KAIRUKI UNIVERSITY

SCHOOL OF MEDICINE

DEPARTMENT OF INTERNAL MEDICINE

DETERMINING CUTANEOUS MARKERS OF DYSLIPIDEMIA AMONG HIV SEROPOSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY ATTENDING CARE AND TREATMENT CLINICS IN DAR ES SALAAM.

By

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A dissertation submitted in partial fulfilment of the requirements for the degree of Masters of Medicine (MMED) in Internal Medicine 2024

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CERTIFICATION

The undersigned certifies that he has read and hereby recommended for submission a Dissertation entitled "DETERMINING CUTANEOUS MARKERS OF DYSLIPIDEMIA AMONG HIV SEROPOSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY ATTENDING CLINICS IN DAR ES SALAAM." in fulfilment of the requirements of the degree of Master of Medicine in Internal Medicine of Kairuki University.

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DECLARATION AND COPYRIGHT

I, Mhina Edward Mlangwa hereby declare that this dissertation is my original work and has not been presented and will not be presented to any other university for similar or any other degree award.

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DEDICATION

I declare this work to my beloved, late mother Bi Safia Pepo, late junior Brother Lugendo Mlangwa, and Late junior Sister Nemgunda, your sufferings were the impetus for me to seek knowledge so that to serve the people, I pray to Almighty GOD, to rest your souls in" Firdaus", Ameen.

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Abstract

Background:

The prevalence of ischaemic heart disease (IHD) in Sub-Saharan Africa has been on the rise among people living with HIV.HIV infection and antiretroviral drugs (ARTs) are both associated with dyslipidemia.

Objective:

This study aimed to determine the prevalence of cutaneous markers of dyslipidemia and associated factors among HIV seropositive on ARTs attending CTCs in Dares Salaam.

Method:

A descriptive cross-sectional study among HIV seropositive individuals aged 18 years and above were enrolled at Kairuki Hospital and Mwananyamala Regional Referral Hospital, from February to July 2024, and a 100% response rate was obtained. The diagnosis of cutaneous markers of dyslipidemia was based on physical examination (Visual inspection by naked eye keenly looking for cutaneous markers). A fasting blood sample was obtained for serum markers of dyslipidemia

Results:

The study recruited 305 people, 21 persons were excluded due to missing data, and a total of 284 were analysed with a response rate of 100%. The mean age of participants was 46.7±10.9, and 182(64.1%). The mean BMI was 26.2±5.5, with 80(28.2%) were overweight. Fifty per cent of participants were on ART for 10 years or more. A total of 17(5.9%) participants were found to have cutaneous markers of dyslipidemia.

No association was found between alcohol consumption, cigarette smoking, and other predictors of dyslipidemia.

Conclusion:

This study found the prevalence of cutaneous markers of dyslipidemia; henceforth heralding the need of incorporating lipid screening as a component of care among HIV seropositive individuals on ARTs, for reducing mortality and morbidity.

LIST OF ABBREVIATION

ATP III	Adult Treatment Program III
CTC	Care and Treatment Centre/clinics
CVD	Cardiovascular Disease
KH	Kairuki Hospital
KU	Kairuki University
MNH	Muhimbili National Hospital
MRRH	Mwananyamala Regional Referral Hospital
NCD	Non-Communicable Disease
NCEP	National Cholesterol Education Program
PLWH	People Living With HIV
TLD	Tenofovir, Lamivudine, Dolutegravir

DEFINITION OF TERMS

In this study, the following definitions were used

HAART: refers to a broad category of treatment regimens usually comprised of three or more antiretroviral drugs

HIV ART+: someone who has been tested and found to be positive with HIV and is on ART

Dyslipidemia As the disturbance in lipids, whereas any of the following, Cholesterol, Triglycerides, and Low-Density Lipoprotein c is elevated, High-Density Lipoprotein c is decreased.

CHAPTER ONE

1.0 INTRODUCTION:

1.1 Background

Cardiovascular disease is among the leading causes of mortality globally accounting for nearly 19 million deaths globally in 2020, and it was estimated 244.1 million were living with ischaemic heart disease[1]. Traditional and modifiable risk factors for this disease include hypertension, diabetes, ageing, cigarette smoking, alcohol consumption and dyslipidemia. Apart from these risk factors, HIV disease itself and ART use are associated with the increase in prevalence and incidence of Ischaemic heart disease and stroke in Sub-Saharan Africa, with dyslipidemia as the prime cause of the ischaemic heart disease[2].

Human Immunodeficiency Virus (HIV), a retrovirus is the causative agent of the disease. HIV exist in two forms, HIV-1 and HIV-2, the latter is exclusively found in Western Africa, while HIV-1 causes a global pandemic and has four subtypes, groups M (major), N, O and P[3,4]. HIV is transmitted through body fluids like blood, semen, vaginal fluids and breast milk from infected lactating mothers, and the most common mode of transmission is sexual intercourse[3,4]

1.1.1 Epidemiology and Burden of HIV Infection

As of 2023, approximately 39 million people globally are living with human immunodeficiency virus (HIV)[5]. About 67% of the 39 million HIV infections were from Sub-Saharan Africa(SSA)[6]. Eastern and central Africa carry the major burden of the disease with 20 million people living with the disease[7]. In Tanzania, the prevalence among adults was estimated to be 4.5%, of which the majority are women with a prevalence of 5.6%[8], Of which 82.7% of adults living with HIV are reported to be aware of their status and 97.9% of them are on ART[8].

1.1.3 HIV Treatment:

Different classes of HIV drugs are in use, including Non-Nucleoside Reverse Transcriptase (NNRTI), Non-Nucleotide Reverse Transcriptase Inhibitors (NRTIs), as the backbone, and Protease Inhibitors (PIs)/Integrase Strand Transfer Inhibitors (INSTIs) as a third medication[9]. Over time different regimens of antiretroviral therapy have been applied, to overcome resistance, and side effects from the drugs, increase compliance and reduce virological and immunological failures[9].

The discovery and introduction of HAART tremendously transformed the management of HIV and AIDS[10]. This has brought about a marked decline in mortality with significant, improvement in quality of life, reduction in the level of transmission, and combating opportunistic illnesses[10], this improvement led to an increase in the population of this cohort to advanced age thus making them prone to dyslipidemia and its associated conditions like coronary artery disease (CAD), stroke and peripheral vascular disease.

1.1.4 Dyslipidemia in the general population and ART use:

Dyslipidemia is defined as a metabolic disturbance in either cholesterol, Triglycerides and lipoproteins, and is defined as an increase in plasma Triglycerides greater than 1.8 mmol/l or a decrease in plasma HDL less than 1mmol/l in males or 1.3 mmol/l in females [11]. Evidence from prospective studies has shown that elevated total cholesterol, low-density lipoprotein (LDL), non-high-density lipoprotein cholesterol(non-HDL-C), triglycerides and apolipoprotein B(ApoB), are important risk factors for cardiovascular disease. Studies have shown evidence of an increase in myocardial infarctions among HIV seropositive individuals caused by dyslipidemia, with 1.5 folds of developing atherosclerotic cardiovascular disease and stroke[12]

HIV induces immune activation, leading to an inflammatory response in the arterial vessel wall, causing endothelial injury and low-density lipoprotein cholesterol (LDL-C) oxidation and atheroma formation. HIV also elevates LDL-C, VLDL-C, and triglyceride-rich lipoprotein levels reduces HDL-C functionality and reverses cholesterol transport. Meanwhile, Antiretroviral therapy (ART) favours lipogenesis, insulin resistance, and abnormalities in adipocyte metabolism[13].

1.1.5 EPIDEMIOLOGY:

Data show variability in the prevalence of dyslipidemia globally[14]. In 2018 a systematic review done in the general population; in Africa reported the prevalence of Total cholesterol to be 25.5% while a previous review ten years earlier reported the prevalence of total cholesterol in Europe to be 54%[15].Study. A cross-section survey in northwestern Tanzania and Southern Uganda revealed a prevalence of 29% and 32% respectively.

According to Global Burden of Diseases, by 2015, approximately 4 million deaths were attributable to dyslipidemia, and 94 million disability-adjusted life years, globally[15,16]. In the study population from the European Study on Cardiovascular Risk Prevention and Management in Usual Daily Practice (EURIKA; N=7641), over 20% of patients had either triglyceride or high-density lipoprotein cholesterol levels characteristic of atherogenic dyslipidemia[17].The prevalence of dyslipidemia varies between HIV+ on ARTs and HIV+ ART naive. A meta-analysis study done in Ethiopia among HIV+ on ARTs revealed a prevalence of up to 67%, with a higher prevalence being total cholesterol and Triglycerides[18], while a study conducted in Dares Salaam Tanzania, reported a prevalence of 76%[19]. Alteration in lipid levels, due to lifestyle or genetic factors, can lead to atherosclerosis and other Cardiovascular complications.

HIV-infected patients on antiretroviral therapy develop an array of changes in lipids which make them vulnerable to the risk of cardiovascular diseases[20,21]. The changes including alteration of

coagulation pattern, immune disturbance, and pro-inflammatory state are associated with plaque formation on blood vessels, ultimately leading to cardiovascular events.

Aetiology:

Dyslipidemia is categorized as primary(familial) dyslipidemias and secondary(acquired) to other conditions (obesity or an unhealthy lifestyle, medications e.g. thiazide, Amiodarone, etc.), the secondary type is the most common[22] Vast studies have shown dyslipidemia is influenced to a large extent by secondary factors[23].

Manifestation:

Dyslipidemia is asymptomatic, usually, the endpoint outcome of cardiovascular events, coronary artery disease (CAD), stroke and peripheral arterial disease, is the first sign of the disease in most of the patients. Severe infiltration of lipids in some organs like the pancreas can cause severe pain, which can be the first sign of this dysregulation. Elevated serum or plasma levels of lipids can be seen during laboratory work-ups, and another manifestation is seen in the cutaneous deposition of lipids whereby there is the formation of xanthomas, which are benign skin lesions with an accumulation of lipid-laden foam cells in the dermis, tendons, and other tissues[24].

The xanthomas include xanthelasma Palpebrarum, eruptive xanthomas, tendinous xanthomas, and plantar xanthomas. Furthermore, dyslipidemia manifests as corneal arcus, an opacity of the peripheral cornea. The xanthomas and cornea arcus are cutaneous markers of dyslipidemia and this study aimed to determine their prevalence among HIV seropositive patients on ART attending CTC clinics in Dar es Salaam.

1.1.5 Cutaneous Markers of Dyslipidemia (Xanthoma) aetiology:

Xanthomas are yellowish tumors under the skin associated with extravasation of serum lipoproteins through vascular walls and local ingestion endocytosis by macrophages, the macrophages with lipoproteins change into rich vacuolated foam cells[25]. On physical examination, these lesions look like small reddish-yellow, non-pruritic tender papules, mostly found in extensor surfaces of extremities and on buttocks and shoulders. Some of these lesions are reversible either by medication or lifestyle changes[25].

