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**SCHOOL OF MEDICINE**  
**DEPARTMENT OF INTERNAL MEDICINE**



**URINARY TRACT INFECTION AMONG PATIENTS WITH HUMAN  
IMMUNODEFICIENCY VIRUS INFECTION ATTENDING SELECTED CARE AND  
TREATMENT CLINICS IN DAR ES SALAAM.**

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**CERTIFICATION.**

The undersigned certifies that he has read and thereby recommended for submission of the dissertation entitled "URINARY TRACT INFECTION AMONG PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION ATTENDING SELECTED CARE AND TREATMENT CLINICS IN DAR ES SALAAM in fulfilment of the degree of Masters in Internal Medicine at Kairuki University.

Supervisor's Signature ..... Date.....

**DECLARATION AND COPYRIGHT.**

I, Catherine Chacha at this moment 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.**

This work has been dedicated to my beloved husband, Mr. Stephen Charles Makundi, and my children; Othniel Stephen, Candace Stephen and Bernice Stephen.

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## **LIST OF ABBREVIATIONS.**

KU	Kairuki University
IDSA	Infectious Diseases Society of America
ESBL	Extended-spectrum $\beta$ -lactamase
NRTIs	Nucleoside Reverse Transcriptase Inhibitors
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitors
PIs	Protease Inhibitors
INSTIs	Integrase strand transfer inhibitors
HAART	Highly active antiretroviral therapy
SDI	Socio-demographic index
ASDR	Age-standardized DALY rate
DALY	Disability-adjusted life years
BUTI	Bacterial Urinary Tract Infection
ELISA	Enzyme-linked immunoassay
RNA	Ribonucleic acid
TMP-SMX	Trimethoprim-sulfamethoxazole
PLWHIV	People Living with HIV

## **OPERATIONAL DEFINITION OF TERMS.**

### **Care and Treatment Clinics.**

They are specialized healthcare facilities that focus on providing comprehensive care, support, and medical treatment for individuals living with HIV.<sup>(1)</sup>

### **People living with HIV. (PLHIV)**

Patients considered to have HIV based on documented positive serological tests (e.g., ELISA and confirmatory tests) and their enrollment in care and treatment clinics for the management of HIV/AIDS in Dar es Salaam <sup>(2)</sup>

### **Urinary Tract Infection**

When a patient exhibits signs of a urinary tract infection (UTI), such as increased frequency of micturition, fever, lower abdominal pain, and painful micturition, the presence of pathogenic microorganisms in the urinary tract in a significant quantity ( $>10^5$  cfu/ml), as well as nitrites, leucocytes, and red blood cells in the urine, is confirmed. However, not all symptoms and confirmation investigations must be there to make UTI <sup>(3)</sup>.

### **Asymptomatic individuals**

Participants who did not exhibit any of the common symptoms of a UTI but who still had a significant bacterial count in their urine culture ( $> 10^5$  CFU/mL) <sup>(4)</sup>

## **ABSTRACT**

**Introduction:** Urinary tract infections are common worldwide and represent a major concern in developing countries among immunocompromised populations. This study aimed to determine the prevalence of UTI by age, gender, marital status and the distribution of the CD4+ lymphocyte count, and viral load among people living with HIV. In addition, the study aimed to determine the common bacterial etiologies of UTI and their susceptibility patterns among people living with HIV attending Care and Treatment Clinics at Dar-es-salaam.

**Methods:** A cross-sectional design was employed, involving interviews, medical record reviews, and laboratory analyses. Descriptive statistics, chi-square analysis, and logistic regression were used for data analysis.

