743 | 0.44-3.123 |
| LDL | ARV use | 1.8 | 1.11-2.9 | 0.01 | 1.2 | 0.658-2.146 |
| | Stage III | 2.34 | 6.3-3.8 | 0.008 | 1.56 | 0.6-3.8 |
| HDL | Age>51 | 2.03 | 1.09-3.78 | 0.02 | 1.795 | 0.95-3.39 |
| | Male sex | 2.26 | 1.43-3.55 | 0.000 | 2.145 | **1.36-3.4** |
| HT | Arv use | 2.54 | 1.321-4.93 | 0.006 | 2.105 | 0.96-4.63 |
| | Age | 1.19 | 1.001-3.79 | 0.05 | 1.409 | 0.69-2.84 |
| | Sex | 1.92 | 1.16-3.12 | 0.01 | 1.897 | **1.11-3.21** |
| | Stage IV | 6.16 | 2.1-18-14 | 0,001 | 3.513 | **1.04-11.9** |

Table 8 shows the independent predictors of CVD risk factors among patients on HAART only.Specificaly use of PI containing regimen was an independent predictor for hypertiglyceridermia,hypercolesterolemia and low high density lipoprotein.

**Table 8:Predictors of CVD risk factors among study subjects on HAART only (n=274)**

| | **univariate** | | | | **multivariate** | | |
|---|---|---|---|---|---|---|---|
| **CVD** | **predictor** | **OR** | **CI** | **P value** | **OR** | **CI** | **P value** |
| ***TG*** | PI use | 6.88 | 3.64-12.97 | 0.000 | 5.31 | **2.71-10.39** | **<0.0001** |
| | ART use >5years | 1.94 | 1.05-3.579 | 0.003 | 2.25 | 1.04-4.87 | 0.213 |
| | Sex | 2.6 | 1.55-4.48 | 0.000 | 1.85 | **1.103-3.406** | **0.041** |
| | Age more than 51 years | 2.82 | 1.42-5.59 | 0.003 | 2.25 | **1.04-4.869** | **0.04** |
| ***TC*** | PI use | 2.39 | 1.335-4.269 | 0.003 | 2.32 | **1.28-4.22** | **0.006** |
| | ARV duration>5years | 1.67 | 0.91-3.065 | 0.09 | 1.11 | 0.69-1.94 | 0.591 |
| ***HDL*** | PI use | 2.55 | 1.433-4.54 | 0.001 | 1.806 | **1.04-3.116** | **0.036** |
| | Sex | 2.14 | 1.26-3.63 | 0.005 | 2.192 | **1.21-3.98** | **0.010** |

# CHAPTER FOUR

## 4.0 DISCUSSION

This study was conducted among HIV patients at MNH Care and treatment Clinic with the aim of assessing the cardiovascular risk factors in this population. Both patients on HAART and HAART naïve were studied.

**Prevalence of CVD risk factors**

The prevalence of dyslipidemia of 83% found in this study was higher than a previous study among HIV patients in Dar es salaam in which the prevalence of dyslipidemia was found to be 76%[28] .The difference in prevalence with the current study could be due to the fact that the previous study studied only the HAART naive patients while the current study studied both HAART naive and HAART experienced patients.These results are similar to those which were reported from Latin American HIV cohort of patients on HAART in which the prevalence of dyslipidemia was reported to be 80 % [58]. It is postulated that the dyslipidaemia is a result of the metabolic effects of the HIV virus itself and the metabolic effects of the HAART.This increases the risk of future cardiovascular events in HIV patients. [14, 15]

On top of the effect of HAART and the HIV virus itself; the dyslipidaemia could also be explained in part by wrong eating habits among HIV affected patients.A common practice in the local population is to encourage HIV patients to 'over-feed' on rich foods so that they mantain their weight and improve immunity In the past 'Thin subjects' were easily identified by society as being HIV infected and the associated social stigma.Thus HIV patients strive to get nutritional support and use food supliments.This may lead to over weight and dyslipidaemia.,

The prevalence of hypercholesterolaemia of 42% in this study is higher than that reported by Swai et in a general multiregional survey 5%-19% [61] . However the current study is from

a specified group of HIV affected patients. It is possible that a factor related to HIV disease and its treatment is responsible for increased hypercholesterolemia.

The prevalence of hypercholesterolemia in the current study is much higher than the one reported by Amstong et al in Dar es salaam among HIV patients who were not on HAART 14% [28] The difference with the current study which constituted the patients who were on HAART\and HAART naive perhaps suggest an additional effect of HAART in causation of hypercholesterolemia.

Prevalence of hypertriglyceridemia in this study was (36%) with males more affected than females.The pattern is similar to that which was reported in South Africa HIV patients in which more HIV males had hypertiglyceridemia than females [62].The prevalence in the current study was higher than that reported by Armstrong et al among HIV patients HAART naive 28% .[28] However the prevalence is lower than that which was reported by Anastos et al in which he reported the prevalence to be 48%[59].The difference in prevalence from the current study could be due smaller sample size in the current study as compared to Anastos et al. High triglyerides levels in HIV patients has been postulated to be due to inflamation with subsequent cytokines release and decreased hepatic clearance related to a role of apolipoprotein E[31]

Prevalence of decreased HDL in this study(50%) is comparable to the South Africa HIV cohort in which was reported to be 46%.[62] The results are also similar to the reports from developed counties in which the prevalence of hypertiglyceridemia in a Latin American HIV cohort was reported to be 46%[58]. HDL are cholesterol scavengers, picking up excess cholesterol from the blood and taking it back to the liver.The lower the HDL levels the more the risk of hypercholesterolemia and hence increased CVD risk.