They affect different parts of the body and organs including eyes (Arcus lipoides), tendons and knees, tophi of gout, and obesity. Are classified as

- **xanthelasma Palpebrarum**
    - This is the most common form of cutaneous xanthoma, an abnormal accumulation of lipid-containing macrophages in the dermis, and it presents as a yellowish plaque /nodule. On palpation, Xanthelasma might feel tender, soft, semisolid, or calcareous.

- **xanthoma Planum Diffusum,**
    - large flat, yellowish plaque lesions involving the neck, upper trunk, buttocks, and flexures. generalized xanthelasma.

- **Xanthoma Tuberosum**
    - Plate-like and flat or semispherical, yellow to yellow-red or yellow-blue nodules and nodes which can reach substantial sizes.

- **Xanthoma eruptivum (Eruptive xanthoma)**
    - The lesions are small and symmetrical, papules or small nodules, light yellow, 2 to 5 mm in diameter surrounded by an erythematous border (an inflammatory halo). They are found mostly on the gluteal regions, extensor surfaces of the extremities and the back.

- **Xanthoma Palmare Striatum/Xanthoma Palmare Papulosum**
    - Yellowish striate discolouration of the creases of both palms *(xanthochromia palmaris)* and of the flexor lines of the fingers.

- **Xanthoma tendinosum articulare.**
    - Affected are chiefly those of the extensor surfaces of the proximal finger joints and over the insertions of the patellar tendons and the Achilles tendons.

- **Corneal arcus**
    - Consist of lipid deposits within the corneal stroma, seen clinically as grey white ring in the inferior, then superior poles of peripheral cornea and later join together.

1.1.5.1 Pathophysiology of Xanthoma:

Xanthoma results from the breakdown of metabolic lipoproteins. VLDL (TG rich), once absorbed in circulation and reaches adipose and muscle tissue, lipoprotein lipase hydrolyses the Triglyceride part and changes it into intermediate low-density lipoprotein (IDL) and then low-density lipoprotein (LDL) which contains exclusively Apo B 100, Apo B 100 binds LDL to the E receptor of hepatic and extrahepatic cells, alteration of these lipoproteins results in defective apoproteins resulting in clinically visible Xanthomas[26,27].

1.1.5.2 Epidemiology of Xanthoma:

Essentially, they affect people of all age groups, however, they are more common from the age of 20s and above. They show a near similar pattern of prevalence between females and males[28].

1.1.5.3 Diagnosis of xanthoma.

Physical examination by visualisation is the first method of evaluating these lesions, followed by systemic workup, including histopathology examination in a few lesions, which mostly reveal numerous foamy and giant cells[24]. For cornea arcus, the gold standard test is slit lamp examination.

1.1.5.4 Management of dyslipidemia (Xanthoma):

Unlike in the general population, management of dyslipidemia among HIV seropositive subjects, poses a challenge to healthcare providers, nevertheless, non-pharmacological and pharmacological approaches are still the mainstay of treatment[29].

1.1.5.5 Non-Pharmacological Approach:

Lifestyle modifications like aerobic exercise like brisk walking of at least 150 minutes per week, have proven to significantly reduce weight and body fat. Also, a diet containing low saturated fats, and consuming food rich in soluble fibres eg legumes and vegetables, have been documented to lower cardiovascular-related risk factors like blood LDL-C.

1.1.5.6 Pharmacological Approach:

hypertriglyceridemia which most often manifests as eruptive xanthomas, is managed by both lifestyle modification and lipid-lowering pharmacotherapy with fibrates in combination with statins (HMG CoA reductase inhibitors) proven to lower these levels. Eruptive xanthomas typically

disappear within weeks of initiating systemic treatment, tuberous xanthomas take some months, while tendinous xanthomas may take years to resolve or even persist indefinitely. Statin (HMG-CoA reductase inhibitors) is the mainstay for the treatment of hypercholesterolemia while fibrates are used in managing hypertriglyceridemia[29].

Ezetimibe the first lipid-lowering drug that inhibits intestinal uptake of dietary and biliary cholesterol is shown to be effective in reducing total cholesterol and LDL-C levels when used alone or in combination with rosuvastatin[30]. Other drugs like Bile sequestrants and PCK9i are also used, depending on availability and type of dyslipidemia[31].

Lifestyle changes and observing health behaviors can aid in combating this rapidly emerging problem[32]. The use of all these measures will help maintain good health in this cohort and lower the cost of managing these conditions by individuals and at the national level, thus increasing productivity.

CONCEPTUAL FRAMEWORK

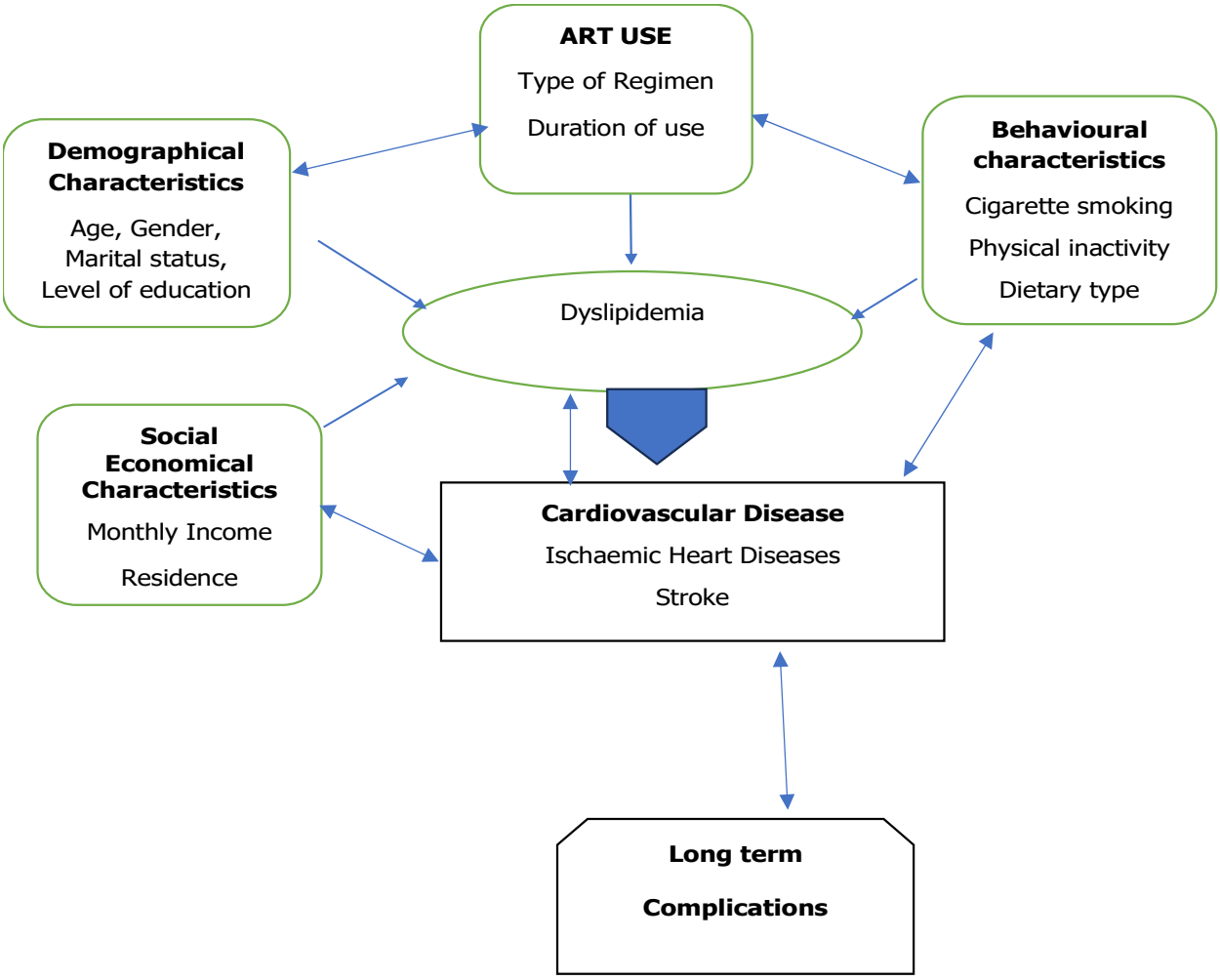

Figure 1. Conceptual Framework

1.2 Problem statement

A marked increase in ART accessibility and effectiveness has aided in a change in HIV/AIDS dynamics whereas mortality has remarkably reduced and life expectancy and quality have improved, however, the risk of diseases, like Atherosclerosis Cardiovascular diseases, have increased[20,33].Dyslipidemia prevalence among HIV seropositive on ARTs is estimated at 73% to 77.5%[34]. with LDL-c comprising the majority[19].

The burden of CVD has major social and economic repercussions and the loss of a productive workforce. According to the Health Sector Strategic Plan cost of the NCD health area is expected to rise from approximately Tsh 820 billion in 2021 to nearly 2 billion in 2025(360 million to 790 million), cardiovascular disease being one of the diseases which are estimated to consume 56% of the budget.

This study aimed to determine the prevalence of cutaneous markers of dyslipidemia among HIV seropositive attending CTC in Dares Salaam.

1.3 Rationale:

Dyslipidemia is increasing among HIV ART+. Despite this noted increase, MOH in Tanzania has not included lipid profile tests as a component of care among HIV seropositive in ARTs in CTCs.

The anecdotally high cost of the test, which ranges from Tsh 10000 To 40000 may be the hindrance of inclusion of the test in CTCs.

The study findings will be used to convince policymakers of the burden of dyslipidemia and the use of cutaneous markers of dyslipidemia, as a screening tool among this risky group, which will help in early detection and intervention.

The present study intends to determine the prevalence of the cutaneous markers in dyslipidemia among HIV seropositive on ART attending CTC in Dares Salaam.

1.4 Research Questions:

1. What is the magnitude and pattern of dyslipidemia among HIV patients on antiretroviral therapy attending CTC clinics in Dar es Salaam Tanzania?
2. What is the pattern of cutaneous markers of dyslipidemia among HIV patients on antiretroviral therapy attending CTC clinics in Dar es Salaam Tanzania
3. What are the associated factors of cutaneous markers of dyslipidemia among HIV patients on antiretroviral therapy attending CTC clinics in Dar es Salaam Tanzania?

1.5 Objectives

1.5.1 Broad Objective:

To determine the prevalence and associated factors of cutaneous markers of dyslipidemia among HIV patients on antiretroviral therapy attending CTC clinics in Dar es Salaam Tanzania.

