# FATTY LIVER DISEASE AND ITS CORRELATES AMONG PEOPLE LIVING WITH HIV ATTENDING CARE AND TREATMENT CLINIC AT TEMEKE REGIONAL REFERRAL HOSPITAL, DAR ES SALAAM, TANZANIA

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# FATTY LIVER DISEASE AND ITS CORRELATES AMONG PEOPLE LIVING WITH HIV ATTENDING CARE AND TREATMENT CLINIC AT TEMEKE REGIONAL REFERRAL HOSPITAL, DAR ES SALAAMTANZANIA

**By**

**Farida Mohamed Mtonga, MD**

**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 Science**
**October, 2021.**

## CERTIFICATION

The undersigned certifies that, they have read and hereby recommend for examination by Muhimbili University of Health and Allied Sciences a dissertation entitled: ***"Fatty Liver Disease and its correlates among People Living with HIV/AIDS attending Care and Treatment Clinic at Temeke Regional Referral Hospital in Dar es Salaam"*** in partial fulfillment of requirement for the degree of Master of medicine in Internal Medicine Muhimbili University of Health and Allied Sciences.

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## DECLARATION AND COPYRIGHT

I, **Dr Farida Mohamed Mtonga** declare that this **dissertation** is my 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: ……..**

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## DEDICATION

This research is dedicated to my beloved parents, Mr. and Mrs. Mohamed Mtonga and my family. Your encouragement and support to my studies development is beyond measure, nothing can ever replace your love and support. I pray to God that He gives you the best in this world and hereafter.

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**LIST OF ABBREVIATION(s)**

| | |
|---|---|
| ALT | Alanine Aminotransferase |
| ART | Antiretroviral Therapy |
| BMI | Body Mass Index |
| CTC | Care and Treatment Clinic |
| ESLD | End stage Liver Disease |
| FLD | Fatty Liver Disease |
| HBV | Hepatitis B virus |
| HCV | Hepatitis C virus |
| HIV | Human Immunodeficiency Virus |
| *IL* | Interleukin |
| IR | Insulin resistance |
| MUHAS | Muhimbili University of Health and Allied Sciences |
| NAFLD | Nonalcoholic Fatty Liver Disease |
| NNRTI | Non-Nucleoside Reverse Transcriptase Inhibitor(s) |
| NRTI | Nucleoside Reverse Transcriptase Inhibitor(s) |
| PIs | Protease Inhibitor(s) |
| PLHIV | People Living with HIV |
| TLD | Tenofovir Disoproxir Fumarate + Lamivudine+ Dolutegravir |
| *TNF* | Tumor Necrosis Factor |
| TRRH | Temeke Regional Referral Hospital |

## DEFINITION OF TERM(S)

Fatty Liver Disease (FLD) was defined as increased hepatic echogenicity compared to right kidney by using abdominal Ultrasound (1)

Dyslipidemia was defined as fasting serum Low Density Lipoprotein (LDL) cholesterol ≥ 130 mg/dl and/or fasting total serum cholesterol ≥ 200 mg/dl (2)

Diabetes mellitus was defined as fasting blood glucose (FBG) ≥7 mmol/L or random blood glucose (RBG) ≥11.1 mmol/L plus hyperglycemic symptoms OR known to be diabetic on management(3).

Central obesity was defined as waist circumference > 90 centimeter in males and >84 centimeter in females (4).

Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure≥ 90 mmHg or known to have hypertension on antihypertensive medication(5).

## ABSTRACT

**Introduction:** Fatty Liver Disease (FLD) is projected to be the leading cause of chronic liver disease among People living with HIV (PLHIV)

**Objectives:** This study aimed at determining the prevalence and associated factors for Fatty Liver Diseases among People living with HIV attending Care and Treatment Clinic at Temeke Regional Referral Hospital in Dar es Salaam, Tanzania.

**Materials and methods**: A hospital-based descriptive cross-sectional study was conducted between

September and November 2020. Consenting adults aged ≥18 years and living with HIV were enrolled in the study. A structured questionnaire was used to collect socio-demographic, anthropometric measurements and clinical characteristics. Patients were fasted for a minimum of 8 hours before undergoing an abdominal USS, using B-mode and 3.5 MHz convex probe transducer (Dawei-DW 580, China, 2020) was done by a single trained investigator. FLD was defined as increase in liver echogenicity compared to the right kidney. Interpretation of USS images was done by a trained investigator and senior radiologist .Independent predictors of FLD were analyzed using multivariate logistic regression; p value of < 0.05 was considered to be statistically significant.

**Results**: A total of 454 patients were enrolled into the study. FLD was seen in 118 patients, making a prevalence of 25.9% (95% CI 22.0%-30.3%). Age group 40-60 years (aOR 1.74; 95% CI: 1.02 – 2.96 p=0.043), overweight (aOR 1.92; 95%CI: 1.05-3.51: p =0.034), obesity (aOR 3.46; 95% CI: 1.80 – 6.65: p < 0.001) and dyslipidemia (a OR: 2.63 95%CI: 1.58-4.39; p < 0.001) were significantly associated with FLD. HIV viral load status, duration on combination antiretroviral therapy had no association with FLD**. .**

**Conclusion and Recommendations**: One out of four PLHIV had FLD. Factors associated with FLD were age 40-60 years, overweight, obesity and dyslipidemia. We recommend weight reduction and regular screening for FLD among PLHIV with above risk factors.

# CHAPTER ONE

## 1.0 INTRODUCTION

### 1.1 Background

#### 1.1.1 Definition of FLD

Fatty Liver Disease (FLD) is the pathological accumulation of fat in the hepatocytes (more than 5%) of total liver weight (6–8). Broadly, FLD can be classified as alcoholic or nonalcoholic. Increasingly, FLD is recognized as a spectrum of diseases comprising of simple steatosis, steatohepatits, and fibrosis (6).

#### 1.1.2 Epidemiology

The prevalence of FLD among PLHIV in the world ranges between 30%- 65%; wider range of variation depending on diagnostic method used (9). Most of the studies reporting these figures were done in America, Europe and Asia. FLD is more common in males compared to females (10,11). In Tanzania, the prevalence of FLD among PLHIV is not known.

By the end of 2019, approximately 38 million people were living with Human Immunodeficiency Virus (HIV) infection globally and 67% were on combination antiretroviral therapy (ART) (12). In Tanzania, coverage of combination ART is about 75% (13). Available combinations ART in our country are Nucleos (t) ide Reverse Transcriptase
Inhibitors (NRTI); Tenofovir, Lamivudine, Emtricitabine, Zidovudine, Abacavir, NonNucleoside Reverse Transcriptase Inhibitors (NNRTI); Nevirapine, Efavirenz, Protease Inhibitors (PIs); Ritonavir, Lopinavir, Atazanavir, and the newly introduced class Integrase Strand Transfer Inhibitor-Dolutegravir.

Chronic liver diseases are the leading cause of morbidity and mortality in this population, due to declining opportunistic infection with wider coverage of effective combination ART (6,14).

### 1.1.3 Pathogenesis and Risk factors

Chronic hepatitis C and B infection, excessive alcohol consumption, metabolic syndrome (dyslipidemia, central obesity, hypertension, and diabetes mellitus) are the leading causes of FLD (7,14). Also genetic disorders of lipid and carbohydrate metabolism like Patatin-like phospholipase containing domain 3 (*PNPL3*) polymorphism have been documented to be the potential cause of FLD(7).

The core pathogenesis towards FLD is insulin resistance(6,7,15). Impaired suppression of hormone-sensitive lipase leads to inappropriate accumulation of fatty acids in the liver due to excessive break down of triglycerides in adipose tissue. In addition, studies have shown that insulin resistance enhances hepatic lipid synthesis (6).

People living with HIV (PLHIV), have additional risk factors which include HIV infection, combination antiretroviral therapy (ART), gut bacterial translocation and HIV-associated lipodystrophy. HIV infection induces chronic inflammation, the release of pro-inflammatory cytokines (*TNF* α and *IL* 6) which leads to insulin resistance (16). Nucleoside reverse transcriptase inhibitors (NRTI) such as Stavudine and Didanosine and Protease Inhibitors (PIs) have been blamed to contribute in pathogenesis of FLD by impairing hepatic mitochondrial γ polymerase causing mitochondrial toxicity and insulin resistance respectively(17).

### 1.1.4 Diagnosis of FLD

The gold standard diagnosis of FLD is histopathological findings on liver biopsy (6,7).However, it is not routinely done since it is an invasive test, associated with several risks; bleeding and infection; as well as requiring high expertise (6). Abdominal ultrasound is an alternative, widely available, noninvasive radiological investigation; it has a sensitivity of 85% and specificity of 94% in diagnosing FLD(18). This method is not sensitive in diagnosing mild FLD and it has inter-observer variability. Transient elastography, a new noninvasive procedure validated for use in diagnosis of FLD where Controlled Attenuation Parameter(CAP) and liver stiffness measurements (LSM) are able to quantify hepatic steatosis and fibrosis respectively(19).

Magnetic resonance imaging proton fat fraction sensitivity in diagnosing FLD is approaching 100 %(6), but is not readily available in developing countries. Moreover computed tomography is reliable alternative means of diagnosis but is associated with a high radiation exposure (20)..

### 1.1.4 Management of FLD

Management of FLD involves multidisciplinary approach; pharmacological and non-pharmacological. Non-pharmacological approach includes weight reduction for those who are obese. This was evidenced in previous study whereby weight loss resulted in decrease of pathological hepatic fat content and hepatic inflammation(21). Healthy diet intake (low calories), regular exercise and cutting down alcohol intake are among life style modification recommended in the management of FLD(6,21,22). PLHIV should be prescribed medication including combination ART which do not cause dysregulated lipid metabolism (22).

There is no definitive pharmacological treatment for FLD, although in previous trials Pioglitazone and Vitamin E have been shown to regress histopathological findings in non HIV infected population (23)**.** In a current single trial done in China among PLHIV, Vitamin E has shown reduction in enzymatic markers of hepatocellular injury and CAP scores (24).

### 1.1.5 Complications of FLD

Hepatic and extra hepatic complications of FLD include liver cirrhosis, hepatocellular carcinoma, cardiovascular diseases and type 2 diabetes mellitus (6,7,25). In elderly, neurocognitive decline and reduced body strength have been reported (26).

### 1.1.6 Prevention

Prevention of FLD involves proper management of components metabolic syndrome such as diabetes mellitus and dyslipidemia. Lifestyle modification including weight reduction, healthy diet intake, and regular aerobic exercise are important preventive measures (6,7,22).