Elevated LDL occurred in 53% of the study subjects being significantly higher in females than in males. The prevalence is lower than that which was reported by Gripson in urban Dar es salaam among HIV patients who are not on HAART ( 67%)[28] The results are lower than that which was reported in Latin American study in which it was found to be 25%[58].The

results from all these studies call for a need for intervention to prevent premature CVD among HIV patients.

The prevalence of Dysglycaemia in this population(16%) was slightly lower than that which was reported in a Jomo Kenyatta HIV cohort in which the prevalence of dysglycaemia was found to be 20.7%.[24]This observed difference could be explained by the fact that dysglycaemia in Kenya study also included patients who had impaired glucose tolerance which was not done in the current study. Prevalence of DM and impaired fasting blood glucose in the the current study were higher than the report from general population [63] .Diabetes Melitus in HIV patients is due to genetic factors or the toxic effects of elevated circulating lipids (beta cell lipotoxicity) as the consequences of lipodystrophy or could be drug induced. [64]

In the present study women were found to be more obese than males. This study was nearly similar to the study which was conducted among HIV patients in Western Kenya in which the prevalence of obesity among female HIV patients and HIV males were 22% and 11% respectively[65] . The prevalence of obesity in this study was similar to that from the general population in Kinondoni district in Dar es Salaam which found an overall prevalence of(19%)[66]. However the prevalence similar to a general population was obtained despite having more than 64% of the study participants in advanced stage of the disease stage III and IV suggest that there is a factor related to HIV or its treatment is responsible for its equalization. Also obesity in this population could be in part explained by a factor related to stigma.The tendency from the community is to encourage the HIV patients to be obese as thinnes could easly reveal their status.

Prevalence of cigarette smoking and excess alcohol intake were low in this population (7% and 9% respectively). The prevalence of excess alcohol intake is lower than that reported in the general population in which it was found to be 17.2%. [67] This lower prevalence perhaps could be due to the fact that majority of the studied patients were already on HAART, and the

tendency is to discourage excess alcohol intake in patients on HAART. The prevalence of cigarette smoking was lower than the reported prevalence among HIV patients in Nigeria which was 22%[68] .This can be explained by probably social differences between the two countries.

Hypertension was more prevalent among males than females with ARV use, age, sex, being its independent predictors. The prevalence is lower than that which was reported among HIV patients in western Kenya[65].Lower tha that which was reported in the Latin America HIV Cohot.[58]The differences from the current study could be explained by regional population rate of hypertension .

**CVD risk factors and HAART status**

The prevalence hypercholesterolemia, hypertriglyceridemia, and high LDL were found to be more prevalent among HIV patients on HAART than HAART naïve patients. Even after adjusting for age and sex HAART use remained to be an independent predictor for hypercholesterolemia and hypetriglyceridermia. The similar pattern has been observed among HIV patients in Kenya[24] and in Cameroon[69]. The difference observed among HAART users and HAART naive patients indicate that HAART use has an additive efffect to that attributed by the HIV virus itself in causation of hypercholesterolemia, hypertriglyceridemia, and high LDL.

The prevalence of decreased HDL was significantly higher among HAART naïve patients than patients on HAART.The similar pattern was observed in Kenya; in which decreased HDL levels were found in 51.3% of HAART naive patients and in 14.6% among HAART users.[24] And a study by Gripson suggested a higher prevalence than the current study 67%[28] The finding in all these studies shows decreased HDL to be more prevalent among HAART naive than HAART users. Longitudinal assessment of patients with HIV seroconversion suggests that there are decreasing HDL and low-density lipoprotein (LDL)

cholesterol at the time of infection, before treatment. With the initiation of HAART, total and LDL cholesterol increase to preinfection levels, but low HDL levels persist [70]

DM prevalence was more among patients on HAART than HAART naive.The results are in keeping with the major trial DAD study[26] and also the Manuthu et al study[24] in which DM was found to be more prevalent among HIV patients on HAART as compared to HAART naive.PI and NRTI therapy are implicated in causation of DM among HIV patients. Mechanism suggested include PIs directly inhibit the uptake of glucose by insulin-sensitive tissues, such as fat and skeletal muscle, and by selective Inhibition of the glucose transporter Glut4[64]

**CVD risk and ARV types**

In this study it was found that the prevalence of dyslipidemia, dysglycaemia, HT and obesity were more prevalent among patients who were on Protease inhibitors (PIs) as compared to other regimens that did not contain PIs. These results are in keeping with the major trial, the DAD study [26]which had reported earlier the high prevalence of dyslipidemia and dyglycaemia among HIV patients on PI. Ritonavir, a PI common in use has been found to be the most notorious cause of dyslipidemia,dysglycaemia and obesity. Ritonavir boosted Lopinavir is the only PI used in the MNH Care and Tretment Clinic as the second line treatment according to Tanzania National HIV treatment guideline.Even after adjusting for other factors PI use remain to be an independent predictors of hypercholesterolemia, hypertriglyceridemia and and low HDL among patients on HAART.

There was no significant difference between the prevalence of all of the CVD factors assesed in the current study between patients who were taking Stavudine and those who were on zidovudine. This is in keeping with the report from Cameroon in which they found the same pattern[69] But however this finding is in contrary to the result from the major trial the DAD trial [26]in which they found that stavudine was more notorious in causing the CVD risk factors as compared to zidovudine. The observed differences of the current study from the

DAD study could be due to drug switch especialy from stavudine to zidovudine commonly due to its side effects including peripheral neuropathy and lipodystrophy .