1.5.2 Specific Objectives

1. To determine social demographic, bahavioural and economic characteristics among HIV patients on antiretroviral therapy attending CTC clinics in hospitals in Dar es Salaam Tanzania
2. To determine the prevalence and patterns of dyslipidemia by serum markers among HIV patients on antiretroviral therapy attending CTC clinics in hospitals in Dar es Salaam Tanzania
3. To determine the prevalence of cutaneous markers of dyslipidemia by social demographic, and clinical characteristics among HIV patients on antiretroviral therapy attending CTC clinics in hospitals in Dar es Salaam Tanzania
4. To determine the type of cutaneous markers of dyslipidemia by social demographic characteristics among HIV patients on antiretroviral therapy attending CTC clinics in hospitals in Dar es Salaam Tanzania.

CHAPTER TWO

2.0 LITERATURE REVIEW:

2.1. Burden of dyslipidemia

Dyslipidemia has appeared to be an important cardiovascular risk factor in sub-Saharan Africa. Studies show that hypercholesterolemia accounts for approximately 60% of ischemic heart disease and nearly 30% of ischemic stroke burden in adults aged 30 and over. Dyslipidemia, especially elevated cholesterol has been shown to vary across regions in sub-Saharan Africa (Belue et al., 2009).

2.1.1 Cutaneous markers of dyslipidemia

Xanthomas are localized lipid deposits in the skin, brought about by lipoproteins passing through the blood vessel wall into the subendothelial layer, whereby they are picked up by macrophages, they are cutaneous manifestations of lipid abnormalities and are signs of atherosclerotic cardiovascular risk. Depending on the types of metabolic disorders, the xanthoma may include triglycerides or cholesterol ester[27]. Studies have demonstrated that the deposition of cholesterol in xanthomas is similar to that in atherosclerotic lesions[26,27].

Clinical and imaging studies have suggested that a positive correlation exists between tendon xanthoma regression and improvement in atherosclerotic disease, which is the main cause of death in dyslipidemic patients[35,36]. In a prospective analysis using Cox-proportional hazards regression models in the Framingham Heart Study, a cohort included 23,376 person-exams, 3,890 (17%) of whom were identified as having corneal arcus during their physical exam. It was found that Corneal arcus was a predictor of both CVD and CHD at 4 years [hazard ratio (HR) = 2.28 and 1.99, respectively] and 8 years of follow-up (HR = 2.52 and 2.35, $p<0.0001$ for all).

Franz et al, reported a case of extreme xanthoma, in a patient with HIV and undetected viral load, five months post antiretroviral therapy switch, where, he developed yellowish lesions on the palmar and digital creases of both hands, furthermore, he developed yellowish lesions on both knee caps and tips of elbows, these findings correlated with hyperlipidemia in this patient. A similar finding of xanthomas was reported four days after a patient regimen changed from efavirenz-based to Dolutegravir, whereby he developed numerous monomorphic yellow-orange papules in extensors on extremities, buttocks and hands[37].

Leung et al reported a case of an HIV patient with massive tendon xanthomas on the metacarpophalangeal and metatarsophalangeal joints, elbows, and patellae, lesions appeared approximately twelve months after initiation of a PI-based regimen (stavudine; lamivudine; saquinavir, and ritonavir); the lesions rapidly grew over the next 18 months. The patient reported having mixed dyslipidemia, before initiation of HAART. This shows dyslipidemia is exacerbated by the use of ART[38].

Ozdol et al, in a study of 100 xanthelasma patients with 100 non-xanthelasma patient age-sex matched, and compared for cardiac risk factors, the rate of atherosclerotic, Framingham risk scores and Lp(a) levels, dyslipidemia was found to be significantly more common in patients with xanthelasma($p=0.001$)[39], this shows that these skin markers can predict the presence of lipid changes in patients. In another study among 80 xanthelasma patients, the prevalence of dyslipidemia was found to be 80% (74-86 at a 90% confidence Interval). (Anjanrai) Ang et al, in examining the association of corneal arcus to cardiovascular disease (CVD) in an adult, ethnic Indian population, reported the corneal arcus is associated with CVD (OR, 1.31; 95% CI, 1.02 to 1.7; $P = .0038$) independent of risk factors, even in those at low risk for vascular disease, higher levels of total_cholesterol (OR, 1.14; 95% CI, 1.05 to 1.24; $P = .002$) associated with this condition.

CHAPTER THREE

3.0 Methodology:

3.1 Study Design:

A cross-sectional hospital-based study was conducted.

3.2. Study Area:

Dares Salaam is located at 6°48' South, 39°17' East on the eastern coast of East Africa. It is a rapidly growing cosmopolitan commercial city of Tanzania with a population of 5 million, it has 5 districts (Ilala, Kinondoni, Kigamboni, Ubungo, Temeke). It has over 1000 registered health facilities and over 50 fully-fledged hospitals. Care and Treatment Clinics for HIV (CTC) are distributed in all five districts.

The study was conducted at the HIV and AIDS care and treatment clinics (CTC) of the Mwananyamala Regional Referral Hospital, a government-owned Hospital with about three hundred bed capacity and CTC which attends a minimum of 80 clients per day divided into two clinics, one starting around 6.00 AM and the second one at 10.00 AM, and Kairuki Hospital a privately owned, has about 100 bed capacity and CTC which serves around 25 clients per day, with only one clinic per day starting around 7.30 AM—both hospitals located in Kinondoni Municipality in Dar es Salaam region. The municipality is the most populated district with a population of 982,328, from the 2022 census, and a geographical area of 269.5 km^2.

3.3. Study duration

The study lasted six months, from January 2024 to July 2024.

3.4. Study Population

HIV patients attending the Care and Treatment Centre in Dar es Salaam Tanzania

3.5. Target population

HIV patients on ARTs attending the Care and Treatment Centre on ARTs in Dar es Salaam Tanzania.

3.6. Sample Size Estimation:

A previously used single population proportion formula for cross-sectional study was used considering the following assumptions:

$$n = \frac{(Z(\alpha/2))^2 P(1-P)/(d)^{2,}}{E^2}$$

n represents the initial sample size;

Z α/2 represents the standardized normal distribution value for the 95% CI = 1.96; attriation of 10% for missing data

P, 77.5% represents the population proportion from a similar study done in Tanzania by Ombeni et al, with a final sample size of 230[19]

E represents the margin of error of 5%. Sample size.

Calculated sample size for this was 270.

3.7. Recruitment of Participants

A simple random sampling technique was used, whereby CTC clinics of each of the 5 districts making the Dares Salaam region, were listed, and randomly two CTCs were selected. By using a random sampling technique, one district was Kinondoni, and from the Kinondoni district, all

CTCs were listed and grouped into Public/Government run versus private/NGO run CTC. Then randomly one CTC was selected from each group. From CTC selected participants were obtained by consecutive recruitment technique. A list of registration numbers of patients expected to attend clinic on a particular day was used to randomly select the study population. Using random numbers, twenty eligible patients were randomly selected as potential study participants on each day. Data were collected throughout the week.

The clinic in charge and principal investigator randomly selected patients to the allocated room for interview and consented patients were recruited in the study.

3.7.1 Inclusion criteria

Adults above 18 years of age, HIV-positive patients attending CTC clinics in Dares Salaam

Those who have signed a written informed consent form.

Those who had fasted for at least 8 hours.

Patients initiated ART treatment and had been on treatment for six months or above

3.7.2. Exclusion criteria

i. Patients fasting less than 8 hours and those who have not fasted at all

ii. Patients with known chronic diseases, liver, renal and autoimmune diseases

iii. Patients using drugs that have the potential to cause dyslipidemia such as Thiazide diuretics, B blockers, Cyclosporine, Estrogen, Growth Hormone, Retinoids, and steroids.

3.8. Data collection procedure

The questionnaire was pretested at Mwananyamala Care and Treatment Clinic before the initiation of the study. Ten participants were interviewed twice on the same day by both the principal investigator and research assistant. The first five interviews were conducted by the principal investigator, while the research assistant completed the other five. The findings from the pretest were used to improve the data tool.

A pretested questionnaire was used by a principal investigator and 2 research assistants, (qualified nurses and Medical Doctors, were trained by the principal investigator) to collect sociodemographic data (age, sex, marital status, employment status and education level), behavioural characteristics and Clinical data.

On the clinic day, the patients were randomly selected and those who met the inclusion criteria were given an information sheet and detailed consent form. These contained purpose, procedures, benefits and risks. The researcher explained the details needed on the questionnaires, ensuring they all understood the questions. The researcher took time with the patients to answer all the questions and clarification was provided by the researcher and the assistants.

The questionnaires were assigned a unique identification number for data capture and to ensure confidentiality. All clinical measurements were carried out on hospital premises between 7.00 am and 10.00 am. Upon arrival, about 4mls of blood samples were collected for serum lipids tests (i.e. High-density lipoprotein, Low-density Lipoprotein, Triglyceride, Total cholesterol) were collected by a qualified phlebotomist. The blood samples obtained were then emptied into red plain vacutainers which were stored in the cooler box and then transported to the Laboratory for analysis on the same day of collection.

3.8.1 Laboratory Biochemical Data.

Blood was centrifuged for 10 minutes at 3,000 rates per minute in 30 refrigerated positions by using Zeny Cntrifuge,800-1, made in China. Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were measured by a Random-access automatic analyzer with photometric reading Biosystems, S.A. Costa Brava, Spain). LDL-C levels were calculated by the Friedewald formula[40].

Quality checks for the results were conducted by running the sample alongside calibrators and controls and a qualified biochemist.

In this study, hypercholesterolemia was defined as total serum cholesterol of >5.17 mmol/L. Hypertriglyceridemia was defined as serum TG of > 1.69 mmol/L, decreased HDL was defined as serum HDL levels of <1.04 mmol/L and increased LDL was considered as serum LDL levels of >3.3 mmol/l[41].

3.8.2. Anthropometric Measures:

A trained healthcare provider measured the participants' weight using the calibrated weighing scales Model PM-200A, serial No. 23060620, made in China, and Seca, manufactured in Germany at Mwananyamala and Kairuki Hospital, respectively. The weight was taken without shoes and in light clothing. Participants stood with feet close together, arms at the side, and body weight evenly distributed. Reading was measured to the nearest 1 kilogram.

The Height was measured by a trained healthcare provider using a Height measuring rod, attached to the same weighing scale measurement was recorded on a health assessment form in meters.BMI was calculated per WHO 2015 guidelines: BMI = Weight (kg)/Height (m).

3.8.3 Physical examination for cutaneous Markers/Xanthomas

Corneal Arcus Diagnosis

The research assistants were trained by photos and videos on different kinds of xanthomas, including cornea arcus, during the examination, the principal investigator and/or research assistant had to stand in front of the subject and ensure that their eyes were at the same level. Diagnosis for cornea arcus was made by the naked eye in natural light and was done by diligently searching for any ring in the peripheral of the cornea whether complete/incomplete and had to be bilateral for it to be counted as a positive finding. Smartphones took photographs and a Dermatologist was consulted to clear doubts about the diagnosis for the cases which were not clearer, the photos were not shared online to keep confidentiality, and were immediately deleted after concluding.