## 1.2 Literature Review

Human Immunodeficiency virus (HIV) infection has been known to be associated with Fatty Liver Disease (FLD). This is due to the ability of the virus to impair the function of peroxisome proliferator-activated receptor gamma (PPARɣ) which leads improper lipid and carbohydrate metabolism (27)**.** In addition, PPARɣ induces chronic inflammatory state, leading to increased production of pro-inflammatory cytokines which increase the production of reactive oxygen species causing hepatic fatty degeneration. Furthermore, HIV infection increases intestinal wall permeability, favoring bacterial translocation. This triggers surge of pro-inflammatory markers leading to insulin resistance, which is a significant step towards FLD pathogenesis (6,7,22). A study done in Asia showed that people living with HIV (PLHIV) were four times likely to have FLD compared to those without HIV (28)

### 1.2.1 Prevalence of FLD

Prevalence of FLD varies significantly across the globe depending on the method of diagnosis. Globally, the prevalence of FLD in a meta-analysis study by Maurice et al among PLHIV by using Abdominal Ultrasound (USS) was 35 %(9)**.** In a study done by Nishijima et al, among PLHIV in Asia who had no chronic hepatitis B nor Hepatitis C virus infection and who were non-hazardous alcohol consumers, the prevalence of FLD by USS was found to be 31%(29). Furthermore in a study done by Morse CG et al among PLHIV without type 2 diabetes mellitus ( T2DM), viral hepatitis nor using alcohol, prevalence of FLD was high (65%) by using histopathological finding of the liver biopsy as a diagnostic test (30)**.**

### 1.2 .3 Risk factors associated with FLD

Studies have revealed contradicting results regarding effects of combination ART towards pathogenesis of FLD. The purpose of combination ART is to maximally suppress the HIV disease progression; hence improve quality of life among PLHIV (6). Despite this desirable positive effect, Protease inhibitors (PIs), Nucleoside Reverse Transcriptase Inhibitors (NRTIs) have been associated with dyslipidemia and metabolic syndrome causing inappropriate accumulation of fat in the liver and peripheral tissues due to their potential of causing mitochondrial toxicity(6,7,25,27).

Studies done by Nishijima et al (29) and Lesi O et al (25) reported that FLD was neither associated with the type nor the duration of combination ART regimen among PLHIV in Asian and Nigerians respectively. On the contrary Price J et al found that initiation of combination ART slowed the progression of FLD to chronic liver disease on patients with suppressed HIV viral load (31). Moreover, in a cross sectional study done in rural Uganda, combination ART was shown to be protective towards progression of FLD to hepatic fibrosis among PLHIV (32).

Previous studies have shown that dyslipidemia is an independent risk factor for development of FLD (14,20,25,29). In a study done by Crum-Cianflone et al in California, among PLHIV, those with hypertriglyceridemia were 1.4 times likely (p value <0.001) to develop FLD than those with normal triglyceride levels (10). Furthermore, in a study done in Nigeria, the prevalence of hypertriglyceridemia among PLHIV with FLD was 7 % and serum low density lipoprotein cholesterol ≥130 mg/dl was significantly associated with FLD (25). Although there are no studies to show relationship between combination ART and FLD in Tanzania, dyslipidemia is very common. Armstrong C et al showed that among a cohort of ART treatment naïve, the prevalence of dyslipidemia was 76% (33) but prevalence of FLD was beyond the scope of that study**.**

PLHIV are more likely to have type 2 diabetes mellitus T2DM (Relative Risk 2.4) compared to the general population (34)**.** In a serial cross sectional study done in United States of America(USA) among 2472 PLHIV, among those with Non Alcoholic Fatty liver Disease (NAFLD), 2176( 88% )of them had T2DM (35). On the contrary, a study done by Nishijima et al among PLHIV, diabetes mellitus was not associated with FLD ,p value= 0.308(29).

Various studies have shown the association between overweight/obesity and FLD (6,7,27,36). A study done in Italy by Guaraldi et al which was assessing prevalence, factors and predictors of NAFLD among HIV patients clearly showed that elevated waist circumference (OR 1.07; 95% CI, 1.03–1.11) was significantly associated with FLD(11). On the contrary, Mohammed S et al found significant proportion of people infected with HIV who were not obese, had FLD (37) suggesting that correlates and pathogenesis of FLD in this group could be different from that occurring in general population.

Hypertension is not uncommon in PLHIV (38,39). As other components of metabolic syndrome, hypertension is associated with chronic inflammatory state which predisposes PLHIV to develop FLD. Paik et al found that 80% of PLHIV who were diagnosed to have FLD were hypertensive(35).Furthermore, In another study done in Asia, demonstrated association between Hypertension and FLD, p value=0.019 (29). In contrary, Lesi O et al (25) did not find significant association (p=0.13) between Hypertension and FLD.

Alcohol is one of the established independent risk factors for FLD(6,7). Hazardous alcohol drinking, intake of more than three units in females and more than four units in males (6,22) increases the risk of developing FLD. Alcohol consumption is not uncommon among PLHIV(39–41) and it has been linked to poor drug adherence(40).A recent local study which was assessing prevalence of alcohol drinking among TB/HIV co-infected patient, the prevalence of heavy alcohol drinking was found to be 15% (40) More over in a study done in Uganda among PLHIV, those who consumed alcohol heavily were more likely to have liver fibrosis, the etiology for FLD was beyond the scope of that study (32). Alcohol is presumed to cause chronic inflammatory state, increasing oxidative stress, bacterial gut translocation, favoring development and progression of FLD

Several studies have shown contradicting results on the contribution of sex on FLD. A study done by Guaraldi et al which used CT-scan as a diagnostic tool in assessing FLD, male sex was significantly associated with FLD ($p < 0.001$)(11). Contrary to that studies conducted in Nigeria (25) and Brazil (10) showed no preponderance of FLD among males.

Normal ageing process of the liver involves impaired regeneration capacity, reduction hepatic blood flow and impaired mitochondrial function (41). A study by Lonardo A et al, showed a decrease of FLD above $6^{th}$ decade of life (42), and this could be due to the fact that the severe form of steatohepatitis results in increased production of adiponectin which is protective against FLD (43)

# CHAPTER TWO

## 2.1 Problem Statement

Fatty liver disease is common among PLHIV with a global prevalence of FLD among PLHIV estimated to between 30%-65 %(9). Liver cirrhosis, one of the fatal complications of FLD causes one million deaths in the world (44). In 2015, the mortality rate due to liver cirrhosis, hepatocellular carcinoma and other liver related diseases in Sub Saharan Africa in the general population was 1.9% (41).

PLHIV are at increased risk of suffering from FLD, due to virus' ability to induce chronic inflammatory state, which leads to poorly regulated lipid metabolism (27). Also viral proteins activate hepatic Kupffer cells and stellate cells towards fibrogenesis, hence leading to liver fibrosis (15,30). Furthermore, the combination antiretroviral therapy (ART) causes undesirable effects which are weight gain and metabolic syndrome leading to insulin resistance which leads to hepatic steatosis (15).

Previous studies done in Tanzania by Nagu TJ et al and Mugusi S et al have revealed that raised serum alanine aminotransferase, a marker of hepatocellular injury, is prevalent among PLHIV (45,46), however the causes for the transaminitis were not fully explored. Furthermore in a local study by Armstrong C et al, this cohort had statistically significant elevated serum triglyceride levels (2). A raised serum triglyceride level is independent risk factor for development of FLD among PLHIV (25). Given that there is limited evidence for the magnitude of FLD and associated factors among PLHIV in our set up, and that FLD contributes to increased morbidity and mortality among PLHIV in Tanzania, this study comes timely to fill this gap. Therefore, this study aims to determine the prevalence and explore associated factors for FLD among people living with HIV in Dar es Salaam Tanzania.

## 2.2 Conceptual Framework

Non communicable and particularly End Stage Liver Diseases (ESLD) is increasingly recognized as non-AIDS cause of mortality and morbidity (3). Major contributors being chronic hepatitis B and C infection, alcoholic and non-alcoholic liver diseases (4). As illustrated below, factors such as diabetes mellitus, obesity, hypertension, dyslipidemia, combination antiretroviral therapy contribute to FLD through inducing insulin resistance hence leading to impaired lipid metabolism (3, 4).

HIV infection impairs gut wall integrity, facilitating translocation of micro-biome from the gut to the liver. This induces insulin resistance due to production of pro-inflammatory cytokines such as TNF α in response to bacterial by products. Moreover, HIV infection worsens FLD as it accelerates progression of FLD from simple steatosis to steatohepatitis, and cirrhosis by increase expression of pro-inflammatory chemokines, which promote liver fibrosis (4).

Combination antiretroviral therapy classes that have been shown to be associated with FLD include early generation Nucleoside reverse transcriptase inhibitors (NRTI) such as Stavudine and Protease inhibitors (PI) such as Indinavir. These induce mitochondrial toxicity augmenting adipocyte cell death; complicating to lipodystrophy and insulin resistance (6,7,22).

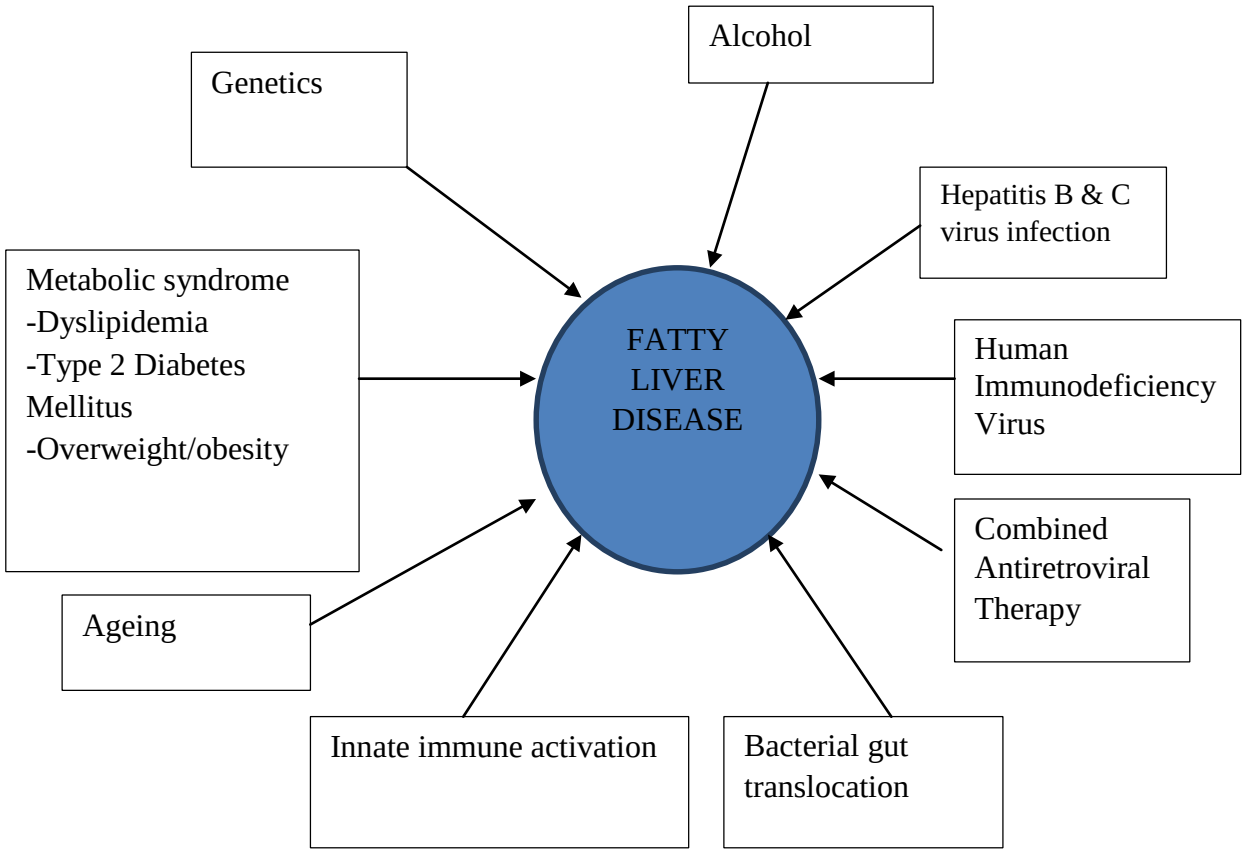


**Figure 1: Diagrammatic presentation indicating pathogenesis and related factors of Fatty Liver Disease**

## 2.3 Rationale

With the lack of local studies conducted on the prevalence of Fatty Liver Disease (FLD) among People Living with HIV (PLHIV), this study serves to provide insight on the magnitude of this problem in our set up.