**CVD risk and HIV WHO clinical stage**

All of the CVD risk factors assseses the prevalences were increasing as the disease advances picking at clinical stage III, but the prevalence were surprisingly dropping in clinical stage IV. This finding is different from what was reported earlier in which the prevalence were found to be increasing with advanced disease as indicated by CD4 levels[24]. The observed difference could be explained by the fact that in the current study WHO clinical staging was used instead of CD4 counts and it is well known that one might be in an advanced WHO stage but with modest CD4 decrease.

**Overall CVD risk**

In this study by use of QRISK2011 mathematical model, the 10 years risk of developing a cardiovascular event was found to be in the low risk levels in majority of the participants. The results are similar to the results from the major trials CREATE 1 trial in which the overall CVD risk was found to be in the lower risk levels(<10%)[71].The results are similar to the Rwanda study where the CVD risk among HIV patients were also found to be in the lower risk levels [59]All these studies have used the CVD risk models which were designed to be used in the general population.However the use of general population models to asses CVD risks in HIV patients has been challenged recently[72, 73]. It is urged that general population models to asses CVD risks may not be fully applicable to HIV infected patients because the models encompasses characteristics that are not directly related to the HIV disease for example the model enquires about a first degree relative who died of heart disease to predict an incresed risk to a person, however the model might overpredict or underpredict the risk because it was not designed for HIV infected patients .Better equations are clearly needed to more accurately predict the risk of CVD in HIV-infected patients.

## 4.1 STUDY LIMITATIONS

Mathematical model used was meant to estimate risk in the general population and so may not be fully applicable to this population, and the model itself despite being adjusted for ethnicity it can estimate CVD risk for people older than 30years.

Due to age limitation from the model used CVD risk could not be assesd in HIV patients aged less than 30 years.

# CHAPTER FIVE

## 5.1 CONCLUSIONS

There is high prevalence of CVD risk factors among HIV patients .

Patients on HAART have high prevalences of traditional coronary risk factors .

The CVD risk profile is higher in those on PI regimen as compaired to other HAART regimen.

Using Q risk 2011 calculator the Overall 10 years risk of developing a cardiovascular event was low in this study population.

## 5.2 RECOMMENDATIONS

- Integration of CVD risk factors assessment and management as part of HIV care and treatment
- Screening of patients and whenever possible, the antiretroviral medication least likely to worsen the dyslipidemia or dysglycaemia should be given.

## REFERENCES

1. UNAIDS/ WHO 2010 AIDS Epidemic update
2. www.tacaids.go.tz
3. Crum NF, R.R., Wegner S, Agan BK, Tasker SA, Spooner KM, Armstrong AW, Fraser S, Wallace MR; Triservice AIDS Comparisons of causes of death and mortality rates among HIV-infected persons: analysis of the pre-, early, and late HAART (highly

active antiretroviral therapy) eras. J Acquir Immune Defic Syndr,February 2006, 1;41(2):194-200.

4. Crum NF, R.R., Wegner S, Agan BK, Tasker SA, Spooner KM, Armstrong AW, Fraser S, Wallace MR; Triservice AIDS Increased Prevalence of Subclinical Coronary Atherosclerosis Detected by Coronary Computed Tomography Angiography in HIV-Infected Men. American Heart Association J, 2009; 120:S463.
5. A book in Cardiovascular risk factors by Henry r. Black, MD, Chapter 3,pg 23-25
6. Pekka Jousilahti, M.E.V., MD; Jaakko Tuomilehto, MD; Pekka Puska, MD, Sex, Age, Cardiovascular Risk Factors, and Coronary Heart Disease.American Heart Association J, 1999;99: p. 165-1172.
7. Pekka Jousilahti, M.E.V, MD; Jaakko Tuomilehto, MD; Pekka Puska, MD, Sex, Age, Cardiovascular Risk Factors, and Coronary Heart Disease ,A Prospective Follow-Up Study of 14,786 Middle-Aged Men and Women in Finland. American Heart Association J, 1999.
8. U Broeckel, C.H., B Mayer, et al. s ; A comprehensive linkage analysis for myocardial infarction and its related risk factors. . J Nature Genetic, 2002. 30: p. 210–214.
9. E Touze, P.R.L.N., Heritability of ischaemic stroke in women compared with men:a genetic epidemiological study, Lancet Neurol. 2007 Feb;6(2):125-33. 2007
10. Ezzati M, H.S., Thun MJ, Lopez AD. . , Role of smoking in global and regional cardiovascular mortality. Circulation J, . 2005; . 112: : p. 489–497.
11. Maat MPM, P.A., Kofflard M et al. , Association of plasma fibrinogen levels with coronary artery disease, smoking and inflammatory markers. . Atherosclerosis., 1996;. 121:185–191.
12. J Mackay, Atlas of Heart Disease and Stroke 2004 World Health Organization. Geneva.
13. Najfian, MedlinePlus Medical Encyclopedia:Hypertension.2005.
14. G De Backer, E.A., K Borch-Johnsen, C Brotons, R Cifkova, J Dallongeville, et al. , European guidelines on cardiovascular disease prevention in clinical practice. Third

joint task force of European and other societies on cardiovascular disease prevention in clinical practice. European Heart Journal., 2003. 24: 1601-10.