A consulted dermatologist was selected randomly out of three from a list of dermatologists attending Kinondoni Derm clinics, the first three from the first three odd numbers were selected, and later one was randomly obtained. About 80-90% of dermatological diagnoses are made by visual examination, it is rarely a biopsy can be entertained.

Xanthelasma Palpebrarum

A thorough history was taken by the interviewer, examination was done on the face, periorbital skin and eyelids, looking for yellowish plaques, papules or nodules, and softy or semisolid in consistency. Photographs were taken and shown to the Dermatologist for a second opinion and to clear ambiguity.

3.8.4 Research tools:

1. Questionnaire: was tested among participants, and repeated on the same participants at different times to test for its validity and reliability.
2. Weighing scale: someone with a known weight was used to check for its reliability in different time intervals
3. Laboratory data: Samples were run alongside calibrators and controls for validity and reliability checks.

3.9.1 Dependent Variable: Visual and Biochemical

Dependent Variable	Independent variable
i.Serum markers	
Total Cholesterol	Age
Triglycerides	Sex.
HDL	Occupation
LDL	Education
ii.Cutaneous markers	
xanthelasma Palpebrarum	Marital status
seen in Hypercholesterolemia.	Duration on ART
xanthoma Planum Diffusum,	CD4 Count level
xanthoma Tendinous,	Smoking
xanthoma Planum Diffusum,	Type of ART regimen
Cornea arcus	Duration of ART
	CD4 COUNT
	Physical activity, use of medication, sedentary lifestyle

3.9.3 Operational definition of variables:

1. The Demographical characteristics[42]:

   These included

   Social characteristics: Age, gender, Marital status

   Economic characteristics: monthly income per month

2. **Behavioral characteristics**: Cigarette smoking, dietary habit, physical activity, Alcohol consumption[43].

3. **Clinical characteristics[43]:** duration of ART use, CD4 count; chronic use of medications, comorbidities, family history of cardiac disease, number of years since the initiation of ART, type of ART regimen used, e.g. dolutegravir-based regimen, Efavirenz-based regimen etc.

4. **Cutaneous markers** meant, xanthelasma Palpebrarum, cornea arcus, eruptive xanthoma and other xanthomas which were seen by the naked eye[44–47].

5. **serum biomarkers** of dyslipidemia: Include Serum Total Cholesterol (TC), Triglycerides (TG), LDL and HDL[48].

6. **Smoking** was defined as current tobacco use or use during the last 3 months.

   Physical activity was defined as at least 150 min of moderate-intensity aerobic physical activity throughout the week or at least 75 min of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous-intensity activity. Patients who did not fulfil this definition were considered **physically inactive[49].**

Hypertension was defined according to World Health Organization recommendation as resting systolic blood pressure (SBP) ≥140 mmHg and or diastolic blood pressure (DBP) ≥90 mmHg or a patient on antihypertensive treatment[50].

overweight was defined as a body mass index (BMI) between 25 and 29.9 kg/m^2 and obesity as a BMI ≥30 kg/m^2[51].

Dyslipidemia as total cholesterol ≥5.2mmol/L, or triglycerides ≥1.7mm0l/L, or LDLC ≥4.2L, or HDLC <1mmol/L[52].

3.10 Data Safety, validation, analysis and presentation

3.10.1. Data safety

Filled questionnaires have been kept under the custody of the researcher to prevent any possible breach of confidentiality. Each variable on the questionnaire had an ID number to simplify easy data entry and analysis. A Microsoft Office-Excel 2010 database was created to store all the information from the filled questionnaires. This information was carefully entered into the database by the researcher.

3.10.2 Data validation checks

This process ensured that data were clean and correct. It will also provide guarantees for fitness, accuracy and consistency for the inputs from the questionnaire through manual checks on the questionnaires.

3.10.3 Data analysis and presentation

Quantitative data were analysed using IBM SPSS software Version 24. Descriptive statistics (percentages, proportions) Were used to determine the prevalence and patterns of dyslipidemia and cutaneous markers, together with other patients' characteristics. T-test was used to compare the lipid parameter means of males and females.

Chi-square was used to describe the distribution of dyslipidemia then univariate analysis and multivariable logistic regression analysis were performed to determine the associated factors.

All variables at the 0.2 level of significance in the univariate were included in the multivariable model. Using backward elimination criteria, variables that had a p-value of < 0.05 using a 95% confidence interval were considered significant. The analysed data were presented as tables, pie charts and bar graphs.

3.10.4. Ethical Consideration and Approval:

Permission was sought from the Kairuki University Institution, Research and Ethics Committee, and permission was sought from each respective facility where the study was conducted. Informed consent was obtained from all participants and a Consent form was administered to the participants. Participants were warned to expect mild pain during blood procurement, which resolves soon after phlebotomy. Those found to have dyslipidemia were informed and advised for the non-pharmacological part and also were advised to seek medical help, as this study had no funds for the pharmacological part. The data obtained have been kept in a confidential vault and will help in managing the participants.

CHAPTER FOUR

4.0 Results

The results presented in this section are from two parts of the study. the first part is from analysis of laboratory data, which analysed serum markers on prevalence, and patterns, of dyslipidemia, the second part is the clinical data which was the broad objective of this research on determining prevalence and patterns of cutaneous markers of dyslipidemia among HIV Seropositive attending care and treatment Clinics in Dares Salaam in the year 2024. The calculated sample size was 270, however, 305 HIV seropositive were randomly selected, of which 21 had missing data from the registry and were excluded from the analysis, two hundred and eighty-four were included in the final analysis.

I: Results based on laboratory Serum analysis:

4.1.1 Table 1. Description of study participants and Socio-demographic characteristics of HIV seropositive on ART attending clinics in Dares Salaam. N 284, 2024

Among 284 HIV seropositive participants included in the analysis, 185 (65.1%) were women. The mean age of participants was 46.7± 10.91 years. The majority of them 240(84.5%) were employed. More than two-thirds of them 185(65.1%) had a monthly income of ≥ 150000 Tsh. About 165 (58.1%) of the participants attained a primary level of education, and forty per cent were married. Table 1

Table 1. The socio-demographic and economic characteristics of participants N= 284

Characteristic		Frequency	Percentage
Sex			
	Male	99	34.9
	Female	185	65.1
Age group			
	18-30	19	6.7
	31-50	163	57.8
	51-70	102	36.2
	>/=70	2	0.7
Occupation			
	Employed	71	25.0
	Unemployed	39	13.7
	Self Employed	169	59.5
	Retired	5	1.8
Education level			
	No formal Education	27	9.5
	Primary School	165	58.1
	Secondary School	63	22.2
	Tertiary Education	29	10.2
Marital Status			
	Single	48	16.9
	Married	115	40.5
	Widow	49	17.3
	Divorced	72	25.4
Monthly Income			
	<Tsh 150000	99	34.9
	>Tsh 150000	185	65.1

4.1.2 Table 2. Description of Behavioural and Clinical Characteristics of HIV seropositive on ART attending CTC in Dares Salaam. N 284, 2024

More than two-thirds 249(87.7%) reported no history of cigarette smoking and one hundred seventy-seven (62.3%) of them had a current history of alcohol consumption. And a majority of them 237(84.6%) were physically active (Table 2). One hundred and eighty-eight 188 (66.2%) had hypertension. The mean BMI was 26.4±5.43, of these, 80(28.2%) were overweight and 69(24.3) were obese, and the majority of them145(50%) had been on ARTs for ten/above years. Most (51.8%) had CD4 counts of more than 350 cells/mm3. A vast number of 278 (97.8%) participants received TLD, 4(1.4%) were on TLE and 2((0.7%) were on Abacavir+Lamivudine+Dolutegravir (Table 2).

Tab 2 Clinical and Behavioral characteristics among HIV Seropositive on ARTs attending CTCs in Daressalaam, N 284

Variable	Frequency	Percentages
Blood Pressure		
SBP		
≥140 mmHg	82	28.9
<140 mmHg	202	71.1
DBP		
≥90 mmHg	67	23.6
<90 mmHg	217	76.4
Mean BMI 26.4±5.4		
Healthy weight	125	44
Overweight	80	28.2
Obese	69	24.2
Underweight	10	3.5
ART Regimen		
TLD	278	97.9
Others	6	2.1
CD4 cell count		
<350 cell/Ul	18	6.3
350-500 cell/ul	119	41.9
>500 cells/ul	147	51.8
Alcohol use		
Yes	107	37.7
No	177	62.3
Cigarette smoking		
Yes	35	12.3
No	249	87.7
Physical Activity		
>600MET-min/week	237	84.6
<600MET-min/week	43	15.4

Abbreviations: N, Number; BMI, Body Mass Index; kg/m2, Kilogram per Meter Square; Antiretroviral Therapy; CD4, Cluster of Differentiation 4; %, Percentage; TDF, Tenofovir Disoproxil Fumarate; 3TC, Lamivudine; ABC, Abacavir; ATV/r, Atazanavir/Ritonavir; AZT, Zidovudine; DTG, Dolutegravir; EFV, Efavirenz; SD, Standard Deviation

4.1.3.1 Table 3. Prevalence and Patterns of Dyslipidemia by Serum makers of HIV seropositive on ART attending CTC IN Dare Salaam by sex N 284. 2024

The prevalence of dyslipidemia by serum markers was 145**(51.1%),** the majority with dyslipidemia were female 87(60.7%). The majority 232(81.7%) had low HDL, and about 77 (27.1%) of study participants had hypercholesterolemia, other lipid profile characteristics are shown in Table 3 below.

Table 3 Distribution of Patterns of Serum Dyslipidemia of HIV Patients on ART in Dares Salaam by Sex N= 284

Dependent Variable	Frequency n (%)	Sex	
		Male	Female
Dyslipidemia			
Yes	145(51.1)	57(39.3)	87(60.7%)
No	139(48.9)	53(38.1)	86(61.9)
High Total Cholesterol	77(27.1)	20(26)	57(74)
High LDL-Cholesterol	57(20.1)	17(29.8)	40(70.2)
Low HDL-Cholesterol	232(81.7)	83(35.8)	149(64.2)
High Triglyceride	38(13.4)	19(50)	19(50)

Dyslipidemia was defined according to NACEP as a TC>5.2mmol/L, and or increased LDL-C>2.6mmol/L, and or decreased HDL-C<1.03mmol/L for males or <1.3mmol/L for females and or TG>1.7mmol/L.
Blood pressure is defined according to WHO Guidelines on Management of Hypertension as Normal (Systolic Blood Pressure < 140 mmHg and Diastolic Blood Pressure <90 mmHg) and not on anti-hypertensive Treatment.