The study will increase awareness among attending clinicians on FLD in PLHIV, increase the emphasis on screening for FLD and consequently improve early detection of the condition. Early diagnosis and addressing factors that cause FLD is known to halt the progression to chronic liver disease. Knowledge of factors associated with FLD in our context will empower clinicians, researchers and public health specialists to plan for necessary interventions and priority areas for primary as well as secondary prevention. Consequently, the study will contribute towards averting health and financial burdens associated with the FLD.

This study could potentially form the basis for larger interventional studies in search of potential therapeutic and/or preventive agents for FLD among PLHIV.

## 2.4 Research Questions

What is the prevalence of FLD among people living with HIV attending CTC at Temeke Regional Referral Hospital (TRRH) in Dar es salaam, Tanzania?

What factors are associated with FLD among people living with HIV attending CTC at TRRH in Dar es salaam, Tanzania?

## 2.5 Objectives

### 2.5.1 Broad objective

To determine the prevalence and factors associated with FLD among people living with HIV attending CTC at TRRH in Dar es salaam, Tanzania.

### 2.5.2 Specific objectives

i. To determine prevalence of FLD among people living with HIV who attend CTC at TRRH
ii. To determine factors associated with FLD among people living with HIV who attend CTC at TRRH

# CHAPTER THREE

## 3.0 MATERIALS AND METHODS

### 3.1 Study design and settings

This was a hospital-based cross-sectional descriptive study, done at Temeke Regional Referral Hospital (TRRH) from September 2020 to November 2020.

### 3.2 Study population

The study included people living with HIV/AIDS attending CTC at TRRH

#### 3.2.1 Inclusion criteria

i. PLHIV on combination Antiretroviral Therapy for one year or more (≥ 1year)
ii. Age ≥ 18 years
iii. Attending HIV care and treatment at TRRH

#### 3.2.2 Exclusion criteria

i. None

### 3.3 Description of study site

The study was conducted at Temeke Regional Referral Hospital (TRRH) in Dar es Salaam. The hospital operates CTC services from Mondays to Saturdays. The CTC serves 7000 clients in total, majority (70%) being cost sharing, and others being health insured and out of pocket. Average number of clients being served per week is 500. Stable clients attend clinic after every three or six months.

The clinic is run by medical officers and nursing officers. The clinic provides services to PLHIV such as combination ART initiation and refill, screening and treatment of opportunistic infections. Baseline laboratory investigations such as Full Blood Count, liver function test

(serum *Alanine aminotransferase* levels), renal function test (serum creatinine) and CD4 cell count measurements are performed prior to initiation of combination ART. Quantitative HIV viral load levels are done six months after initiation of combination ART. Clients with HIV viral load <1000 copies/mil, the test is repeated after six months. If on repeat test, the HIV viral load <1000copies/mil; the test is being done on annually. If after six months post initiation of combination ART, HIV viral load remains >1000copies/mil, the client will have to be subjected to Enhanced Adherence and Counseling, and the test repeated after three months. According to Tanzania National HIV/AIDS guideline, the presence of HIV viral load > 1000copies/mil for a minimum of six months is regarded as virological failure. Screening for Non-Communicable Diseases is not routinely performed in the clinics we selected.

### 3.4 Sample size estimation

To determine the minimal sample size required the following for formula for cross sectional studies was used $n=z^2 \times p(1-p)/ \square^2$ n= minimum sample size z =standard normal deviation (1.96)

p=Prevalence of alcohol consumption among patient with HIV diagnosed to have FLD by Abdominal USS done by Lesi A.O et al in Nigeria was 20%
(25).

$\square$ = maximum likely error taken as 4% $n= 1.96^2 \times 0.20(1-0.20)/0.04^2$ n= 384

Taking non response rate as 10%

The minimum sample size obtained was 422, Prevalence of alcohol consumption was used in sample size calculation considering its established association with FLD and it provided large sample size.

### 3.5 Sampling method

Consecutive recruitment was used to enroll study participants during data collection. PLHIV were introduced to the study during morning health session upon attendance at Care and Treatment Clinic (CTC). Informed consent was obtained from PLHIV who were willing to participate in the study, after being clearly explained and understanding the purpose of the study. Recruitment process was conducted on clinic days until the required sample size was attained.

### 3.6 Data collection procedure

#### 3.6.1 Patient interview

The investigator and two assistants collected research data. Assistants were employed qualified nurses who had been working at Care and Treatment Clinic (CTC) for more than 3 years. They were trained for 2 days on how to take anthropometric measurements. Assistants were also familiarized into nature of interview that was used to gather data using structured Swahili questionnaire. They were also collecting blood samples for laboratory investigations.

The structured questionnaires were pre-tested for data collection from a convenience sample of PLHIV at Temeke Regional Referral Hospital for three consecutive days. This helped to identify and address shortcomings before the actual start of data collection

The questionnaire comprised of 4 sections; socio-demographic, clinical, laboratory and radiology sections for data collection.

#### 3.6.2 Clinical examination

**Blood Pressure Measurement**

Blood pressure measurements were taken in sitting position after rest for five minutes using a calibrated automated sphygmomanometer *Omron*® with the left arm positioned on the same level as the heart. The cuff was placed approximately 1/2" above the elbow, centered the arrow to align with the middle finger. Then it was wrapped firmly around the arm using the cloth

fastening. The study participant was asked to keep still and without talking during measurement. The START/STOP button was pressed and inflation started. Systolic and diastolic blood pressures displayed in the monitor were then recorded.

A set of three readings were taken, and the average of the readings was considered as the study participant's office blood pressure (BP).

**Anthropometric measurements**

Study participants' heights were measured using a stadio-meter with the shoes off, and without head caps and results were recorded to the nearest 0.5 centimeter.

Without shoes and by using calibrated weighing SECCA scale, study participants' weights were recorded to the nearest 0.5 kilogram.

Body Mass Index (BMI) was calculated as weight in kilograms divided by height in metres squared. BMI was interpreted as per WHO recommendation that is underweight BMI < 18 $kg/m^2$, normal 18.5 $kg/m^2$ and 24.9 $kg/m^2$, overweight BMI between 25$kg/m^2$ and 29.9$kg/m^2$, and obese > 30 $kg/m^2$ (4).

**Waist circumference**

Waist circumference was measured by using non-stretchable tape at the midline point from the lower margin of the last palpable rib and the top of iliac crest

**Neck Circumference**

Neck circumference in centimeter (cm) was measured below was measured by using non-stretchable tape measure just above the cricoid cartilage and perpendicular to the long axis of the neck. Study participants were kindly asked to extend the neck to facilitate measurement. Starting from the small prominence of the thyroid cartilage, light pressure was applied using the forefinger and middle finger, moving downwards to find a small space and subsequently the cricoid cartilage.

**Hip circumference** was measured at the level of maximal gluteal protrusion (females only) by using a non-stretchable tape.

**Body fat percent**

Body fat percent was calculated using the following anthropometric measurements; neck circumference, waist circumference, hip circumference, and height (both in inches) using the following formula (47).

The equation for women was:

% body fat= [163.205 x Log10 (waist + hip – neck)] – [97.684 x Log10 (height)] – 78.387

The equation for men was:

% body fat= [86.010 x Log10 (waist – neck)] – [70.041 x Log10 (height)] + 36.76

The following were predicted healthy (normal ranges) body fat percent according to sex and age group (48).

**Table 1: Healthy body fat percent ranges**

| Age | Healthy Body %(women) | Healthy Body %(Men) |
|---|---|---|
| 20-39 | 21%-32% | 8%-19% |
| 40-59 | 23%-33% | 11%-21% |
| 60-79 | 24%-35% | 13%-24% |

### 3.6.3 Laboratory Methods

**Fasting/Random Blood Glucose**

Under sterile procedure, capillary fingertip blood glucose measurement was done for each study participant on attendance at the clinic. Fasting /Random blood glucose were measured by using the G*lucoPlusTM* glucometer and reported in mmol/l.

**Serum Lipid profile**

Aseptically, 5mls of whole blood was drawn from median cubital vein then collected in vacutainer tubes (BD, NJ USA) for measurements of low density lipoprotein (LDL) cholesterol and total cholesterol. A minimum 8 hours of fasting were the prerequisite for this investigation. For those who consented and did not meet the required hours of fasting, socio-demographic and anthropometric measurement were done, and kindly requested to come early morning (from 8.00 am) working days for completion of fasting serum lipid measurement. At Temeke Regional Referral Hospital laboratory the collected sample was allowed to clot. Clear serum was obtained by centrifugation at 3000rpm for five minutes, then collected by using Pasteur pipette and stored in refrigerator at 4 degrees Celsius. Serum lipids (Low Density Lipoprotein cholesterol and total cholesterol) were measured by using calibrated Erba XL-100 /Clinical chemistry (Transansia Biomedicals, India/20 and reported in mg/dl**.**

**HIV/RNA viral load**

HIV RNA viral load measurements were done every six months as per national CTC protocols. Our study used recorded results taken within six months period as uploaded in electronic data base or patient file(s). For study participants who did not have recent viral load results, about 5mls of whole blood sample was collected in EDTA bottle. Plasma HIV 1 RNA levels were tested using the Abbott m2000system (Abbott Molecular Inc., Wiesbaden, German).Upon any delay in processing the samples, plasma was kept in a refrigerator at 2 -8 Degree Celsius for not more than five (5) days or frozen at -20 degree Celsius or lower temperature for longer storage.5 mL of venous blood was kept in the plasma preparation tube containing EDTA gel (shelf life of

6 hours) and centrifuged. Plasma was taken to the viral load testing machine for extraction in 3 hours and amplification and followed by detection for 3 hours to get the RNA measure. HIV /RNA <1000 copies/ml was regarded as virological suppression (13)**.**

### 3.6.4 Abdominal Ultrasonography

Abdominal USS was done after fasting for at least 8 hours, study participants whom had not were not fasted for the required duration were kindly requested to come the next morning or any day of their convenience. FLD assessment was done using a 3.5 MHz convex probe transducer (Dawei-DW 580, China, 2020) using a B mode. Abdominal USS was performed by a trained investigator. Study participants' particulars (age, sex, CTC card number) were entered in the USS machine and the machine was set on abdominal examination mode. Investigator asked the participant to lie on left lateral position, with the right arm raised above his/her head to widen the intercostal acoustic window. Ultrasound gel was applied over the right subcostal margin along mid axillary line. The transducer placed over the gel in parasagittal plane for visualization of cross-section of right liver and kidney.

A minimum of two images upon breath holding after deep inspiration for few seconds were frozen and saved. Stored images were interpreted by a trained investigator and a senior radiologist. Upon discordance, the interpretation of the senior radiologist was taken as final.

### 3.7 Data management and analysis

Questionnaires were checked for consistency, validity and missing information before data entry. Data entry was done using Epi Data software version 3.1. The prevalence of Fatty Liver Disease (FLD) was calculated as total number of study participant with FLD divided by total number of people living with HIV attending CTC at Temeke Regional Referral Hospital enrolled in the study.

Categorical variables were summarized using proportions and were compared using Chi square test. Continuous variables were summarized by means (SD) or medians (IQR) and analyzed using Student's t-test or Chi square test.