15. Yusuf S, Lonn E, Bosch J. Lipid lowering for primary prevention. *Lancet*. Apr 4 2009;373(9670):1152-5
16. Brussels., I., International Diabetes Federation Diabetes and Cardiovascular Disease:. A Time to Act, 2001.
17. National Diabetes Fact Sheet. Department of Health and Human Services, USA., 2005. .
18. DM Nathan, P.C., JY Backlund, et al. , Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. New England Journal of Medicine., 2005. 353(25): p. 2643-2653.
19. DE Warburton, C.N., SS Bredin. , Health benefits of physical activity:. Canadian Medical Association Journal., 2006. 174((6)): p.:801-9.
20. Urbanus RT, S.B., Roest M, Rosendaal FR, de Groot PG, Algra A, Antiphospholipid antibodies and risk of myocardial infarction and ischaemic stroke in young women in the RATIO study: a case-control study. Lancet Neurol, . 2009 Nov;. 8: p. 98-1005.
21. World Health Organization. , Obesity and Overweight:, September 2006.( Factsheet 311).
22. R Jackson, R.S., and R Beaglehole, Alcohol consumption and risk of coronary heart disease.BMJ 1991 July:303(6769):211-216
23. Armin Imhof, W.K. and Alcohol inflammation and coronary heart disease. J Addiction Biology, 9 JUN 2006: p. 1293-1299.
24. Group., T.D.S., Class of antiretroviral drugs and the risk of myocardial infarction. N Engl J Med, 2007. 356: p. 1723-35.
25. Friis-Møller, N.W., R.; Reiss, P.; Thièbaut, R.; Kirk, O.;, et al., Cardiovascular disease risk factorsin HIV patients-association with antiretroviral thrapy. Results from the DAD study. AIDS, , 2003. 17, : p. 1179-93.
26. Fontas, E.v.L., F.; Sabin, A.; Friis-Møller, N.; Rickenbach,, et al., Lipid profiles in HIV-infected patients receiving combination antiretroviral therapy:are different

antiretroviral drugs associated with different lipid profiles? J. Infectious diseases, 2004. 189: p. 1056-74.

27. E M Manuthu, M.D.J., G N Lule, E Karari and Prevalence of dyslipidemia and dysglycaemia in HIV infected patients Journal: East African medical journal, 2008. 85(1):10-7.
28. Armstrong C, L.E., Okuma J, Spiegelman D, Guerino C, Njelekela M, Grinspoon S, Fawzi W, Hawkins C., Dyslipidemia in an HIV-positive antiretroviral treatment-naive population in Dar es Salaam, Tanzania. J Acquir Immune Defic Syndr, 2011. ;57(2):141-5.
29. Constans J, P.J., Peuchant E, and e. al., Plasma lipids in HIV-infected patients: a prospective study in 95 patients. . Eur J Clin Invest 1994. 24: p. 416-206.
30. E Bernal, M.M., S Padilla, and others. , High-Density Lipoprotein Cholesterol in HIV-infected Patients: Evidence for an Association with HIV-1 Viral Load, Antiretroviral Therapy Status, and Regimen Composition. . AIDS Patient Care and STDs., May 15, 2008.
31. C Grunfeld, M.P., W Doerrler, J K Shigenaga, , Lipids, lipoproteins, triglyceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. JCEM. 74: 1045-52;.
32. Baril, L.B., I.; Valantin, M.A.; Bruckert, E.; Bonnefont-Rousselot, D.; Coutellier, A.; Caumes, E.; Katlama, C.; Bricaire, F, Low lipolytic enzyme activity in patients with severe hypertriglyceridemia on highly active antiretroviral therapy. . AIDS, 2001, . 15,415-17.
33. Schmitz, M.M., G.M.; Walli, R.; Bogner, J.; Bedynek, A.;Seidel, D.; Goebel, F.D.; Demant, T., Alterations of apolipoprotein B metabolism in HIV-infected patients with antiretroviral combination therapy. J. Acquir. Immune Defic. Syndr., 2001, 26, 225-35. J. Acquir. Immune Defic. Syndr.: p. 2001, 26, 225-35.
34. Liang, J.S.D., O.; Cooper, D.A.; Jamil, H.; Deckelbaum, R.J.; Ginsberg, H.N.; Sturley, S.L. , HIV protease inhibitors protect apolipoprotein B from degradation by the

proteasome: a potential mechanism for protease inhibitor-induced hyperlipidemia. Nat. Med J., 2001, 7, 1327-31.

35. Lichtenstein KA, W.D., Moorman AC, et al, Clinical assessment of HIV-associated lipodystrophy in an ambulatory population. AIDS Patient Care and STDs., 2001. 15: p. 1389-1398.
36. Steven Grinspoon, M.D., and Andrew Carr, M.D., Cardiovascular Risk and Body-Fat Abnormalities in HIV-Infected Adults. N Engl J Med, 2005. 352:: p. 48-62.
37. Carr, A.S., K.; Chisholm, D.J.; Cooper, D.A. , Pathogenesis of HIV protease inhibitor-associated syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance. ,. Lancet 1998. 351: p. 1881-83.
38. Carr, A.S., K.; Burton, S.; Law, M.; Freund, J.; Chisholm, and D.A. D.J.; Cooper, A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. AIDS, 1998. 12: p. F51-F58.
39. Carr, A.C., D., Adverse effects of antiretroviral therapy. . Lancet, 2000. 356: p. 1423-30.
40. Mallal, S.A.J., M.; Moore, C.B.; James, I.R.; McKinnon, E.J., Contribution of nucleoside analogue reverse transcriptase inhibitorsto subcutaneous fat wasting in patients with HIV infection. AIDS, 2000. 14: p. 1309-16.
41. Murata H, H.P., Mueckler M. , The mechanism of insulin resistance caused by HIV protease inhibitor therapy. J Biol Chem, 2000. 275: p. 20251-4.
42. Jack E. Burkhalter, C.M.S., Rosy Chhabra, Jamie S. Ostroff, Bruce and D. Rapkin, Tobacco use and readiness to quit smoking in low-income HIV-infected person. Nicotine & Tobacco Research J, Volume 7, Number 4.
43. Desalu O.P, Olokoba AB, Adekoya AO, Danburam A, Salawu FK, Midala J., Prevalence and determinants of tobacco smoking among HIV patients in North Eastern Nigeria. Afr J Med Med Sci. 2009 Jun;38(2):103-8