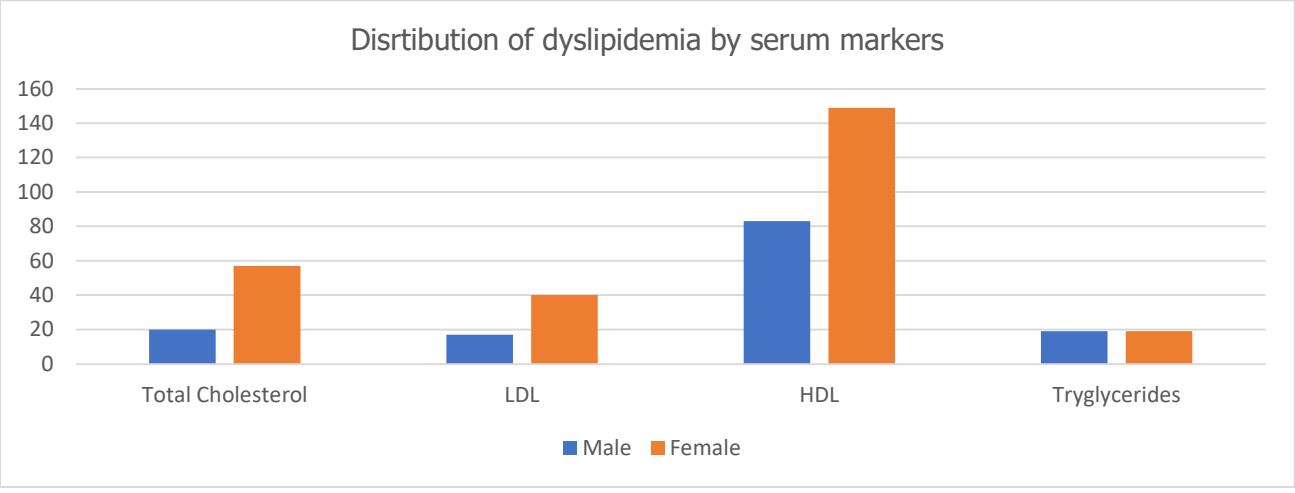

Fig.2 Bar graph showing the distribution of serum markers of dyslipidemia stratified by sex

4.1.3.2 Table 4. **Prevalence of Dyslipidemia by Serum makers by Age group among HIV seropositive on ART attending CTC in Dare Salaam, N 284. 2024**

The majority of participants with dyslipidemia were in between the age group of 31-50,77(53.1%), the most predominant dyslipidemia was found to be low HDL,232(81.7%), total cholesterol was higher in the age group, 51-70, while LDL-c was more on age group, 31-50, which was significant: table 4.

Table 4 Serum dyslipidemia and lipid profile patterns of Study Participants by Age N= 284

Characteristic	Frequency n (%)	20-30	31-50	51-70	≥71	P Value
Dyslipidemia						
Yes	145(51.1)	7(4.8)	77(53.1)	59(40.7)	2(1.38)	0.816
No	139(48.9)	12(8.6)	84(60.4)	43(30.9)	0(0)	
High Total Cholesterol	77(27.1)	3(3.9)	35(45.5)	37(48.1)	1(1.3)	0.533
High LDL-Cholesterol	56(19.7)	3(5.4)	29(51.8)	23(41.1)	1(1.8)	*0.23
Low HDL-Cholesterol	232(81.7)	4(1.41)	31(13.4)	16(6.8)	1(0.43)	0.45
High Triglyceride	38(13.4)	3(7.9)	23(60.5)	12(31.6)	0	0.73

Dyslipidemia was defined according to NACEP as a TC>5.2mmol/L, and or increased LDL-C>2.6mmol/L, and or decreased HDL-C<1.03mmol/L for males or <1.3mmol/L for females and or TG>1.7mmol/L.
Blood pressure was defined according to WHO Guidelines on Management of Hypertension as Normal (Systolic Blood Pressure < 140 mmHg and Diastolic Blood Pressure <90 mmHg) and not on anti-hypertensive Treatment.

II: Results based on Physical Examination:

4.2.1 Distribution of cutaneous markers of dyslipidemia among HIV seropositive on ART attending CTC in Dares Salaam N 284, 2024

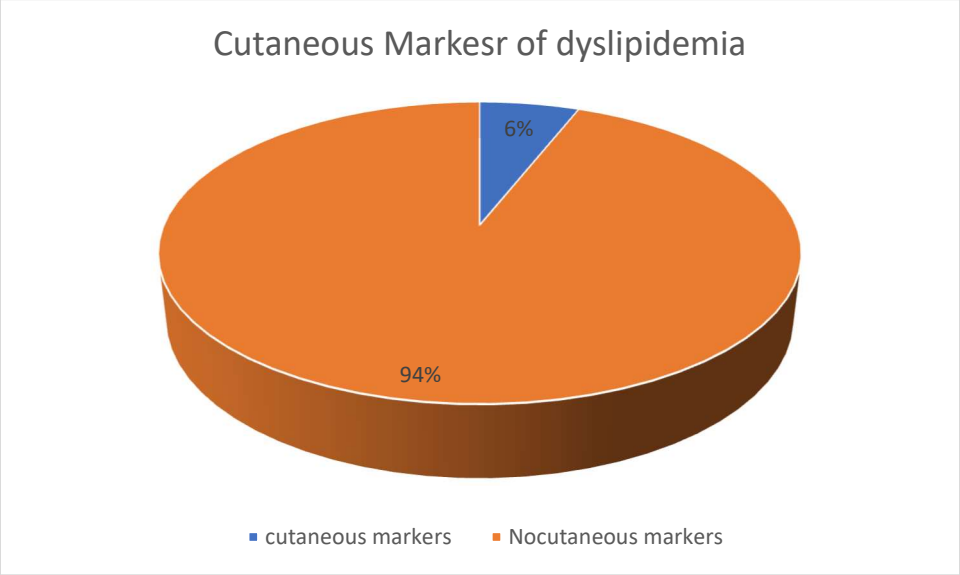

Fig. 2 shows the distribution of cutaneous markers of dyslipidemia among HIV seropositive on ART attending CTC in Dares Salaam

4.2.2: Table 5. Distribution of cutaneous markers of dyslipidemia among HIV seropositive on ART attending CTC in Dares Salaam by Social Demographic Characteristics. N284, 2024

The prevalence of cutaneous makers was 17(5.9%), and females were predominantly affected 12(70.5%), Age group and sex were not statistically significant. Prevalence of cutaneous markers was found more in females by 7(85.7%). The majority with cutaneous markers were in the age group 31-50. Table 5.

Table 5 Prevalence of Cutaneous Markers of dyslipidemia by Social demographic characteristics N= 284

Characteristic		Overall	Cutaneous Markers		P Value
			Yes(%)	No(%)	
Overall	Distribution	284	17(5.9)	267(94.01)	
	20-30	19	0(0)	19(100)	0.148
	31-50	161	8(5)	153(95)	
	51-70	100	7(7)	93(93)	
	≥71	2	2(50)	1(50)	
	Sex				
	female	185	12(6.5)	173(93.5)	
	Male	99	4(4)	95(96)	0.574
	Total	284	16	268	

4.2.3: Table 6. Distribution of cutaneous markers of dyslipidemia by clinical characteristics of HIV Seropositive on ART attending CTC in Dares Salaam, 2024.

The majority of those with cutaneous markers, 9(52.9) belonged to CD4 Count 350-500 cells/µL and about 278(97.8) were using TLD, with a few 6(2.1) on other ARTs. Physical inactivity p= 0.018, was statistically significant in multivariate analysis.CD4 count, ART regimen and duration of ART use were not statistically significant. Table 6.

Table 6 Prevalence of Cutaneous Markers of dyslipidemia by Clinical characteristics N= 284

Characteristic	Overall	Cutaneous Markers		P Value
CD4 Count		Yes(%)	No(%)	
<350	18(6.3)	1(6.2)	17(6.3)	
350-500	137(48.2)	9(52.9)	129(48.1)	0.9
>500	129(45.4)	7(5.4)	122(94.6)	
ART Regimen				
TFD+3TC+DTG	278(97.9)	17	261(97.8)	
Other 1st line ARTs	6(2.1)	0	6(2.2)	0.72
Duration of ART Use				
<5 years	81(28.5)	5(31.2)	76(28.4)	
5-10 years	59(20.8)	3(18.8)	56(20.9)	
>10 years	144(50.7)	8(50)	136(50.7)	0.325
Duration HIV diagnosis				
<5 years	59(20.8)	4(25)	55(20.8)	
5-10 years	92(32.4)	5(31.2)	87(32.5)	
> 10 years	133(46.8)	7(43.8)	126(47)	0.658
Hypertension (SBP)				0.693
yes	82(28.9)	6(7.3)	76(92.7)	
no	202(71.1)	8(4)	194(96)	
Hypertension (DBP)				0.215
yes	67(23.6)	3(4.5)	64(95.5)	
No	217(76.4)	11(5.1)	206(94.9)	
Alcohol Consumption				0.811
yes	108(38)	5(4.6)	103(95.4)	
No	176(62)	9(5.1)	167(94.9)	
Cigarette smoking				0.027
yes	37(13)	0(0)	37(100)	
no	247(87)	14(5.7)	233(94.3)	
Physical Activity				0.031
MET-min/week>600	237(84.6)	9(3.8)	228(85.7)	
MET-min/week<600	43(15.4)	5(11.6)	38(88.4)	

4.2.4. Distribution of type of cutaneous markers of dyslipidemia among HIV seropositive on ART by social demographic Characteristics. N 284, 2024

Four types of markers were observed, Xanthelasma Palpebrarum 9, cornea arcus was second most 6, and other types of xanthomas 2, (eruptive and tendon) both were found in female. in xanthelasma Palpebrarum, females were majority,6, while in cornea arcus, male,5, were the majority. Fig.3, no statistical significance for age group, gender, education level and monthly income.