Univariate logistic regression analysis was used to identify factors associated with FLD. All variables with p values <0.2 at univariate analysis were entered into multivariate logistic regression models. In addition, sex was added into the multivariable model despite being non-significant at univariate analysis as it is a known confounder a priori. The odds ratio (OR) and 95% confidence interval (95%CI) were used to estimate the association of each variable with FLD. All statistical analyses were performed with The Statistical Package for Social Sciences (SPSS) version. 26, $p < 0.05$ was considered significant.

**Outcome variable**

**Fatty Liver Disease**

Fatty Liver Disease (FLD) as a categorical variable in this study was defined as presence of hepatic steatosis presented as increased hepatic echogenicity compared to the right kidney.

The following were the grades of FLD (8).

Grade 0: Normal liver echogenicity

Grade 1: Mild, increase in fine echoes in liver parenchyma with a normal visualization of diaphragm and intrahepatic vessel borders

Grade 2: Moderate, increase in fine echoes with slightly impaired visualization of intrahepatic vessels and diaphragm

Grade 3: Marked, increase in fine echoes with poor or non-visualization of the intrahepatic vessel borders, diaphragm, and posterior right lobe of the liver

**Independent Variables**

The following variables were used to assess their association with FLD among people living with HIV (PLHIV) on combination ART attended Care and Treatment Clinic (CTC) at Temeke Regional Referral Hospital.

Age, sex, level of education, marital status, current history of alcohol consumption, type of alcohol containing drink consumed, hazardous alcohol consumption, ever history of cigarette smoking, hypertension, central obesity, body mass index ($kg/m^2$), body fat percent, diabetes mellitus, Low density cholesterol (mg/dl), total density cholesterol (mg/dl), dyslipidemia, HIV viral load status, current combination ART regimen and duration on combination ART.

**Hypertension**

Hypertension was defined as systolic blood pressure ≥ 140mmHg and/or diastolic blood pressure ≥ 90 mmHg or known to have hypertensive on antihypertensive medication (5).

**Central obesity**

Central obesity was defined as per WHO guideline as waist circumference >90 centimeter in males and > 84 centimeter in females (4).

**Diabetes mellitus**

Study participant was regarded to have diabetes mellitus if (FBG ≥7 mmol/L) OR RBG ≥11.1mmol/l plus hyperglycemic symptoms (3). OR study participant is known to be diabetic and has been on anti-diabetic management.

**Dyslipidemia**

In this study dyslipidemia was defined as fasting serum LDL cholesterol levels ≥ 130 mg/dl and/or total serum cholesterol levels ≥ 200 mg/dl (2)

**Hazardous alcohol drinking**

Significant alcohol drinking was defined as drinking more than four and more than three alcohol units per occasion for males and females respectively (4). This was equivalent of taking more than two regular beers (approximately 350 mils, 5% alcohol) for females and more than three for males

**Duration of combination ART**

In this study, duration of combination ART was regarded as the number of years the patients has been on combination ART. Study participant was asked for the first ever CTC card if he/she has for documentation of duration. For those who did not have their first treatment CTC card, we relied upon self-report.

**Current combination ART duration**

Current combination ART regimen was defined as the combination ART regimen used by study participant for minimum duration of 6 months. This information was recorded from recorded from study participant's patient CTC card.

### 3.8 Ethical clearance and patient disposal

Ethical approval for conducting this research was obtained from the MUHAS research and publication committee of MUHAS. Permission to conduct the study was obtained from the administration of Temeke Regional Referral Hospital administration. Written informed consent from participants was obtained prior recruitment to the study. Study participants were informed of the study objectives possible risks that may occur, their right to participate, that their withdrawal would not affect their disease management.

Confidentiality was ensured throughout the study period. Questionnaires were stored in a safe locker, whose keys were managed by the principal investigator. Abnormal clinical findings were communicated with the attending clinicians for appropriate disposal and/or referrals of patients.

# CHAPTER FOUR

## 4.0 RESULTS

Between September and November 2020, a total of 454 study participants were recruited into the study as shown in the flow chart (**Figure 2**)

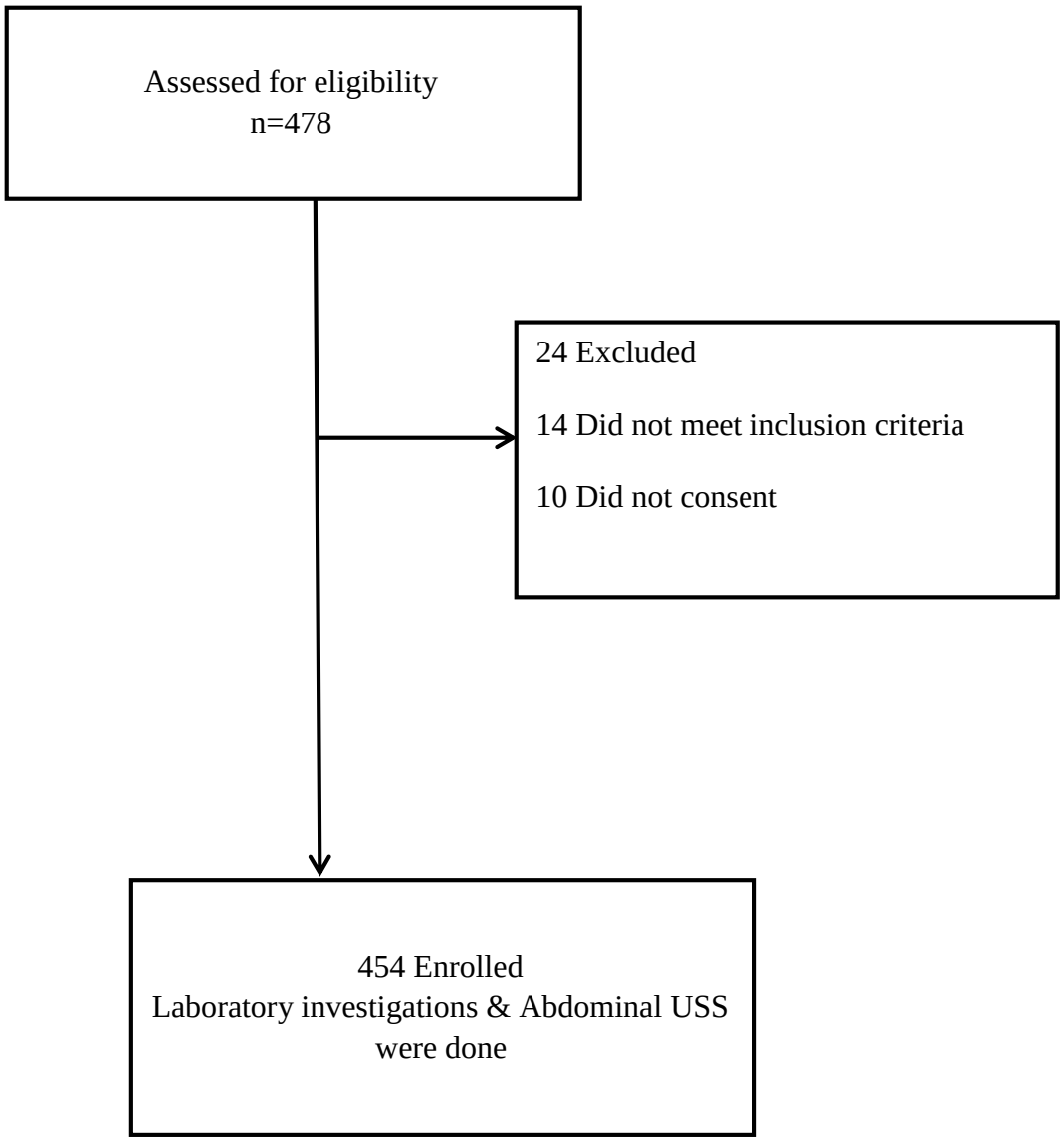


**Figure 2: The flow diagram of recruitment procedure among People Living with HIV at Temeke Regional Referral Hospital**

### 4.1 Socio-demographic characteristics of study participants are summarized in Table 2.

A total of 454 People living with HIV (PLHIV) at Temeke Regional Referral Hospital (TRRH) HIV Care and Treatment Clinic (CTC) were enrolled in this study.

The median age of the study participants was 44 years (IQR 38, 49). Majority (57.7%) of them were in the age category of 40-60 years. Most of them were female 330 (72.7%) and 292 (64.3%) had attained primary level of education. Current alcohol consumption was reported in 82 (18.1%), and 14 (17.1%) among alcohol consumers took hazardous amounts of alcohol. Majority 73(89.0%) reported to be consuming regular beer, 9 (11.0%) were taking local brews and spirits. One sixth 73(16.1%) of our study participants were current cigarette smokers.

Age between 40-60 years and history of current alcohol consumption were associated with FLD among PLHIV, (p value =0.021, p value=0.034) respectively

**Table 2: Socio-demographic characteristics of People Living with HIV at Temeke Regional Referral Hospital HIV Care and Treatment Clinic with and without Fatty Liver Disease n=454.**

| | | Fatty Liver Disease | | | |
|---|---|---|---|---|---|
| **Variable** | **Category** | **Yes (%)** | **No (%)** | **Total** | **p-value** |
| Age(years) | <40 | 31 (18.8) | 134 (81.2) | 165 | **0.021** |
| | 40-60 | 77 (29.4) | 185 (70.6) | 262 | |
| | >60 | 10 (37.0) | 17 (63.0) | 27 | |
| Sex | Male | 30 (24.2) | 94 (75.8) | 124 | 0.592 |
| | Female | 88 (26.7) | 242 (73.3) | 330 | |
| Marital status | Single | 30 (22.7) | 102 (77.3) | 132 | 0.128 |
| | Married | 45 (24.6) | 138 (75.4) | 183 | |
| | Divorced | 20 (25.3) | 59 (74.7) | 79 | |
| | Widow/widower | 23 (38.3) | 37 (61.7) | 60 | |
| Level of education | Informal Primary | 6 (22.2) | 21 (77.8) | 27 | 0.949 |
| | | 76 (26.0) | 216 (74.0) | 292 | |
| | Secondary | 32 (26.2) | 90 (73.8) | 122 | |
| | College/university | 4 (30.8) | 9 (69.2) | 13 | |
| Current Alcohol consumption | Yes | 29 (35.4) | 53 (64.6) | 82 | **0.032** |
| | No | 89 (23.9) | 283 (76.1) | 372 | |
| Hazardous alcohol consumption | Yes | 4 (28.6) | 10 (71.4) | 14 | 0.761 |
| | No | 25 (36.8) | 43 (63.2) | 68 | |
| Cigarette smoking | Yes | 17 (23.3) | 56 (76.7) | 73 | 0.565 |
| | No | 101 (26.5) | 280 (73.5) | 381 | |

*Hazardous alcohol consumption; drinking >3 and >4 units of alcohol per occasion in males and females respectively*(4)

### 4.2 Clinical characteristic of study participants

In clinical characteristic of study participants (**Table 3**), hypertension was found among 161(35.5%) and diabetes mellitus was found in 31(6.8%). Fasting serum LDL cholesterol ≥ 130 mg/dl and fasting total serum cholesterol ≥200 mg/dl were found among 68 (15.0%) and 84 (18.5%) respectively. Some study participants presented with both elevated LDL and total cholesterol, thus were counted once, 101(22.0%) were found to have dyslipidemia. Nearly half of study participants 226 (49.7%) were overweight and obese. A total of 301(66.3%) had high body fat percent.

The median (Interquartile Range) duration on combination ART use was 7 (4, 11) years. Majority of the recruited PLHIV 422 (93.0%) had attained HIV viral suppression. Most of study participants 439 (96.7%) were on Dolutegravir based antiretroviral therapy (Tenofovir + Lamivudine + Dolutegravir (TLD) at the time of the study.