44.Reynolds, N. R., Neidig, J.L., & Wewers, M.E. (2004). Illness Representation and Smoking Behavior: A Focus Group Study of HIV-Positive men. Journal of the Association of Nurses in AIDS Care, 15(4), 37-47.

45. Gazzaruso C, B.R., Garzaniti A, Giordanetti S, Fratino P, and e.a. Sacchi P, Hypertension among HIV patients:prevalence and relationships to insulin resistance and metabolic syndrome. :. J Hypertens, 2003. 21: p. 1377–1382.
46. Chow D, S.S., Richmond-Crum S, Shikuma C Epidemiological evidence of increasing blood pressure in HIV- 1-infected individuals in the era of HAART. Antivir Ther, 2000: p. 31–32.
47. Mattana J, S.F., Sankaran RT:, Absence of age-related increase in systolic blood pressure in ambulatory patients with HIV infection. Am J med, 1999: p. 232–237.
48. RussellRoss,B. Arherosclerosis: an inflammatory disease. N Engl J Med, 1999. 340: p. 115 -226.
49. Stary HC, C.A., Glagov S, Guyton JR, Insull W Jr, Rosenfeld ME, et al. , A definition of initial fatty streak and intermediate lesion of atherosclerosis: a report from the Committee on Vascular Lesions of the sf Council on Arteriosclerosis,. American Heart Association J., 1994. 89: p. 2462-2478.
50. Galis ZS, S.G., Lark MW, Libby P. , Increased expression of matrix metalloproteinases and matrix degrading activity in vulnerable regions of human atherosclerotic plaques. J Clin Invest, 1994. 94: p. 2493-2503.
51. Schönbeck U, M.F., Sukhova GK, Murphy C, Bonnefoy JY, Fabunmi RP, et al, Regulation of matrix metalloproteinase expression in human vascular smooth muscle cells by T lymphocytes: a role for CD40 signaling in plaque rupture? Circ Res, 1997. 81: p. 448 -454.
52. Naghavi M, L.P., Falk E, Casscells SW, Litovsky S, Rumberger J, et al., From vulnerable plaque to vulnerable patient: a call for new definitions and risk assessment strategies: . Part I. Circulation, 2003. 108: p. 1664 -1672.
53. Triant VA, L.H., Hadigan C, Grinspoon SK., Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab, 2007. 92: p. 2506-12.
54. Anderson KM, O.P., Wilson PWF, Kannel WB, Cardiovascular disease risk profiles. Am Heart J, 1991. 121: p. 293-8.

55. Brindle P, E.J., Lampe F, Walker M, Whincup P, Fahey T, et al, Predictive accuracy of the Framingham coronary risk score in British men: prospective cohort study. BMJ, 2003. 327: p. 1-6.
56. John F Potter2, N.R.P., Margaret M Robins1, Jane Skinner, Performance of the ASSIGN cardiovascular disease risk score on a UK cohort of patients from general practice. Heart and education in Heart J, 2010(.203364).
57. Carol Coupland, Y.V., , John Robson, Margaret May, Peter Brindle,, Derivation and validation of QRISK, a new cardiovascular disease risk score for the United Kingdom: prospective open cohort study BMJ, 2007: p. 335 : 136 doi: 10.1136/bmj.39261.471806.55.
58. Leite, R., Metabolic profile and cardiovascular risk factors among Latin American HIV-infected patients receiving HAART Cahn, . Braz J Infect Dis 2010;14(2):158-166].
59. Kathryn Anastos1, François Ndamage3, Dalian Lu4,, Lipoprotein levels and cardiovascular risk in HIV-infected and uninfected Rwandan women AIDS Research and Therapy 2010, 7:34.
60. Triant VA, L.H., Hadigan C, Grinspoon SK. , Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab, 2007. ; 92: p. 2506–2512.
61. Swai, M., Kitange HM et al, .Low prevalence of risk factors for coronary heart diseases in rural Tanzania. Int J Epidemiol.1993;August;22(4):651-9.
62. Julius H, B.D., Ricci E, Wing J, Basu JK,, The burden of metabolic diseases amongst HIV positive patients on HAART attending The Johannesburg Hospital. . Curr HIV Res. 2011 Jun;9(4):247-52. doi: 10.2174/157016211796320360.
63. Aspray TJ,Mugusi F,A.R Rashid Seif, Rural and urban differences in diabetes prevalence in Tanzania : The role of obesity, physical inactivity and urban living. Royal society of tropical medicine and hygiene, 2000 Nov,94(6):637-44
64. McGarry JD ,Dysregulation of fatty acid metabolism in the etiology of type 2 diabetes. J Diabetes. 2002;51:7–18