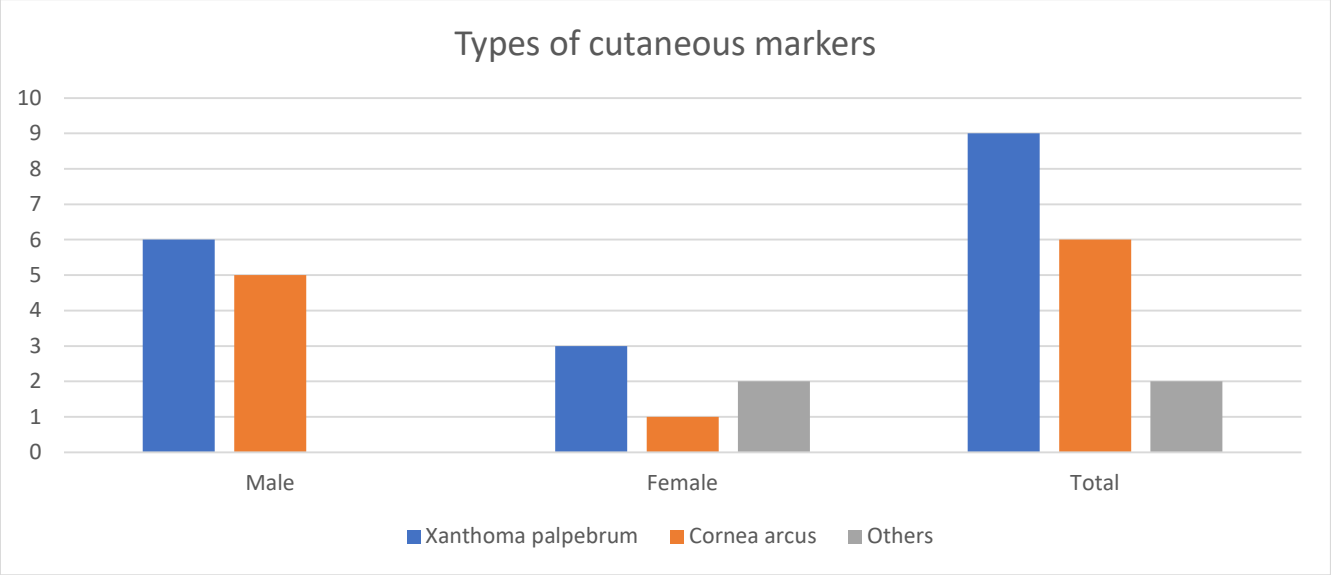

Fig: 3, showing types of cutaneous markers among HIV seropositive on ART attending CTCs in Dares salaam.

4.2.5. The correlation between cutaneous markers of dyslipidemia and predictors.

(age, gender, BMI, Hypertension, Physical activity, Cigarette smoking, Alcohol consumption, ART use, Current ART Regimen, Duration of ART use).

Results of logistic regression

Analysis of predictors showed that being on ART for more than 10 years COR 2.286(0.249-31.706), unemployed OR (1.722(0.406-7.309), married, COR1.009(0.189-5.379), tertiary education,1.032(0.061-17.24) were not associated with cutaneous markers, Table 7 and 8.

Table 7 Association between cutaneous markers among HIV seropositive on ART attending CTC in Dares Salaam and study variable by multiple regression N 284

	Cutaneous markers					
	Univariate Analysis			Multivariate Analysis		
Cutaneous markers	Odds ratio	P>z	[95% conf. interval]	Odds ratio	P>z	[95% conf. interval]
Age	1.035	0.148	0.988 - 1.085			
Sex (Male)	1.331	0.574	0.490-3.613			
Primary School	0.949	0.948	0.195-4.609			
Secondary School	1.051	0.956	0.182-6.060			
Tertiary Education	1.033	0.975	0.137-7.814			
Married	3.396	0.256	0.412-27.95			
Alcohol consumption	0.882	0.811	0.316-2.418			
Cigarette smoking	0.883**	0.027	0.193-4.031	0.862	0.669	0.189-3.943
Physical inactivity	1.767**	0.031	0.547-5.700	1.770**	0.018	0.549-5.709
Duration on ART						
5 -10 Years	Table C16n	0.416	0.407-8.787			
>10 years	1.94	0.325	0.518-7.263			
CD4 Level (350-500 cells/ul)	1.063	0.902	0.397-2.845			
Occupation						
Unemployed	1.722	0.461	0.406-7.309			
Self Employed	0.845	0.786	0.251-2.844			
Duration HIV diagnosis						
10 years	1.073	0.925	0.247- 4.666			
>10	1.355	0.658	0.353-5.196			
SBP	1.004	0.693	0.982- 1.026			
DBP	1.021	0.215	0.987- 1.056			

Hypertension	1.808	0.239	0.674- 4.846
BMI	1.081**	0.035	0.998- 1.177

Table 8. Association between xanthelasma palpbrarum among HIV seropositive on ART attending CTC in Dares Salaam and study variable by multiple regression N 284

	Univariate Analysis			Multivariate Analysis		
Xanthelasma palpebrarum	Odds ratio	P>z	[95% conf. interval]	Odds ratio	P>z	[95% conf. interval]
Age	1.045**	0.019	0.979-1.114	1.041	0.271	0.969-1.118
Sex (Male)	0.524	0.426	0.106-2.573			
Primary School	1.06	0.959	0.120-9.379			
Secondary School	1.049	0.969	0.092-12.07			
Tertiary Education	1.032	0.982	0.062-17.24			
Married	1.291	0.772	0.230-7.233			
Alcohol consumption	0.809	0.769	0.198-3.306			
Cigarette smoking	0.829	0.862	0.101-6.832			
Physical inactivity	2.887**	0.045	0.693-12.07	2.719	0.183	0.624-11.84
Duration on ART						
5 -10 Years	0.681	0.756	0.060-7.692			
>10 years	1.717	0.514	0.339-8.713			
CD4 Level (350-500 cell)	1.923	0.362	0.470- 7.858			
Occupation						
Unemployed	0.538	0.598	0.054-5.361			
Self Employed	0.621	0.523	0.144-2.676			
Duration since HIV diagnosis						
10-May	0.205	0.175	0.021-2.021			
>10	0.729	0.673	0.168-3.157			
SBP	1.018	0.172	0.992- 1.046			
DBP	1.019	0.402	0.975- 1.066			
Hypertension	2.527	0.175	0.663- 9.638			
BMI	1.169***	0	0.039- 1.315	1.161**	0.018	1.025-1.314

CHAPTER SIX

6. DISCUSSION

6.1 Introduction

HIV and ART use has been established to cause dyslipidemia[34,53–55]The alarming increase in ischaemic heart diseases and ischaemic stroke incidence among HIV patients. is a study that examined dyslipidemia in both serum and cutaneous, however, the broad objective was to determine the prevalence of cutaneous markers of dyslipidemia, among HIV seropositive ARTs attending Care and Treatment centres in Dar es Salaam.

6.2 Discussion

Findings in the serum markers of dyslipidemia revealed that 145(51.1%) had dyslipidemia, which was slightly low compared to a study done on similar subjects and in a similar region which reported a prevalence of approximately 75%[19] , that can be attributed most probably to the type of ART regimen used which was Efavirenz 98(42.4%), which is associated with increasing Triglycerides and VLDL-C[56] whilst in the current study majority used a Dolutegravir-based regimen 278(97.9%), which is associated with lower HDL-c and is associated with increasing atherosclerosis risk in HIV participants and increase in weight gain, this is similar to findings from other studies which revealed,[22,57,58]Moreover this study revealed an increase in BMI> above twenty five,249(52.5%), similar to other study[19,59].

In the broad objective of this study prevalence of the overall cutaneous marker of dyslipidemia was found to be 17(5.9%), and females were found to be the majority,9(52.9%), the preponderance of females was also revealed by another study[60,61], of which women were 64.7%. hormonal factor is attributed to this manifestation. In this study 47% were found to have cornea arcus, which is nearly similar to a study done in Iran by Hashemi et al which revealed a prevalence of 42.3%, however, the study in Iran was on a population above 60 years, which is not as much risk for dyslipidemia compared to participants in the current study[62].

In this study prevalence of cornea arcus was found to increase with age group, this is similar to reports from other studies[62].

The education level associated with an increase in cornea arcus, in this study is primary education but, this is similar to another study in Iran, by Hashemi et.al which revealed prevalence to be higher in the university education level[62].

The social economic level is a protective factor, but this is different from the finding in this study.

In this study overall prevalence of Xanthelasma was found to be the most prevalent marker,52.9%, followed by cornea arcus, which is inconsistent to a study done in Denmark, which revealed cornea arcus to be more prevalent, this can be due to the fact that, Copenhagen study had more than 12000 participants and age range 20-93, and it wa a prospective study for over thirty years[63]. Furthermore, among participants with xanthelasma Palpebrarum, females were predominant with 57.1%, this preponderance of females is associated with hormonal mechanism[64].

Another finding was of one participant grouped in other xanthomas, who was found to have eruptive xanthomas, which were present only on the elbows and this finding is similar to other documented cases which showed the presence of various forms of eruptive xanthomas in HIV seropositive, on which is one of the study this occurred after a switch of medication to Dolutegravir within a week[25,37,65], however in this study, the patient noticed them many months after being on the Dolutegravir regimen, There may be a genetic component involved in the manifestation of this condition, more people need to be studied to find the variability of manifestation.

Study limitation:

A Cross-sectional study which has limited generalizability

Diagnosis of cutaneous markers was done by using naked eyes, which could miss some subtle changes, especially in the cornea arcus, the use of eye aide equipment like a slit lamp could increase sensitivity. Also, absence of similar study for comparison is another limitation of the study. Also the study has not tested for sensitivity and specificity of cutaneous markers of dyslipidemia as compared to serum markers which is considered gold standard.

Strength of the study.

This is the first of its kind in this cohort, thus paving the way for further studies/research on the same subject. The large number of study participants is another strength of the study, statically oriented, and structured in a standard manner.

Conclusion

Findings from this study provide evidence for the presence of cutaneous markers of dyslipidemia among HIV Seropositive on ART attending Care and Treatment Centre in Dar es Salaam, which implies that this cohort is at greater risk of cardiovascular and metabolic diseases. This finding adds value to the previously done studies among the cohort, which shows the prevalence of dyslipidemia, which has direct implications in cardiovascular and ischaemic diseases, and heralding the need to incorporate it in a bundle of care among the group.

Recommendation:

It is strongly recommended that screening of dyslipidaemia be incorporated as a component of care among HIV seropositive subjects, and that cutaneous markers, to be used as a screening tool especially for the risk groups for dyslipidemia. this test being cost effective, and easy to perform, will aid in early diagnosis and management, ultimately reducing morbidity, mortality.

Another similar study with eye aid equipment like a slit lamp can be performed to increase the sensitivity of not missing even minor changes which the naked eye alone could have missed. Furthermore, this study recommends another study to be performed to determine sensitivity and specificity of cutaneous markers against biochemical markers (which is considered gold standard) in diagnosis of dyslipidemia.

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Appendix 1: Questionnaire (English)

Cutaneous markers of dyslipidemia among HIV patients on Antiretroviral therapy attending CTC clinics in Dar es Salaam

Date…… Code…… Time……

Venue:……

Please answer the following questions by putting a tick on the appropriate answer.