Diabetes mellitus, overweight, obesity, central obesity, fasting serum total cholesterol ≥ 200 mg/dl, fasting serum Low

Density Lipoprotein (LDL) cholesterol ≥ 130 mg/dl and dyslipidemia were found to increase likelihood of FLD and significantly associated with FLD, (all p value <0.05).

HIV associated factors which were; type of current combination ART, HIV viral load status, and median duration on combination ART were not with FLD.

**Table 3: Clinical characteristics of People living with HIV at Temeke Regional Referral Hospital HIV Care and Treatment Clinic, with and without Fatty Liver Disease n=454**

| | | Fatty Liver Disease | | | |
|---|---|---|---|---|---|
| **Variable** | **Category** | **Yes (%)** | **No (%)** | **Total** | **p–Value** |
| Diabetes mellitus | Yes | 18 (58.1) | 13 (41.9) | 31 | **0.036** |
| | No | 105 (24.8) | 318 (75.2) | 423 | |
| Hypertension | Yes | 42 (26.1) | 119 (73.9) | 161 | 0.972 |
| | No | 76 (25.9) | 217 (74.1) | 293 | |
| LDL cholesterol (mg/dl) | ≥130 mg/dl | 33 (48.5) | 35(51.5) | 68 | **<0.001** |
| Total cholesterol(mg/dl) | ≥200 mg/dl | 33 (39.3) | 51 (60.7) | 84 | **0.002** |
| Dyslipidemia | Yes | 41(40.6) | 60(59.4) | 101 | **<0.001** |
| | No | 77(21.8) | 276(78.2%) | 353 | |
| Central obesity | Yes | 38(19.3) | 159(80.7) | 197 | **0.004** |
| | No | 80(31.1) | 177(68.9) | 257 | |
| BMI categories | Underweight | 5 (16.7) | 25 (83.3) | 30 | **<0.001** |
| | Normal | 34 (17.2) | 164 (82.8) | 198 | |
| | Overweight | 36 (28.8) | 89 (71.2) | 125 | |
| | Obese | 43 (42.6) | 58 (57.4) | 101 | |
| Body fat percent | Low | 9 (22.5) | 31 (77.5) | 40 | 0.206 |
| | Normal | 23 (20.4) | 90 (79.6) | 113 | |
| | High | 86 (28.6) | 215 (71.4) | 301 | |
| Median duration of ART (IQR) years | | 6 (4,10) | 7 (3,11) | | 0.975 |
| Current ART regime | DTG based | 112 (25.5) | 327 (74.5) | 439 | 0.233 |
| | PI based | 6 (40.0) | 9 (60.0) | 15 | |
| HIV viral load status | Suppressed | 111 (26.3) | 311 (73.7) | 422 | 0.582 |
| | Not suppressed | 7 (21.9) | 25 (78.1) | 32 | |

*Normal ranges for **body fat percent** as per age category and sex; 20-39 yrs (**21%-32%** F, **8%19%** M), 40-59yrs (23**%-33%**F, **11%-21%**M), 60-79yrs (**24%-35%**F, **13-24%**M)*
*BMI=Body Mass Index; ART= Antiretroviral Therapy; PI=Protease Inhibitor;*
*IQR=Interquartile range; LDL=Low Density Lipoprotein: HIV=Human Immunodeficiency Virus; DTG based=Tenofovir Disoproxil Fumarate+ Lamivudine+ Dolutegravir, PI based =Abacavir+lamivudine+Lopinavir/r, Tenofovir+Lamivudine+Atazanavir/r; Abacavir+lamivudine+ Atazanavir/r*

### 4.3 Prevalence and distribution of Fatty Liver Disease (FLD) among People living with HIV at Temeke Regional Referral Hospital HIV Care and Treatment Clinic

Among the 454 study participants who underwent Abdominal USS, FLD was present on 118 participants (25.9 %) 95%CI= 22% - 30.3 %**, Figure 3.**

With four grades of FLD, where by Grade 0 FLD was regarded as normal, Grade 1(mild) was the most common form of FLD, found among 97(82.20%), **Figure 4.**

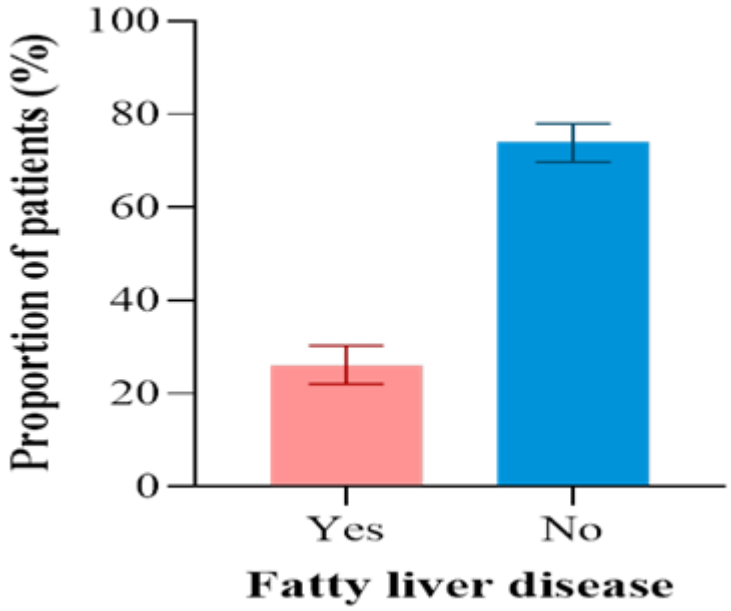


***Figure 3:*** **Prevalence of Fatty Liver Disease among People living with HIV at Temeke Regional Referral Hospital HIV Care and Treatment Clinic**

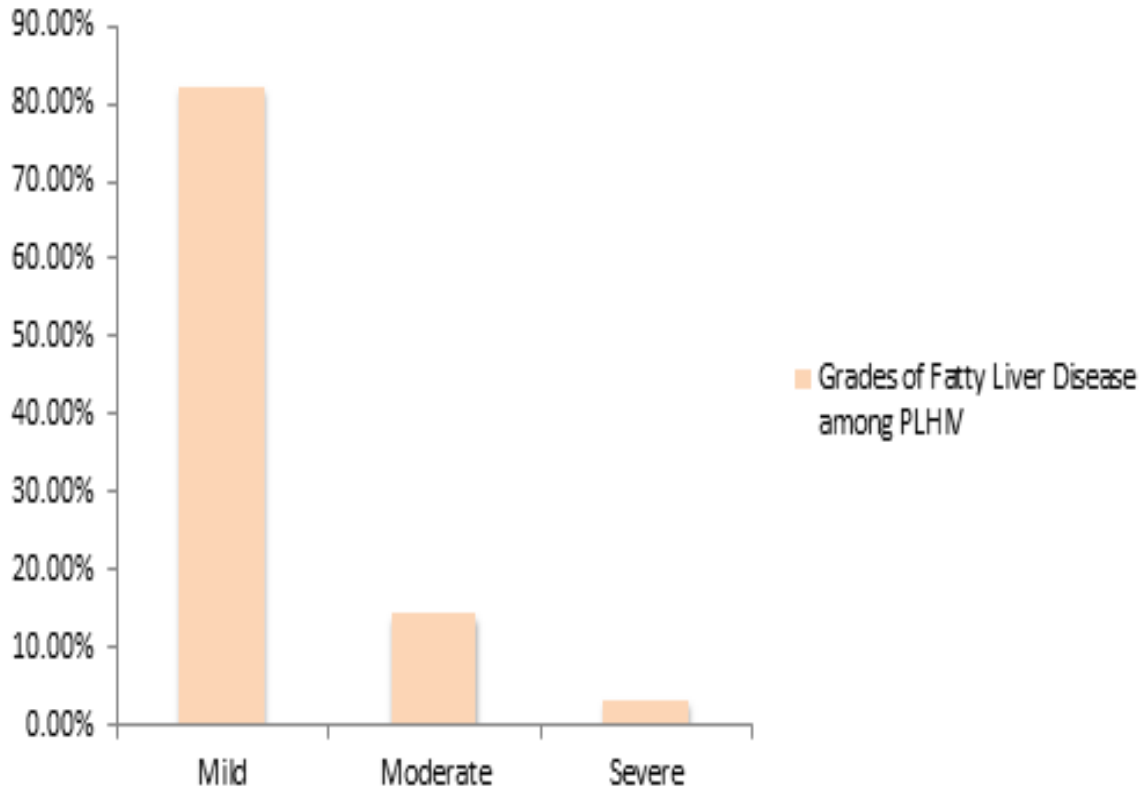


*Figure 4:* **Distribution of severity of Fatty Liver Disease among People living with HIV (PLHIV) at Temeke Regional Referral Hospital (TRRH) HIV Care and Treatment Clinic (n = 454)**

### 4.4 Factors associated with Fatty Liver Disease (FLD) among People living with HIV

Factors associated with FLD are presented in univariate and multivariate analysis table (**Table 4)**.

In univariate logistic regression analysis, Diabetes mellitus (cOR 2.19; 95%CI: 1.04 – 4.62 p value=0.040), central obesity (c OR 1.89; 95%: 1.21-2.94; p value =0.005) and current history of alcohol consumption (cOR 1.74; 95% CI: 1.04 – 2.90; p-value =0.034) demonstrated positive association with FLD.

Factors associated with FLD in multivariate logistic regression analysis were; age between 40-60 years (aOR 1.74; 95% CI: 1.02 – 2.96; p value= 0.043), overweight (aOR 1.92; 95% CI: 1.05-3.51; p value =0.034), obesity (aOR 3.46; 95% CI: 1.80-6.65; p value <0.001) and dyslipidemia (aOR 2.63; 95% CI 1.58-4.39; p value<0.001).