66. Gerald S. Bloomfield1*, J.W.H., Hypertension and Obesity as Cardiovascular Risk Factors among HIV Seropositive Patients in Western Kenya Plos one, July 2011

66. Grace Shayo and Mugusi F.M., Prevalence of obesity and associated risk factors among adults in Kinondoni municipal district, Dar es Salaam Tanzania. BMC Public Health 2011, 11:365

67. Joseph Mbatia [1], R.J., *, Nicola Singleton [3] and Bethany White Prevalence of Alcohol Consumption and Hazardous Drinking, Tobacco and Drug Use in Urban Tanzania, and Their Associated Risk Factors Int. J. Environ. Res. J Acquir Immune Defic Syndr. Public Health 2009, 6, 1991-2006; doi:10.3390/.

68. Desalu O.P, Olokoba AB, Adekoya AO, Prevalence and determinants of tobacco smoking among HIV patients in North Eastern Nigeria. Afr J Med Med Sci. 2009 Jun;38(2):103-8.

69. Eric Walter Pefura Yone1, Awa Foueudjeu Betyoumin3, André Pascal Kengne, First-line antiretroviral therapy and dyslipidemia in people living with HIV-1 in Cameroon: a cross-sectional study. AIDS Research and Therapy 2011, 8:33

70. Riddler SA, S.E., Cole SR, et al., Impact of HIV infection and HAART on serum lipids in men. . JAMA 2003;289:2978-82.

71. M. Aboud, A.E., 1 L. Pomeroy, , Cardiovascular risk evaluation and antiretroviral therapy effects in an HIV cohort: implications for clinical management the CREATE 1 study . Int J Clin Pract, August 2010, 64, 9, 1252–1259.

72. Nina Friis-Møller1, a.S.W.W., Can the Risk of Cardiovascular Disease in HIV-Infected Patients Be Estimated from Conventional Risk Prediction Tools? Clinical Infectious Diseases J ; 2007,45:1082–4.

73. Law MG, F.-M.N., El-Sadr WM et al. , The use of theFramingham equation to predict myocardial infarctions in HIV-infected patients: comparison with observed events in the D:A:D Study. HIV Med J 2006; 7:218-30.

# 6 ANNEX II: CARDIOVASCULAR RISKS ASSESMENT TOOL.

QRISK®2-2010 cardiovascular disease risk calculator

Welcome | Information | Publications | About | Copyright | Contact Us | Software

About you

Age:

Sex: ○ Male ○ Female

Ethnicity: Black African

Leave blank if unknown

Postcode:

Clinical information -- check those that apply

Diabetic? ☐

Had a heart attack, angina, stroke or TIA? ☐

Angina or heart attack in a 1st degree relative < 60? ☐

Current smoker? ☐

Chronic kidney disease? ☐

Atrial fibrillation? ☐

On blood pressure treatment? ☐

Rheumatoid arthritis? ☐

Leave blank if unknown

Cholesterol/HDL ratio:

Systolic blood pressure (mmHg):

Body mass index

Weight (kg):

Height (cm):

Calculate risk over 10 years. Calculate

# 7 ANNEX III: QUESTIONNAIRE

1. Questionnaire No----------
2. Patient hospital No----------
3. Name of the patient----------
4. Age(years)----------
5. Sex M---------- F-------
6. Tribe----------
7. Address , telephone no patients---------- close relative----------
8. Level of education A.No formal education
    A. Primary education
    B. Secondary education
    C. certificate
    D. Advanced diploma /Degree

HIV history

9. When were you first diagnosed to have HIV (Years of diagnosis)----------
10. Are you on ARV Yes ----- No--------
11. If yes, for how long (years)----------
12. Types( from the records)----------
13. since initiation of ARV were they changed at some point in time? Yes .....No.....
14. If Yes; types duration of use reasons for changing

    ..... ..... .....
    `

Family and social history

15. Are you a smoker currently 1. Yes------- No----------
16. If Yes, for how long.....
17. How many cigarete per day?.....
18. If no; were you a smoker in the past? Yes ..... No.....
19. If yes, when did you stoped?.....
20. Do you drink alcohol? Yes..... No .....
21. If yes which type?.....
22. How much per week?.....
23. Do you have a first degree relative who died suddenly at age at age <60 years
    Yes..... No.....

Past medical history

24. Have you ever suffered a stroke Yes----------No----------
25. Have you ever suffered a TIA Yes----------No----------
26. Have ever suffered of angina (description of angina will be given) Yes----------No----------
27. Are you hypertensive Yes---------- no----------
28. Are you an any antihypertensive Yes ---------- No----------
29. Are you diabetic Yes ---------- No----------
30. are you on any treatment for diabetes. Yes.....No.....
31. Do you have rheumatoid arthritis Yes ----------No----------
32. Have ever been told that you have eleveted serum lipids? Yes.....no.....
33. Are you on any lipid lowering drugs Yes ---------- No----------

Examination findings

Weight ---------- Height----------

Blood pressure 1---------- 2---------- Average----------

Pulse rate ----------AF, Yes ---------- No----------

Clinical stage of the disease----------

Laboratory results

Serum cholesterol----------

HDL levels----------

Fasting blood glucose----------

RBG----------

Renal function test----------

DODOSO

**Taarifa binafsi**

1. Namba ya dodoso .....
2. Namba ya jalada .....
3. Umri(miaka) .....
4. Jinsia
    a. Kike .....
    b. Kiume .....
5. Kabila .....
6. Mahali unakoishi .....
    a. Namba yako ya simu .....
    b. namba ya ndugu wa karibu .....
7. Kiwango cha elimu
    a. sijasoma
    b. elimu ya msingi
    c. elimu ya sekoondari
    d. cheti
    e. stashaha/shahada