SECTION A: SOCIO-DEMOGRAPHIC AND ECONOMIC DATA

S/N	Response			ID.		
1	Age (years)					
2	Site of CTC					
3	Gender	Male Female	1 2			
4	Marital status	Single Married Widowed Divorced/Separated	1 2 3 4			
5	Religion	Muslim Christian Others Specify…… ……	1 2 3 4			
6	Residence (Urban or Rural)	Ilala Kinondoni Temeke				

7	Level of Education (choose one from the categories)	None Primary school Secondary school College	1 2 3 4			
8	Duration living with HIV	6 months- 5 years >5 years >10 years				
9	Duration on ART	6 months- 5 years < 5 years >5 years >10 years				
10	Type of Regimen in use	1.TDF+3TC+DTG 2.ABC+3TC+DTG 3.TDF+FTC+DTG				
11	CD4 Count	<200 cell/Ul 350-500 cell/Ul >500 cell/uL	1 2 3			
12	Type of Diet					

Risk factors						
13	Is there any history of chronic disease, like Liver, Renal, Autoimmune diseases, diabetes mellitus,Hypertension?					
14	Do you use any of the following drugs?	Thiazide diuretics, B blockers, Cyclosporine, Oestrogen, Growth Hormone, Retinoids, steroids	1.Yes 2.No	If yes, go to qn 10		
15	For how long	< 7 days ➢ 7 days				
Travel to and from places The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to a place of worship.						
16	Do you walk or use a bicycle (*pedal cycle*) for at least 10 minutes	Yes No	1 2	If No, go to qn7		

	continuously to get to and from places?			If No, go to qn 10		
17	In a typical week, on how many days do you walk or bicycle for at least 10 minutes	Number of days				
18	How much time do you spend walking or bicycling for travel on a typical day?	> 30 minutes <30 minutes	1 2	If 1 go to qn 11		
Recreational activities **The next questions exclude the work and transport activities that you have already mentioned.** **Now I would like to ask you about sports, fitness and recreational activities (leisure).**						
19	Do you do any vigorous-intensity sports, fitness or	Yes No	1 2			
20	In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational (*leisure*) activities?	Number of days	1-2 3-4 5-7			
21	How much time do you spend doing vigorous-	Hours/Minutes				

	intensity sports, fitness or recreational activities on a typical day?					
22	Do you do any moderate-intensity sports, fitness or recreational *(leisure*) activities that causes a small increase in breathing or heart rate such as brisk walking,(*cycling, swimming, volleyball*)for at least 10 minutes continuously?	Yes 1 No 2 If No, go to P16				
24	In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational (*leisure*) activities?	Number of days				
25	How much time do you spend doing moderate-intensity sports, fitness or recreational (*leisure*) activities on a typical day?	Hours: minutes				

Sedentary behaviour

The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent [sitting at a desk, sitting with friends, travelling in a car, bus, train, reading, playing cards or watching television], but do not include time spent sleeping.

26.	How much time do you usually spend sitting or reclining on a typical day?	Hours minutes				

Appendix II: Dodoso (Questionnaire-Kiswahili Version)

MABADILIKO YA NGOZI KUTOKANA NA KIWANGO KIKUBWA CHA MAFUTA/ KOLESTROLI MWILINI MIONGONI MWA WAGONJWA WANAOISHI NA VIRUSI VYA UKIMWI(VVU) WANAOTUMIA DAWA ZA KUFUBAZA VVU

Tafadhali jibu maswali haya kwa kuweka alama ya tiki kwenye jibu sahihi kwako **SEHEMU**

A: MAELEZO BINAFSI NA UCHUMI

S/N	**Swali/Hali**			**Namba ya Utambuzi**		
1	Umri(miaka)					
2	Kituo cha CTC					
3	Jinsi	Mwanaume Mwanamke	1 2			
4	Marital status	Hajaolewa/oa Ameolewa/oa Mjane/mgane Kuachika/tengana	1 2 3 4			
5	Dini	Muislam Mkiristo Nyingine…….	1 2 3			
6	Wilaya ya Ukaazi	Ilala Kigamboni Kinondoni Temeke				

		Ubungo				
7	Kiwango cha elimu(chagua kutoka kwenye orodha)	Sijasoma Shule Msingi Shule Sekondari Chuo	1 2 3 4			
8	Aina ya Chakula	1.Mboga za Majani Na Matunda	1.Mara nyingi 2. kiasi, 3. Mara chache			
8	Muda wa kuishi na maambukizi	<miaka 5 >Miaka 5 >Miaka 10				
9	Muda wa kuwa kwenye Dawa za ART	< Miaka 5 >Miaka 5 >Mika 10				
10	Aina ya Rejimu ya dawa	1.TDF+3TC+DTG 2.ABC+3TC+DTG 3.TDF+FTC+DTG				
11	Kiwango cha mwisho cha CD4 Count	<200 cell/Ul 350-500 cell/Ul >500 cell/uL	1 2 3			

Maswli kuhusu kutembea na mazoezi Yafuatayo ni maswali kuhusu muda unaotumia kutembea na mazoezi.						
9	Unatumia muda gaani kutembea kwa miguu au kutendesha baisikeli kwa siku?	> dakika 30 <chini ya dakika30	1 ndiyo 2 Hapana	Kama 1 nenda swali 11		
Kujiburudisha Maswalli yafuatayo hayahusu kazi ama kusafiri kwako ambapo ushataja. Ningependa kukuuliza kuhusu michezo, mazoezi na kujiburidisha wakati wako mwenyewe.						
10	Je hufanya mazoezi au michezo ya kukutoa jasho?	Ndiyo Hapana	1 2			
11	Ndani ya wiki uanatumia siku ngapi kufanya mazoezi ya kukutoa jasho?	Number of days	1-2 3-4 5-7			
12	Kwa siku unatumia muda gani kufanya mazoezi ya kutoa jasho?	Saa/Dakika				
13	Kwa siku unatumia muda gani kufanya	Saa: Dakika				

	maoezi yanayo fanya moyo Kwenda mbio?					

Tabia bwanyenye/bwete

Swali lifuatalo ni ya kuhusu kuketi na kupumzika kazini, nyumbani, kusafiri kutoka sehemu moja hadi nyingine ama na marafiki pamoja na muda (kukaa ofisini, kukaa na marafiki, kusafiri kwa gari, basi, treni, kusoma, au kuangalia televisheni) bila kuhusisha muda wa kulala.

14	Je unatumia muda gani kukaa na kupumzika kwa siku?	Saa: Dakika	Saa: Dakika:			

Appendix III: Information Sheet

Greetings Sir/Madam

My name is Dr. Mhina Mlangwa, studying at Hubert Kairuki Memorial University. I am conducting a study on the cutaneous manifestation of dyslipidemia among HIV patients on AR patients attending CTC clinics in hospitals in Dares Salaam.

Purpose of the Study

This study aims to determine the prevalence of cutaneous markers of dyslipidemia among HIV seropositive patients on ART attending CTC clinic in this hospital.

What does Participation Involve?

It involves taking a brief history and physical examination of the patient, which will be followed by several investigations; some of which may be unique to some patients. These will include

- Biochemical analyses and Anthropometry

Confidentiality

All information/photography obtained from you during the conduct of this study will remain confidential, and will only be shared with you and other personnel involved in your care.

Risks

There are several inconveniences that you may experience. The blood tests may cause some pain, a skilled health practitioner will draw blood by following all sterile procedures and will try to minimize pain as much as possible. If you notice anything abnormal like prolonged bleeding, please notify the nurse/health practitioner immediately.

Benefits

All the investigations done will be filled in your records and will be used in your care.

Rights to Participate and Withdraw

You are free to decide whether or not to participate in this study, and you may decide to withdraw at any time after you have consented.

Who to Contact

If you have any questions about this study,

Please contact me, Dr Mhina Mlangwa, Department of Internal Medicine, Hubert Kairuki Memorial University (HKMU),70 Chwaku Street-Mikocheni P.O.Box 65300, Dar-es-Salaam, Tanzania, Mobile: 0766747478.

If you have any questions about your rights as a participant in this study,

Please contact Prof. Kabalima, The Chairman of the IREC, HKMU, P.O.Box 65300, Dar-es-Salaam. Tel: 022 2700021-4.

Appendix IV FOMU YA IDHINI **ID No.....**

Nathibitisha kwamba nimesoma (au kusomewa) na kuelewa maelezo yote hapo juu. Na kwa hiyari yangu, bila kushurutishwa ninakubali kushiriki katika utafiti huu.

Sahihi ya mgonjwa _____

Jina la mgonjwa _____

NB: Mbadala anaweza kusaini badala ya mgonjwa ikiwa mgonjwa hawezi, au hana ufahamu timamu.

Sahihi ya Mbadala _____

Jina la Mbadala _____

Sahihi ya Shahidi _____

Jina la Shahidi _____

Appendix V: Health Assessment Record Form

ID No……	**Date and time of sample collection……**
1. Blood Pressure	Systolic Blood Pressure ……(mmHg)
	Diastolic Blood Pressure…… (mmHg)
2. Fasting Lipid Profile	TC.....(mmol/l)
	HDL.....(mmol/l)
	LDL.....(mmol/l)
	TGs.....(mmol/l)
3. Body weight	.....(Kg)
4. Height	.....(M)
5. Body mass index	.....
6. Year of HIV diagnosis	.....

7. Current ART regimen

1). TDF+3TC+DTG

2).ABC+3TC+DTG

3). TDF+FTC+DTG

8. Duration of ART Use

1). 6 Months- 5years

2). > 6 years 5

3). > 10 years

9. Current CD4 Count

1) <200 cell/Ul

2) 350-500 cell/Ul

3) >500 cell/uL

10. History of any chronic use of medications eg

Thiazide diuretics, B blockers, Cyclosporine, Oestrogen, Growth Hormone, Retinoids, steroids

11. History of concomitant Chronic diseases and names

12. cutaneous – dyslipidemia, if yes, go qn 13

13. site of cutenous dyslipidemia

1.Eyes

2.Eyelids

3.Torso

4. Tendon

5. Metaphalanges

Appendix VI: Permission for data collection from Regional referral hospital in Dar es Salaam.

HUBERT KAIRUKI MEMORIAL UNIVERSITY,
P.O.BOX 65300,
DAR ES SALAAM.
29th FEBRUARY 2023

CHAIRPERSON,
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE,
HUBERT KAIRUKI MEMORIAL UNIVERSITY,
P.O.BOX 65300,
DAR ES SALAAM.

U.F.S
CHAIRPERSON, INTERNAL MEDICINE DEPARTMENT, Forwarded for consideration 29/02/2024
HKMU.

Dear Sir/Madam,

REF: ETHICAL CLEARANCE FOR DISSERTATION RESEARCH WORK.

Kindly refer to the heading above. I am Dr Mhina Edward Mlangwa, MMed year III student with registration number HK/PG/IM/22/0026 from the Internal Medicine Department. I am about to start collecting data for the dissertation research work titled **CUTANEOUS MARKERS OF DYSLIPIDEMIA AMONG HIV SEROPOSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY ATTENDING CLINICS IN DAR ES SALAAM**.