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**Table 4: Univariate and multivariate analysis of the factors associated with Fatty Liver Disease among People Living with HIV at Temeke Regional Referral Hospital HIV Care and Treatment Clinic n=454**

| | | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|
| **Variable** | **Category** | **cOR** | **95% CI** | **p - value** | **aOR** | **95% CI** | **p – value** |
| Age | >60 | 2.54 | 1.06 – 6.09 | **0.036** | 2.32 | 0.86 – 6.27 | 0.097 |
| | 40- 60 | 1.80 | 1.12 – 2.89 | **0.015** | 1.74 | 1.02 – 2.96 | **0.043** |
| | < 40 | Ref | | | | | |
| Sex | Female | 1.14 | 0.71 – 1.84 | 0.593 | 0.68 | 0.36-1.27– | 0.224 |
| | Male | Ref | | | | | |
| Marital status | Widow/widower | 2.11 | 1.09 – 4.09 | 0.026 | 1.67 | 0.77-3.60 – | 0.19 |
| | Divorced | 1.15 | 0.60 – 2.21 | 0.669 | 1.08 | 0.53-2.191 – | 0.84 |
| | Married | 1.11 | 0.65 – 1.88 | 0.702 | 0.97 | 0.58-1.74 – | 0.91 |
| | Single | Ref | | | | | |
| Current alcohol consumption | Yes | 1.74 | 1.04 – 2.90 | **0.034** | 1.69 | 0.95-2.98 | 0.07 |
| | No | Ref | | | | | |
| BMI(kg/m² ) | Obesity | 3.58 | 2.08 – 6.14 | **< 0.001** | 3.46 | 1.80-6.65 | **< 0.001** |
| | Overweight | 1.95 | 1.14 – 3.33 | **0.014** | 1.92 | 1.05 – 3.51 | **0.034** |
| | Underweight | 0.97 | 0.35 – 2.70 | 0.945 | 1.03 | 0.35-3.03 | 0.95 |
| | Normal | Ref | | | | | |
| Body fat percent | High | 1.57 | 0.93 – 2.64 | 0.092 | 0.57 | 0.26-1.23 | 0.16 |
| | Low | 1.14 | 0.48 – 2.72 | 0.774 | 0.73 | 0.28-1.87 | 0.51 |
| | Normal | Ref | | | | | |
| Central obesity | Yes | 1.89 | 1.21-2.94 | **0.005** | 1.73 | 0.78-3.89 | 0.18 |
| | No | Ref | | | | | |
| Dyslipidemia | Yes | 3.21 | 1.77-5.82 | **<0.001** | 2.63 | 1.58-4.39 | **<0.001** |
| | No | Ref | | | | | |
| Diabetes mellitus | Ye | 2.19 | 1.04 – 4.62 | **0.040** | 1.14 | 0.49-2.62 | 0.75 |
| | No | Ref | | | | | |

*Key: cOR =Crude Odds Ratio; aOR= Adjusted Odds Ratio; Ref= Reference group*

# CHAPTER FIVE

## 5.0 DISCUSSION, STUDY STRENGTHS AND LIMITATIONS

### 5.1 Discussion

In this study we aimed at determining the prevalence and factors associated with Fatty Liver Disease (FLD) among People living with HIV (PLHIV) at Temeke Regional Referral Hospital (TRRH) HIV Care and Treatment Clinic (CTC). We have found that one out of four among PLHIV had FLD. Predictors of FLD were age category of between 40-60 years, overweight, obesity and dyslipidemia.

The prevalence of FLD among PLHIV in our study was 25.9%. This prevalence is higher compared to prevalence in the general population (13.9%) as it has been revealed in a recent study by Simalene N (49). This could be attributed with presumably higher rates of HCV/HBV co-infection among PLHIV as revealed in previous studies (50,51) which compound the pathogenesis of FLD. Neither our study nor that by Simalene, determined the serological status of HBV and HCV infection in study participants. However previous studies have shown that HBV/HCV infections are higher among PLHIV than in the general population in Tanzania (51). study by Lesi O et al (25) among Nigerians on combination ART, showed the prevalence of FLD was 13.3%.The lower prevalence found by Lesi O et al) could be due to smaller sample size and exclusion of those with prior history of heavy alcohol consumption. On the other hand, the high prevalence found in our study is in keeping with Pezzini and colleagues who found that the prevalence of FLD by using Abdominal USS was 31.6% (10) among Brazilians. Like Tanzania, the prevalence of co-infections with HBV/HCV and HIV is as high as 4.4% among Brazilians PLHIV (52). Moreover, FLD was found on 45 (73%) of 62 study participant by Morse CG et al using histopathological results from liver biopsies taken from HIV mono-infected individuals (30). Diagnostic tool and race greatly influence the presence of FLD and histopathology is the gold standard test for FLD (6,7,22).

Our study found that dyslipidemia, was independently associated with FLD. Similar to our findings, previous studies have shown the association between serum levels of low density lipoprotein (LDL) cholesterol ≥ 130 mg/dl and FLD (10,14,25). Elevated levels of LDL cholesterol have been shown to impair lipid metabolism, increasing insulin resistance leading to excessive delivery to and storage of fatty acids in the liver (53).

Obesity is a well-documented risk factor for development of FLD. Several previous studies have shown association between obesity and FLD among PLHIV (10,25,28,29,54). In the current study, high body mass index was correlated with central obesity and strongly associated with FLD. Obesity causes insulin resistance which impairs hormone sensitive lipase, and leads to increased accumulation of fatty acids in the liver (3). Lipodystrophy, an adverse effect of combination ART, is blamed for high BMIs and central obesity in this cohort due to peripheral adipocyte death hence abnormal fat content. (3). In our study abnormal fat distribution (lipodystrophy) was not assessed in its entirety and we acknowledge it as our limitation. However, truncal obesity was significantly associated with FLD while overall high body fat percent was not significantly associated with FLD at multivariate analysis. The absence of statistical significance should be taken with caution as could result from absence of validated tools for assessing body fat percent to African population.

In keeping with our findings at univariate analysis, several studies have identified the role of diabetes mellitus (DM) in the development of FLD risk factor for FLD (30,54) due to accompanying insulin resistance. We failed to show independent association in multivariate analysis ($p = 0.75$) due to low proportion (6.8%) of participants with DM in our study.

Alcohol consumption is not uncommon among PLHIV in our setting (40) and has been linked to poor ART adherence (22,40). In our study, we found current alcohol consumption was significantly associated with FLD in univariate analysis. Our results are in agreement with a study by Lesi O et al (25), although the association was not statistically significant. The association is brought about by alcohol's pleotropic effects of inducing mitochondrial toxicity and gut bacterial translocation due to increase intestinal permeability leading to chronic

inflammatory state; leading to insulin resistance (6,7,22). On the contrary, in our study hazardous alcohol consumption was not statistically significantly associated with FLD. This finding may have arisen from measurement error of the amount consumed due to self-reporting bias and fear of disappointing the health care workers.

Contrary to known evidence of ART with abnormalities of lipid metabolism, our study did not find any association between FLD and type of current combination ART regimen (p-value =0.233). There is conflicting literature between combination ART and FLD. Literature provides some evidence on development of FLD among PLHIV, studies have been producing varying results in scientific community. Nucleoside Reverse Transcriptase Inhibitors (NRTI) such as Stavudine, Didanosine and Protease Inhibitors e.g. Indinavir are known to induce mitochondria toxicity and lead to impaired lipid metabolism. In our study, majority (96.7%) were on 2NRTI+Integrase strand transfer inhibitor (Tenofovir Disoproxil Fumarate+ Lamivudine + Dolutegravir). This can be attributed to the less hepatotoxic effects of Tenofovir (3) and lack of prior history of combination ART among our study participants. A study done among Asians, in which even prior history of Stavudine and Didanosine was enquired, they failed to show association between NRTI and FLD (29). On the contrary a study by Guaraldi et al in Italy found that, exposure to NRTI was independently associated with FLD (8) .

In our study contrary to what is previously reported a high HIV viral load was not significantly associated with FLD (p=0.582). It is known that high HIV viral load induces chronic inflammatory state, the release of cytokines leads to insulin resistance; a culprit of FLD (3, 4). In the recent years, due to global policy change in HIV treatment and preventing strategy, starting ART as soon as the diagnosis is made and early combination ART as well as effective viral suppression may be the reason why this association between combination ART and FLD has not been observed. In our study only 3.3% of study participants had detectable viremia. Similarly, Lesi O et al did not find association between FLD and median copies of HIV RNA load.

In the current study we could not establish association between sex and FLD. Previous studies have reported varying results regarding the effect of sex on FLD. A study done by Guaraldi N et al, in Italy (8) and Pezzini MF et al (7) in Brazil, showed that male sex was independently associated with FLD. Contrary to that, studies done by Lesi O et al (25) and Nishijima et al (29) showed no association between FLD and male sex. Over representation of female (72.7%) in our study could be the reason for this.

Noteworthy, this study revealed ages between 40 and 60 years is an independent risk factor for FLD. Different from previous studies (10,25,29)), we found an association between this age group and FLD. The relationship between increasing age and FLD could be a result of either; impaired mitochondrial function and increase of oxidative stress as a result of aging or a reflection of accumulated effect of viral inflammation over time (55). With more advanced age, it is expected to have advanced FLD (steatohepatitis), which is associated with higher levels of adiponectin that reduces hepatic fat content (43). Also the lack of association of FLD for those who aged more than 60 years in our study could be due to their low proportion (5.9%).

Despite lack of association between hypertension and FLD in our study, we have found high prevalence of hypertension (35.5%), and this is in keeping with the global prevalence of hypertension revealed in a systematic review and in meta -analysis study was 34.7%,( 95% CI: 27.4%, 42.8%) among PLHIV on combination ART(56). In the current study, we found that even those who knew their hypertension status (9.2%) were not on regular antihypertensive medications. This could be due to the lack of integration of non-communicable diseases care and management at CTCs.

### 5.2 Study Strengths and Limitations

This study used Abdominal USS in assessing the presence of Fatty Liver Disease (FLD) among People living with HIV (PLHIV) on combination antiretroviral therapy. To our knowledge this is the first local study which determined the magnitude and factors associated with FLD among PLHIV.

The prevalence of FLD among PLHIV is high in our setup which has never been documented previously. At this point, we have local data showing high prevalence of a potentially fatal but reversible condition. Factors that may contribute to FLD were clearly ironed out providing a platform for intervention studies or/and programmatic approach to reducing the burden in our setting. Our relatively larger sample size allowed for exploration of many factors.

This study was cross-sectional in nature done in a single centre, Temeke Regional Referral Hospital (TRRH). Since the hospital caters for patients from Temeke, is likely that selection bias will present PLHIV at a slightly lower socioeconomic status(57). According to demographic and health survey of the year 2015-2016 Temeke is among the three major districts in Dar es Salaam city. The use of B mode Abdominal USS in assessment of FLD, has the following limitation; less sensitivity (60.9-65%) in detecting mild hepatic steatosis (> 5% of hepatocyte infiltrated with fat) (58). This could lead to underestimation of FLD. Also abdominal USS is associated with inter-observer variability.

We did not ask history of combination ART regimen used prior to the current period of study. This could be the reason for not finding association between combination ART and FLD, since some of the potential NRTIs which cause metabolic derangement Stavudine and Didanosine were incorporated in our previous National HIV/AIDS standard treatment guideline but are no longer included. In our study, hazardous alcohol consumption did not show association with FLD, this could be a contribution of report bias and we were unable to quantify amount (units) of alcohol consumption on those who were taking local brews and spirit. Due to their low proportion 9(11.0%), we don't believe this could alter our study findings.

# CHAPTE SIX

## 6.0 CONCLUSION AND RECOMMENDATIONS

### 6.1 Conclusion

Fatty Liver Disease (FLD) occurs in one out of four PLHIV on combination ART in Temeke Regional Referral Hospital. Factors associated with FLD in our study include, age between 40-60 years, obesity, overweight and dyslipidemia. Alcohol consumption, diabetes mellitus and central obesity were significantly associated with FLD at univariate analysis but not multivariate analysis.

### 6.2 Recommendations

Based on our findings this study has the following recommendations

A similar study to be conducted at a different setting in Tanzania to validate our study findings.

Periodic screening of fatty liver diseases using abdominal ultrasonography is recommended among overweight or obese PLHIV, those aged 40 - 60 years and dyslipidemia (serum LDL ≥ 130 mg/dl and /OR total cholesterol ≥200 mg/dl).

To assess value of inclusion of cheap and cost effective interventions such as nutritional assessment and advice and in Fatty Liver Disease as well as the overall patient outcomes

An interventional study to find appropriate management strategies of Fatty Liver Disease among People Living with HIV (PLHIV) is recommended.

## REFERENCES


1. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328–57.

2. Liu E, Armstrong C, Spiegelman D, Chalamilla G, Njelekela M, Hawkins C, et al. First-line antiretroviral therapy and changes in lipid levels over 3 years among HIV-infected adults in Tanzania. Clin Infect Dis. 2013;56(12):1820–8.