**Historia kuhusu ugonjwa wako**

8. Uligundulika mwaka gani kuwa na maambukizi ya virusi vya ukimwi ? 20.....or 19.....
9. Je unatumia dawa za kupunguza makali ya ugonjwa wa ukimwi?
    **a.** Ndiyo .....
    **b.** Hapana .....
10. Kama ndiyo, umetumia dawa kwa muda gani sasa?
    **a.** Miaka .....
    **b.** Chini ya mwaka mmoja
11. Taja aina ya dawa anazotumia mgonjwa ( toka katika faili)
    **a.** .....

**b.** .....

**c.** .....

12. Je tangu kuanza dawa umewahi kubadilishiwa dawa

**a.** Ndiyo .....

**b.** Hapana .....

13. Kama ndiyo; Taja aina ya dawa zilizotumika

| | | | |
|---|---|---|---|
| **i.** | Aina za dawa | muada aliotumia | sababu kubadilisha |
| **ii.** | ..... | ..... | ..... |
| **iii.** | ..... | ..... | ..... |
| **iv.** | ..... | ..... | ..... |

**Hitoria ya familia na mambo ya kijamii**

14. Je unavuta sigara?

**a.** Ndiyo .....

**b.** Hapana ..... (Nenda Swaili Na. 17)

15. Kama ndiyo, umevuta kwa muda gani sasa? Miaka .....

16. Je unavuta sigara ngapi kwa siku? .....

17. Kama hapana, uliwahi kuvuta sigara siku za nyuma

**a.** Ndiyo .....

**b.** Hapana .....

18. Kama ndiyo lini uliacha kuvuta sigara? Mwaka .....

19. Je unakunywa pombe?

**a.** Ndiyo .....

**b.** Hapana .....

20. Kama ndiyo ni aina gani ua pombe?

a. Bia/pombe za nafaka

b. Waini

c. Pombe kali

21. Kiasi gani kwa wiki?

**a.** Kwa wastani nakunywa kwa siku ..... kwa wiki

**b.** Kwa wastani nakunywa chupa ..... kwa mara moja

22. Je unandugu aliyewahi kufariki ghafla akiwa na umri chini ya miaka sitini?
    **a.** Ndiyo .....
    **b.** Hapana .....

**Historia yako ya kiafya**

23. Je umewahi kupata kiarusi
    **a.** Ndiyo .....
    **b.** Hapana .....
24. Kama ndiyo hali hiyo ilidumu kwa muda gani?
    a. Chini ya masaa 24
    **b.** Zaidi ya masaa 24
25. Je umewahi kupata maumivu ya upande wa kushoto wa kifua yanayopungua ukipumzika
    **a.** Ndiyo .....
    **b.** Hapana .....
26. Je unatatizo la shinikizo la damu?
    **a.** Ndiyo .....
    **b.** Hapana .....
27. Kama ndiyo, unatumia dawa za shinikozo la damu?
    **a.** Ndiyo .....
    **b.** Hapana .....
28. Je unatatizo la ugonjwa wa kisukari?
    **a.** Ndiyo .....
    **b.** Hapana .....
29. kama ndiyo, unatumia dawa za kisukari?
    **a.** Ndiyo .....
    **b.** Hapana .....
30. Je unaugonjwa wowote sugu wa viungo?
    **a.** Ndiyo .....

**b.** Hapana .....

31. Je Uliwahi kuambiwa viwango vyako vya mafuta katika damu (Cholesterol) vimepanda?

**a.** Ndio .....

**b.** Hapana.....

32. Kama ndiyo, unatumia dawa zozote za kushusha kiwango cha mafuta mwilini?

**a.** Ndiyo ..... **b.** Hapana.....

# 8 APPENDIX IV: CONSENT FORM

## CONSENT FORM

Title: Assessment of risk factors for cardiovascular diseases among HIV infected patients attending Muhimbili National Hospital Care and Treatment Clinic

**Greetings,** I am Dr Amina Mgunya, a resident in the department of Internal Medicine. I would like to conduct the study above as a necessary requirement for fulfillment of my postgraduate studies .

The purpose of the study is to assess risk factors for cardiovascular diseases among HIV infected patients attending Muhimbili National Hospital Care and Treatment Clinic

This study requires you to participate so that important information can be obtained from you regarding your health.

If you agree to participate in the study, you will be interviewed, and a detailed clinical history will be requested. A blood sample will also be requested from your.

Confidentiality:
All information collected on questionnaires will be entered into computer with identification number. The questionnaires will be handled with greater secrecy in order to maintain confidentiality.

There is no risk associated with this study

Taking part in this study is completely voluntary. If you choose not to participate in the study, you will continue to receive all services that are normally provided in the clinic

If you agree to take part in this study, you will be evaluated for Cardiovascular risk factors, and in case of any appropriate measure will be taken including appropriate advice or prescription of medication if required.

If you have any question about the study, you can contact Dr Amina Mgunya 0784821207 and Dr J. Lwakatare, Department of Internal Medicine , MUHAS. If you have questions about your

rights as a participant, you may contact Prof Aboud, Chairman of MUHAS Research and Publications Committee. P.O.BOX **65001 Dar es Salaam.**

Do you agree?
Participant agrees…….. Participant does NOT agree……

I, _____have read/been told of the contents of this form and understood its meaning; hence, I do agree to participate in this study.