I, therefore, kindly request to be given ethical clearance for this important activity.

Attached is my proposal for the mentioned activity.

I hope my request will be considered.

Yours faithfully,

Mhina Mlangwa

KAIRUKI HOSPITAL

Incorporated in the Kairuki Health and Education Network

Tel: *255-22-2700021/4*
+255-653723707 **(mobile)**
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70 Chwaku Street
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Dar es Salaam
Tanzania

E-mail: info@ kairuki hospital.org

web: www.kairuki hospital.org

KH/HKMU/MM/6/2024

21/6/2024

HUBERT KAIRUKI MEMORIAL UNIVERSITY (HKMU)
P.O.BOX 65300
Dar es salaam
Tanzania

RE; PERMISSION TO **Dr MHINA MLANGWAMmed INTERNAL MEDICINE** TO COLLECT DATA FOR RESEARCH TITLED: DETERMINING CUTANEOUS MARKERS OF DYSLIPIDEMIA AMONG SEROPOSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY ATTENDING CLINICSIN DAR ES SALAAM.

Refer to the above heading

This is to inform you that permission to collect data for your research titled: : **DETERMINING CUTANEOUS MARKERS OF DYSLIPIDEMIA AMONG SEROPOSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY ATTENDING CLINICSIN DAR ES SALAAM.**

Has been granted.

Thank you for understanding and cooperation.

KAIRUKI HOSPITAL P. O. Box 65300 DAR-ES-SALAAM

Emmi Masinga
HOSPITAL ADMINISTRATOR

THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

Telephone Address:

Telephone: 022-2760500

Mwananyamala Regional
Referral Hospital,
P.O.Box 61665
Dar es Salaam.

RE: NO.: MA. 239/240/01/118

DATE: 21ᵈ May, 2024

Director,
Kairuki University,
P.O.BOX 65300,
Dar es Salaam.

RE: MHINA MLANGWA TO CONDUCT HER RESEARCH IN MWANANYAMALA REGIONAL REFERRAL HOSPITAL

The captioned subject refers

2. May you be informed that your prescribed request for your bonafide student **Mhina Mlangwa** To conduct ~~her~~ His Research in our Institution through your referred **No. KU/PT/30.5/476** letter dated **8TH May, 2024**, is asserted.

3. The Institution charges **100,000/=**, as a Research fee. The payments are to be made upon reporting.

4. May ~~she~~ He report to the Administration and HR department head for further instruction.

Thanks.

Atugonza kyaruzi
RESEARCH COORDINATOR
FOR: MEDICAL OFFICER INCHARGE
MWANANYAMALA REGIONAL REFERRAL HOSPITAL

COPY:
Head of Internal Medicine Department - **MWANANYAMALA REGIONAL REFERRAL HOSPITAL**

Student - **Mhina Mlangwa**

KAIRUKI UNIVERSITY (KU)

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Ref. No. KU/IREC/27.10/445 **02nd May 2024**

Dr. Mhina E. Mlangwa,
Kairuki University,
P.O. Box 65300,
Dar es Salaam, Tanzania.

RE: ETHICAL CLEARANCE CERTIFICATE FOR CONDUCTING HEALTH RESEARCH.

I am pleased to inform you that the research titled: **Determining Cutaneous Markers of Dyslipidemia Among HIV Seropositive Patients on Antiretroviral Therapy Attending Clinics in Dar Es Salaam (Mlangwa M.E., 2024)** has been granted ethical approval.

This approval is in effect for one year from the above date. Any changes in the procedures should be reported to the Institutional Research Ethics Committee. Significant changes will require the submission of a revised request for ethical approval. You will be required to submit **study progress report** every six months.

Permission to publish your findings should be sought from the National Institute for Medical Research (NIMR) before submission to a publisher and not concurrently.

CHAIR PERSON

Name: Prof. Fredrick Kaijage

Signature:

SECRETARY

Name: Prof. Columba Mbekenga

Signature:

KAIRUKI UNIVERSITY
P. O. Box 65300
DAR ES SALAAM

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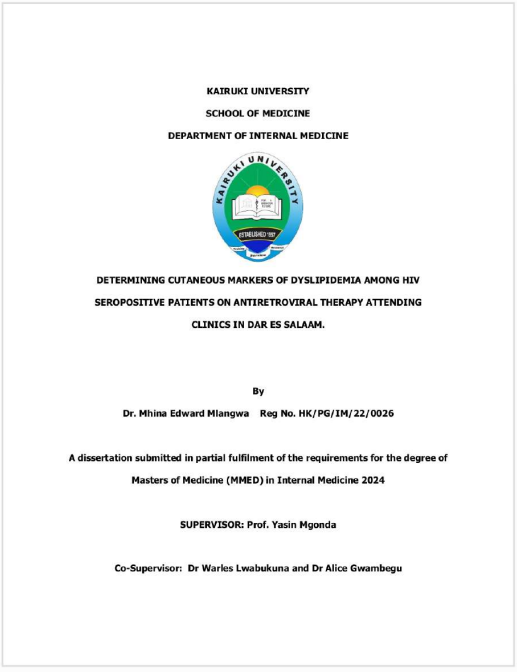


KAIRUKI UNIVERSITY

SCHOOL OF MEDICINE

DEPARTMENT OF INTERNAL MEDICINE

DETERMINING CUTANEOUS MARKERS OF DYSLIPIDEMIA AMONG HIV SEROPOSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY ATTENDING CLINICS IN DAR ES SALAAM.

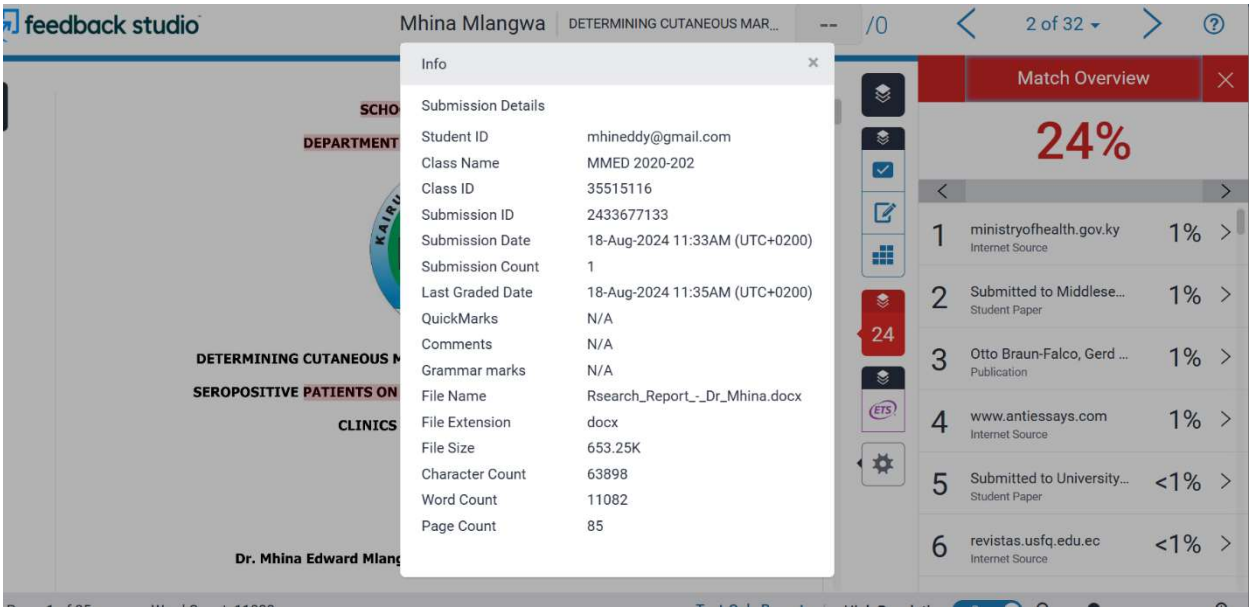
By

Dr. Mhina Edward Mlangwa Reg No. HK/PG/IM/22/0026

A dissertation submitted in partial fulfilment of the requirements for the degree of Masters of Medicine (MMED) in Internal Medicine 2024

SUPERVISOR: Prof. Yasin Mgonda

Co-Supervisor: Dr Warles Lwabukuna and Dr Alice Gwambegu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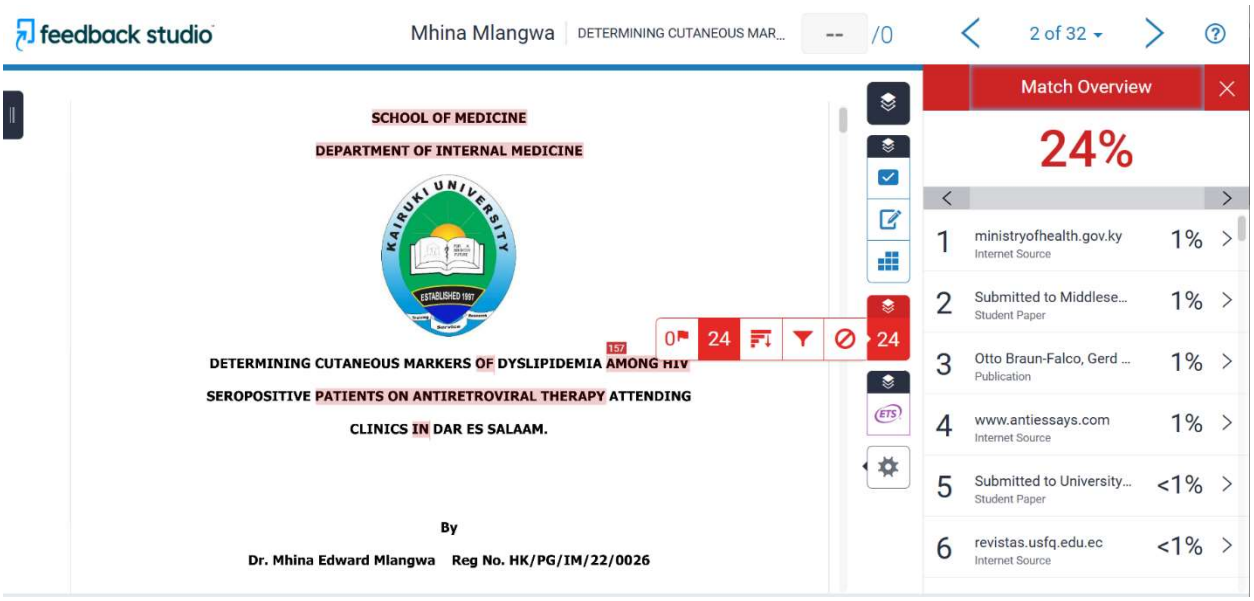
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