3. Pippitt K, Li M, City SL, Gurgle UHE, College U, City SL. Diabetes Mellitus: Screening and Diagnosis. 2016;

4. An Y, Yi S, Fitzpatrick A, Gupta V, Prak PR, Oum S, et al. Appropriate Body Mass Index and Waist Circumference Cutoff for Overweight and Central Obesity among Adults in Cambodia. PLoS One. 2013;8(10).

5. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. Clinical Practice Guidelines 2020 International Society of Hypertension Global Hypertension Practice Guidelines International Society of Hypertension. 2020;1334–57.

6. van Welzen BJ, Mudrikova T, El Idrissi A, Hoepelman AIM, Arends JE. A Review of Non-Alcoholic Fatty Liver Disease in HIV-Infected Patients: The Next Big Thing? Infect Dis Ther [Internet]. 2019;8(1):33–50. Available from: https://doi.org/10.1007/s40121-018-0229-7

7. Seth, Sherman shermake@ucmail uc edu. Fatty liver disease in persons with HIV infection. Top Antivir Med. 2019;27(2):75–82.

8. Cruz JF, Cruz MAF, Machado Neto J, Santana DS de, Oliveira CC da C, Lima SO. Prevalence and sonographic changes compatible with fatty liver disease in patients referred for abdominal ultrasound examination in Aracaju, SE. Radiol Bras. 2016;49(1):1–5.

9. Maurice JB, Patel A, Scott AJ, Patel K, Thursz M, Lemoine M. Prevalence and risk factors of nonalcoholic fatty liver disease in HIV-monoinfection. Vol. 31, Aids. 2017. 1621–1632 p.

10. Pezzini MF, Cheinquer H, de Araujo A, Schmidt-Cerski CT, Sprinz E, Herz-Wolff F, et al. Hepatic steatosis among people living with HIV in Southern Brazil: prevalence and risk factors. Sci Rep. 2020;10(1):1–6.

11. Guaraldi G, Squillace N, Stentarelli C, Orlando G, D'Amico R, Ligabue G, et al. Nonalcoholic Fatty Liver Disease in HIV- Infected Patients Referred to a Metabolic Clinic: Prevalence, Characteristics, and Predictors. Clin Infect Dis. 2008;47(2):250–7.

12. UNAIDS. Global HIV and AIDS statistics 2019 Fact sheet. Glob HIV AIDs ststistics, World AIDS day 2019 Fact Sheet. 2019;1(June):1–6.

13. MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER EAC. The United Republic of Tanzania. Development. 2019;7(5,371,780,231.09):2,274,923,575.00-29.08.

14. Crum-Cianflone N, Dilay A, Collins G, Asher D, Campin R, Medina S, et al. Nonalcoholic fatty liver disease among HIV-infected persons. J Acquir Immune Defic Syndr. 2009;50(5):464–73.

15. Coronel-Castillo CE, Qi X, Contreras-Carmona J, Ramírez-Pérez OL, Méndez-Sánchez N. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis in HIV infection: a metabolic approach of an infectious disease. Expert Rev Gastroenterol Hepatol [Internet]. 2019;13(6):531–40. Available from: https://doi.org/10.1080/17474124.2019.1599284

16. Gutierrez AD, Balasubramanyam A. Dysregulation of glucose metabolism in HIV patients: Epidemiology, mechanisms, and management. Endocrine. 2012;41(1):1–10.

17. Dekkers CC, Westerink J, Hoepelman AIM, Arends JE. Overcoming obstacles in lipid-lowering therapy in patients with HIV-A systematic review of current evidence. AIDS Rev. 2018;20(4):205–19.

18. Hernaez R, Lazo M, Bonekamp S, Kamel I, Brancati FL, Guallar E, et al. Diagnostic accuracy and reliability of ultrasonography for the detection of fatty liver: A meta-analysis. Hepatology. 2011;54(3):1082–90.

19. Perazzo H, Cardoso SW, Yanavich C, Nunes EP, Morata M, Gorni N, et al. Predictive factors associated with liver fibrosis and steatosis by transient elastography in patients with HIV mono-infection under long-term combined antiretroviral therapy. J Int AIDS Soc. 2018;21(11):1–9.

20. Macías J, Pineda JA, Real LM. Non-alcoholic fatty liver disease in HIV infection. AIDS Rev. 2017;19(1):35–46.

21. Harrison SA. Effect of Weight Loss , Diet , Exercise and Bariatric Surgery on Nonalcoholic fatty liver disease. Clin Liver Dis [Internet]. 2015; Available from: http://dx.doi.org/10.1016/j.cld.2015.10.008

22. Dinani A, Khan A, Dieterich D. Emerging prevalence of fatty liver disease in HIV. Future Virol. 2021;16(1):59–73.

23. Sanyal AJ, Chalasani N, Kowdley K V., McCullough A, Diehl AM, Bass NM, et al. Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis. N Engl J Med. 2010;362(18):1675–85.

24. Sebastiani G, Saeed S, Lebouche B, De Pokomandy A, Szabo J, Haraoui LP, et al. Vitamin e is an effective treatment for nonalcoholic steatohepatitis in HIV mono-infected patients. Aids. 2020;34(2):237–44.

25. Lesi OA, Soyebi KS, Eboh CN. Fatty liver and hyperlipidemia in a cohort of HIV-positive africans on highly active antiretroviral therapy. J Natl Med Assoc [Internet]. 2009;101(2):151–5. Available from: http://dx.doi.org/10.1016/S0027-9684(15)30828-2

26. Guaraldi G, Lonardo A, Maia L, Palella FJ. Metabolic concerns in aging HIV-infected persons: From serum lipid phenotype to fatty liver. Aids. 2017;31(March):S147–56.

27. Verna EC. Non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in patients with HIV. Lancet Gastroenterol Hepatol [Internet]. 2017;2(3):211–23. Available from: http://dx.doi.org/10.1016/S2468-1253(16)30120-0

28. Lui G, Wong VWS, Wong GLH, Chu WCW, Wong CK, Yung IMH, et al. Liver fibrosis and fatty liver in Asian HIV-infected patients. Aliment Pharmacol Ther. 2016;44(4):411–21.

29. Nishijima T, Gatanaga H, Shimbo T, Komatsu H, Nozaki Y, Nagata N, et al. Traditional but not HIV-related factors are associated with nonalcoholic fatty liver disease in asian patients with HIV-1 infection. PLoS One. 2014;9(1):1–6.

30. Morse CG, McLaughlin M, Matthews L, Proschan M, Thomas F, Gharib AM, et al. Nonalcoholic steatohepatitis and hepatic fibrosis in HIV-1-monoinfected adults with elevated aminotransferase levels on antiretroviral therapy. Clin Infect Dis. 2015;60(10):1569–78.

31. Price JC, Thio CL. Liver Disease in the HIV-Infected Individual. Clin Gastroenterol Hepatol [Internet]. 2010;8(12):1002–12. Available from: http://dx.doi.org/10.1016/j.cgh.2010.08.024

32. Stabinski L, Reynolds SJ, Ocama P, Laeyendecker O, Ndyanabo A, Kiggundu V, et al. High prevalence of liver fibrosis associated with HIV infection: A study in rural Rakai, Uganda. Antivir Ther. 2011;16(3):405–11.

33. Armstrong C, Liu E, Okuma J, Spiegelman D, Guerino C, Njelekela M, et al. Dyslipidemia in an HIV-positive antiretroviral treatment-naive population in Dar es Salaam, Tanzania. J Acquir Immune Defic Syndr. 2011;57(2):141–5.

34. Duncan AD, Goff LM, Peters BS. Type 2 diabetes prevalence and its risk factors in HIV: A cross-sectional study. PLoS One. 2018;13(3):1–11.

35. Paik JM, Henry L, Golabi P, Alqahtani SA, Trimble G, Younossi ZM. Presumed Nonalcoholic Fatty Liver Disease Among Medicare Beneficiaries With HIV, 2006–2016. Open Forum Infect Dis. 2020;7(1):2006–16.

36. Krahn T, Martel M, Sapir-Pichhadze R, Kronfli N, Falutz J, Guaraldi G, Lebouche B, Klein MB, Wong P, Deschenes M, Ghali P, and Sebastiani G. Ac ce pt e d us cr ip. 2008;1–34.

37. Siddiqui MS, Cheang KL, Luketic VA, Boyett S, Idowu MO, Patidar K, et al. Nonalcoholic Steatohepatitis (NASH) Is Associated with a Decline in Pancreatic Beta Cell (β-Cell) Function. Dig Dis Sci. 2015;60(8):2529–37.

38. Chillo P, Bakari M, Lwakatare J. Echocardiographic diagnoses in HIV-infected patients presenting with cardiac symptoms at Muhimbili National Hospital in Dar es Salaam, Tanzania. Cardiovasc J Afr. 2012;23(2):90–7.

39. Njelekela M, Muhihi A, Aveika A, Spiegelman D, Hawkins C, Armstrong C, et al. Prevalence of hypertension and its associated risk factors among 34,111 HAART Naïve HIV-Infected adults in Dar es Salaam, Tanzania. Int J Hypertens. 2016;2016.

40. Mwiru RS, Nagu TJ, Kaduri P, Fawzi W, Mugusi F. Prevalence and factors associated with alcohol drinking among HIV and tuberculosis co-infected patients in Dar es Salaam, Tanzania. AIDS Care - Psychol Socio-Medical Asp AIDS/HIV. 2018;30(2):173–7.

41. Tajir K, Shimizu Y. Liver physiology and liver diseases in the elderly. World J Gastroenterol. 2013;19(46):8459–67.

42. Lonardo A, Lombardini S, Scaglioni F, Ballestri S, Verrone AM, Bertolotti M, et al. Fatty liver, carotid disease and gallstones: A study of age-related associations. World J Gastroenterol. 2006;12(36):5826–33.

43. Van der Poorten D, Samer CF, Ramezani-Moghadam M, Coulter S, Kacevska M, Schrijnders D, et al. Hepatic fat loss in advanced nonalcoholic steatohepatitis: Are alterations in serum adiponectin the cause? Hepatology. 2013;57(6):2180–8.

44. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. J Hepatol [Internet]. 2019;70(1):151–71. Available from: https://doi.org/10.1016/j.jhep.2018.09.014

45. TJ Nagu, M Kanyangarara, C Hawkins E Hertmark, G Chalamila, D Spiegelman, F Mugusi, and W Fawzi. NIH Public Access. Elev alanine Amin Antiretrovir HIVinfected African patients Magnit risk factors. 2013;13(9):541–8.

46. Mugusi SF, Sando D, Mugusi FM, Hawkins C, Aboud S, Fawzi WW, et al. Risk Factors for Alanine Aminotransferase Elevations in a Prospective Cohort of HIV-Infected Tanzanian Adults Initiating Antiretroviral Therapy. J Int Assoc Provid AIDS Care. 2019;18:1–10.

47. Shaheen A, Javed N, Azam F, Liaquat A, Khan M, Alam SM, et al. Comparison of Bioelectrical Impedance and Navy Seal Formula to Measure Body Composition in Medical Students. Cureus. 2019;11(5).

48. Gallagher D, Heymsfield SB, Heo M, Jebb SA, Murgatroyd PR, Sakamoto Y. Healthy percentage body fat ranges: An approach for developing guidelines based on body mass index. Am J Clin Nutr. 2000;72(3):694–701.

49. Simelane NN. Prevalence Of Fatty Liver Disease And Associated Factors Among Outpatients At Muhas Academic Medical Centre , tanzania. :1–14.

50. Nagu TJ, Bakari M, Matee M. Hepatitis A, B and C viral co-infections among HIV-infected adults presenting for care and treatment at Muhimbili National Hospital in Dar es Salaam, Tanzania. BMC Public Health. 2008;8:1–7.