Signature_____ (Participant), Date_____

Signature_____ (Researcher), Date_____

**APPENDIX NO 2**

**FOMU YA RIDHAA**

**Utafiti kuhuru viashiria hatarishi vya kupata magonjwa ya moyo na mishipa ya mfumo wa damu miongoni mwa wagonjwa wanaoishi na virusi vya ukimwi katika hospitali ya taifa Muhimbili**

`

Salaaam!

Mimi naitwa Amina Mgunya ni mwanafunzi wa udhamili Chuo Kikuu cha Sayansi za Afya. Nafanya utafiti kuhuru viashiria hatarishi vya kupata magonnjwa ya moyo na mishipa ya mfumo wa damu miongoni mwa wagonjwa wanaoishi na virusi vya ukimwi katika hospitali ya taifa Muhimbili

**Jinsi ya kushiriki**

Kama utakubali kushiriki katika utafiti huu ,nita kuhoji maswali machache kuhusu ugonjwa wako na nitakuchukua damu kwa ajili ya vipimo.

**Madhara/usiri**

Hakuna madhara yoyote yanayotegemewa kutokana na utafiti huu.Taarifa za ugonjwa wako zitatunzwa kwa kutumia herufi maalum ili kuwa na usiri

**Uhuru wa kushiriki** ;

Kushiriki kwenye utafiti ni hiari yako.

Unaweza kujitoa wakati wowote. Kama utachagua kutoshiriki, utaendelea kupata huduma kama kawaida hapa hospitalini.

**Faida ya utafiti**

Ukishiriki kwenye utafiti huu , utachunguzwa kama unakiashiriria chochote cha kupata magonjwa ya moyo  na kama unacho chochote utatibiwea au kupewa  ushauri.

**Taarifa**

Kuna kamati ya kusimamia udhibiti wa Utafiti huu.

Endapo unahitaji kupata maelezo kuhusu haki zako au taarifa ,wasiliana na Dr Amina Mgunya 0784821207  au  Dr J. Lwakatare,  wa chuo kikuu cha Afya na tiba Muhimbili. Kama unaswli lolote kuhusu haki yako kama mshiriki wasiliana na  Prof Aboud, ambaye ni mwenyekiti wa bodi ya utafiti chuo kikuu cha  Afya na Tiba Muhimbili,  kwa S.L.P  **65001 Dar es Salaam**

Baada ya maelezo hayo , Je unakubali kushiriki kwenye utafiti? (weka alama)  ya vema,
Ndiyo.....Hapana.....
Mimi ....., nimeelezwa na nimesoma maelezo
haya.  Maswali yangu yamejibiwa.
Nimekubali kushiriki katika utafiti huu.
Sahihi ya mtafiti..... Tarehe…….

Sahihi ya Mtafiti ..... . Tarehe……

# Annex V

**Table 9:WHO clinical staging for HIV**

| Clinical Stage 1 |
| --- |
| • Asymptomatic<br>• Persistent generalized lymphadenopathy |
| Clinical stage 2 |
| • Moderate unexplained weight loss (<10% of presumed or measured body weight)<br>• Recurrent respiratory infections (sinusitis, tonsillitis, otitis media, and pharyngitis)<br>• Herpes zoster<br>• Angular cheilitis<br>• Recurrent oral ulceration<br>• Papular pruritic eruptions<br>• Seborrheic dermatitis<br>• Fungal nail infections |
| Clinical stage 3 |
| • Unexplained severe weight loss (>10% of presumed or measured body weight)<br>• Unexplained chronic diarrhea for >1 month<br>• Unexplained persistent fever for >1 month (>37.6°C, intermittent or constant)<br>• Persistent oral candidiasis (thrush)<br>• Oral hairy leukoplakia<br>• Pulmonary tuberculosis (current)<br>• Severe presumed bacterial infections (eg, pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)<br>• Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis<br>• Unexplained anemia (hemoglobin <8 g/dL)<br>• Neutropenia (neutrophils <500 cells/µL)<br>• Chronic thrombocytopenia (platelets <50,000 cells/µL) |
| Clinical stage 4 |
| • HIV wasting syndrome, as defined by the CDC (see Table 3, above)<br>• *Pneumocystis* pneumonia<br>• Recurrent severe bacterial pneumonia<br>• Chronic herpes simplex infection (orolabial, genital, or anorectal site for >1 month or visceral herpes at any site)<br>• Esophageal candidiasis (or candidiasis of trachea, bronchi, or lungs)<br>• Extrapulmonary tuberculosis<br>• Kaposi sarcoma<br>• Cytomegalovirus infection (retinitis or infection of other organs) |

- Central nervous system toxoplasmosis
- HIV encephalopathy
- Cryptococcosis, extrapulmonary (including meningitis)
- Disseminated nontuberculosis *Mycobacteria* infection
- Progressive multifocal leukoencephalopathy
- Candida of the trachea, bronchi, or lungs
- Chronic cryptosporidiosis (with diarrhea)
- Chronic isosporiasis
- Disseminated mycosis (eg, histoplasmosis, coccidioidomycosis, penicilliosis)
- Recurrent nontyphoidal *Salmonella* bacteremia
- Lymphoma (cerebral or B-cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy
- Symptomatic HIV-associated cardiomyopathy