51. Hawkins C, Christian B, Ye J, Nagu T, Aris E, Chalamilla G, et al. Prevalence of hepatitis B co-infection and response to antiretroviral therapy among HIV-infected patients in Tanzania. Aids. 2013;27(6):919–27.

52. Brandão NAA, Pfrimer IAH, Martelli CMT, Turchi MD. Prevalence of hepatitis B and C infection and associated factors in people living with HIV in Midwestern Brazil. Brazilian J Infect Dis [Internet]. 2015;19(4):426–30. Available from: http://dx.doi.org/10.1016/j.bjid.2015.02.001

53. Sun DQ, Liu WY, Wu SJ, Zhu GQ, Braddock M, Zhang DC, et al. Increased levels of low-density lipoprotein cholesterol within the normal range as a risk factor for nonalcoholic fatty liver disease. Oncotarget. 2016;7(5):5728–37.

54. Rivero-Juárez A, Camacho A, Merchante N, Pérez-Camacho I, Macias J, Ortiz-Garcia C, et al. Incidence of Liver Damage of Uncertain Origin in HIV Patients Not Co-Infected with HCV/HBV. PLoS One. 2013;8(7):7–12.

55. Thio CL and Nwulia OF. Liver disease, HIV and aging. Physiol Behav. 2018;176(5):139–48.

56. Xu Y, Chen X, Wang K. Global prevalence of hypertension among people living with HIV: a systematic review and meta-analysis. J Am Soc Hypertens [Internet]. 2017;11(8):530–40. Available from: http://dx.doi.org/10.1016/j.jash.2017.06.004

57. Tanzania Ministry of Health. Tanzania Demorgraphic and Health Survey Indicator Survey (TDHS-MIS) 2015-2016. Dar es Salaam, Tanzania, Rockville, Maryland, USA MoHCDGEC, MoH, NBS, OCGS, ICF. 2016;1(1):1–630.

58. Ferraioli G and Monteiro LBS. Ultrasound-based techniques for the diagnosis of liver steatosis. World J Gastroenterol. 2019;9327(40).

# APPENDIX

## Appendix I: Questionnaire

QUESTIONNAIRE NO……

SOCIODEMOGRAPHIC DATA

1. Age ……. years
2. Sex ( F/ M)
3. Marital status
   a) Single b) married c) divorced d) widow/ widower
4. Level of education
   a) Formal ---- Primary/ secondary/ college (or university)
   b) Non Formal

ASSESSMENT OF FLD RISK FACTORS

5. Do you smoke cigarette?
   a) Yes b) No
6. Do you consume Alcohol?
   a) Yes b) No
7. If Yes
   a) Which type alcohol do you consume?
   b) What is the average number of drinks do you consume the day when drinking
   c) For how long have you been consuming alcohol?

8. For how long are you on combination ART? ..... (years)
9. Have you ever experienced increase in urine output, thirst and amount of feeding?
   a) Yes b) No

10. Have you ever been told to have Diabetes mellitus?
    a) Yes b) No
11. If yes, are using any anti-diabetic drugs?
    a) Yes b) No
12. Have you ever been told to have abnormal lipid levels?
    a) Yes b) No
13. If yes, are you using any lipid lowering drugs?
    a) Yes b) No c) I don't know
14. Have you ever been told to have Hypertension?
    a) Yes b) No
15. Are you using anti-hypertensive medication?
    a) Yes b) No

PHYSICAL EXAMINATION

16. Blood pressure …….mmHg
17. Body weight …… kg
18. Height …….. meters
19. Neck circumference……centimeter
20. Waist circumference ……..centimeter
21. Hip circumference……..centimeter

RAPID DIAGNOSTIC TEST

22. Random/fasting blood glucose ……. mmol/L

LABORATORY INVESTIGATION TESTS RESULT

23. Serum Low Density Lipoprotein Cholesterol levels……..mg/dl
24. Total serum cholesterol……..mg/dl

**INFORMATION TO BE OBTAINED FROM PATIENT FILE**

25. Current combination ART regime……

26. Current HIV RNA viral load……..

27. Other drugs consumed by the client……

28. ABDOMINAL USS RESULTS

    a) None / Grade 0 ( )
    b) Mild Fatty Liver/ Grade 1 ( )
    c) Moderate Fatty Liver/ Grade 2 ( )
    d) Severe Fatty Liver/ Grade 3 ( )

**Appendix 11: Dodoso**

**DODOSO NAMBARI……..**

**Swahili version**

1. Umri ……..
2. Jinsia ( KE/ME) 3.
   Hali ya ndoa
   a) Sina ndoa b) nina ndoa c) mtalaka d) mjane
4. Kiwango cha elimu
   a) Elimu rasmi----------msingi/sekondari/chuo
   b) Elimu isiyo rasmi
5. Je, unavuta sigara?
   a) Ndio 6. b) Hapana c
   Je, unatumia kilevi?
   a) Ndio b) Hapana

7. Kama ndio
   a) Unatumia aina gani ya kilevi?
   b) Je unakunywa wastani wa kiasi gani( chupa ngapi)?
   c) Umetumia kilevi kwa muda gani?
8. Ni kwa muda gani unatumia dawa za kufubaza virusi vya Ukimwi? .....(mwaka/ miaka).
9. Je umewahi kuhisi au kuambiwa una dalili za ugonjwa wa kisukari kama vile kukojoa sana, kuhisi njaa sana au kuongeza kiwango cha ulaji chakula?
   a) Ndio b) Hapana
10. Umewahi kuambiwa una ugonjwa wa kisukari?
    a) Ndio b)Hapana

11. Kama ndio, je unatumia dawa kwa ajili ya kutibu ugonjwa wa kisukari?

a) Ndio b) Hapana

12. Je umewahi kuambiwa una uwiano usio sawa wa kiwango cha mafuta mwilini?

a) Ndio b) Hapana

13. Je unatumia dawa zinazosaidia kuweka sawa viwango vya mafuta katika mwili ?

a) Ndio b) Hapana

14. Je umewahi kuambiwa una shinikizo la damu?

a) Ndio b) Hapana

15. Je unatumia dawa za kutibu shinikizo la damu?

a) Ndio b) Hapana

16. Msukumo wa damu …….mm Hg

17 Uzito kilogramu…….

1.8Urefu mita……

19. Mzingo wa shingo sentimita…….

20. Mzingo wa kiuno ni sentimita……

21. Mzingo wa nyonga sentimita……..

**VIPIMO VYA DAMU**

22. Sukari ya damu bila mpangilio/ ya kufunga…….mmol/L

23. Kiwango cha lehemu ( LDL) katika mwili……..mg/d

24. Kiwango cha lehemu( total cholesterol)…….mg/dl

**TAARIFA ZITAKAZONUKULIWA KUTOKA KATIKA FAILI LA MGONJWA**

25. Aina ya kundi la dawa zinazofubaza VVU anazitumia mshiriki utafiti……

26. Kiwango cha virusi mwilini( ndani ya miezi sita) ni ……..

27. Aina ya dawa zingine anazotumia mshiriki utafiti……..

**VIPIMO VYA RADIOLOJIA**

28. Kiwango cha mafuta kwa kutumia teknolojia ya Ultrasound

a) Daraja sifuri
b) Daraja la kwanza
c) Daraja la pili
d) Daraja la tatu

**Appendix II: Informed Consent- English Version**

Consent to participate in the study titled Fatty Liver Disease among People living with HIV attending CTC at Temeke Regional Referral Hospital (TRRH) Dar es Salaam Tanzania.

**Greetings:** I am Dr. Farida Mtonga, a postgraduate student doing research titled Fatty Liver Disease and its correlates among People living with HIV attending CTC clinic at TRRH, in Dar es salaam, Tanzania.

**Purpose of the study:** To determine the prevalence and factors associated with Fatty Liver Disease among people living with HIV

**What participation involved:** If you agree to participate in this study, your medical information will be used for research purpose-but will not be linked to you directly.

**Confidentiality:** All information collected will be entered into a computer with identification numbers only, no names included.

**Risk:** We expect no harm to happen to you during the course of this study.

**Right to withdrawal:** Taking part in this study is completely voluntary and refusal to participate or withdrawal will not involve penalty or loss of any benefits to which you are entitled.

**Benefits:** The results from this study will be used as evidence based for proposing routine screening of risk factors and presence of Fatty Liver Disease.

**Approval:** This study has sought approval from proper and informed authorities.

**Questions:** If you have any questions concerning your right as a participant, you may contact

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Do you agree; Study participant…….
I…… have read the consent form and my questions have been answered and I agree to participate in this study.

Signature: Participant……...
Signature of investigator…… Date

of signed consent…….

**Appendix III: Informed Consent - Swahili Version**

Ruhusa ya kushiriki utafiti kuhusu ugonjwa wa ini ya mafuta miongoni mwa watu wenye maambukizi ya Virusi vya Ukimwi wanaohudhuria kliniki ya dawa za kufubaza makali ya VVU katika hospitali ya rufaa ya mkoa Temeke

Mimi naitwa Dr. Farida Mtonga ni mwanafunzi wa uzamili chuo kikuu cha tiba Muhimbili. Ninafanya utafiti kuangalia ugonjwa wa ini ya mafuta miongoni mwa watu wenye maambukizi ya Virusi vya Ukimwi wanaohudhuria kliniki ya dawa za kufubaza makali ya VVU katika hospitali ya Rufaa ya mkoa Temeke

**Dhumuni la utafiti huu:** Kujua wingi wa ugonjwa wa ini ya mafuta na kuona kama kunatofauti katika viashiria vya ugonjwa huu miongoni mwa watu wenye maambukizi ya Virusi vya Ukimwi wanaohudhuria kliniki ya dawa za kufubaza makali ya VVU katika hospitali ya Rufaa ya Mkoa Temeke

**Ushiriki:** Kama unakubali kushiriki huu utafiti, taarifa zako za matibabu zitatumika kwenye utafiti huu pekeyake.

**Usiri:** Taarifa zote za uchunguzi zitaingizwa kwenye kompyuta na nambari ya utambulisho; jina halite nukuliwa.

**Madhara:** Tunategemea kwamba hakuna madhara yoyote yatokanayo na utafiti huu.

**Haki ya kujitoa kwenye utafiti:** Kushiriki katika utafiti huu ni hiari na kutokubali kushiriki au kujitoa hauta adhibiwa au kupoteza haki yako ya matibabu.

**Kutokea kwa madhara:** Tunategemea kwamba hakuna madhara yoyote ya tokanayo na utafiti huu. Hatahivyo kama madhara ya mwili yakitokea kutokana na utafiti huu utatibiwa kulingana na kanuni na taratibu za matibabu ya Tanzania.

Faida za kushiriki kwenye  utafiti:

Kama utakubali kushiriki kwenye utafiti huu, faida utakazopata ni pamoja na kuonwa na kufuatiliwa kwa ukaribu na daktari anayefanya utafiti. Tunatumaini kwamba taarifa zinazopatikana zitawanufaisha wengine pia.

Kwa mawasiliano zaidi:

Kama unamaswali kuhusu utafiti huu uwehuru kuwasiliana na **Prof.**

**Tumaini Nagu, Msimamizi wa utafiti**.

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Je umekubali kushiriki? ……

Mimi ……

Nimesoma maelezo na kuyaelewa vizuri, na nimekubali kushiriki kwenye utafiti huu.

Sahihi ya mshiriki ……

Sahihi ya mtafiti …… Tarehe ……..……