**Results:** The study found that urinary tract infection had a prevalence of 30.6%, was common in participants above 35 years and most specifically in those aged between 35- and 44 years, accounting for 37% of cases. The female gender and married participants were the most affected, with respective rates of 69.9 % and 78.5%. Participants with undetectable viral loads had a low chance of developing UTI (OR=0.1; 95% CI=0.05-0.2). Conversely, participants with a CD4+ lymphocyte count >500 (OR=0.2, 95% CI=0.11-0.3) had a decreased risk of presenting with UTI compared to those with a CD4+ lymphocyte count <500 (OR=3.4; 95% CI=2.0-5.7). In addition, participants who take alcohol had significant ( $p=0.012$ ) high risk (AOR=2; 95% CI=1.1-3.5) to present with Urinary tract infection. E.coli, followed by Klebsiella pneumonia, was the most isolated, with respective rates of 51.6% and 29.2%. Ciprofloxacin and Nitrofurantoin were the most active drugs, with 63% and 53%, respectively, against isolated bacteria, both gram-positive and negative. The least effective antibiotic agent was ampicillin, which showed high resistance at 66.3% and sensitivity at 5.6% in all isolated bacteria.

**Conclusion:** The prevalence of UTI by age and gender among People Living with HIV attending Care and Treatment Clinics in Dar-es-salaam was relatively average compared to that reported in the literature. Participants with low CD4+ lymphocyte count <500 and those with unsuppressed viral load had a high risk of presenting UTI. On the other hand, gram-negative bacteria (E.coli and Klebsiella pneumonia) were prevalent bacteria isolated. Nitrofurantoin, ciprofloxacin, and ceftriaxone were the most sensitive antibiotic agents, with ampicillin being the least sensitive to all isolated bacteria.

**Recommendations:** Use nitrofurantoin, ciprofloxacin, and ceftriaxone as the empirical antibiotic agents in People Living with HIV with undetectable viral load. In addition, patients should be selected by culture and sensitivity before prescribing ampicillin and cotrimoxazole in managing UTIs.

## **CHAPTER ONE**

### **1.0. INTRODUCTION.**

#### **1.1 BACKGROUND INFORMATION.**

##### **1.1.1. Definition of Urinary Tract Infection.**

Urinary Tract Infection (UTI) is the presence of pathogenic microorganisms in the urinary tract that are usually associated with inflammatory response (pyelonephritis, cystitis, urethritis). When a urinary tract infection affects one or both kidneys, it is called pyelonephritis. In contrast, when the same disease affects the lower parts of the same system, it is referred to as either cystitis or urethritis. These infections account for a significant number of emergency department (ED) visits <sup>(5)</sup>.

##### **1.1.1.1. Epidemiology of UTI.**

Urinary Tract Infections are one of the most common infections worldwide<sup>1</sup>. Data from the global burden of Disease study, done in 2019 in 204 countries reported 404.61 Million UTI cases and 236,790 deaths<sup>(6)</sup>

The prevalence of UTIs in Africa varies from country to country and geographical location. E.g., in Ghana, the prevalence is 15.9%, in Senegal 4.5% and 12.3% in Nigeria<sup>(7)</sup>. E.coli is the most predominant isolated uropathogen in most studies with 46.4%<sup>(8)</sup>. Senegal has the lowest recorded prevalence, potentially due to better healthcare access, improved hygiene practices and effective antimicrobial stewardship. Understanding these disparities helps identify factors that could lower UTI prevalence in Tanzania, particularly focusing on infection control and healthcare delivery.

Few studies in Tanzania have shown a prevalence range of 16.7% to 41%<sup>(9)</sup>. For instance, Mlugu and colleagues' study in Morogoro reported a point prevalence of 41% with elders reporting five times higher odds of UTI compared to adolescents in the sample<sup>(10)</sup>. In Mlugu's findings, E.coli was the commonest bacteria isolated<sup>(11)</sup>. They displayed moderate

susceptibility to nitrofurantoin and ciprofloxacin. More than half (51.5%) of all E. coli isolates were biofilm-forming<sup>(12)</sup>. Besides, they demonstrated significantly higher antibiotic resistance compared to non-biofilm-forming bacteria<sup>(13)</sup>. However, the study was done with a general outpatient sample, with young adults predominating the sample and no exact magnitude is known among adults living with HIV and AIDS. Besides, it is not clear whether the sample from Morogoro residents could be safely assumed to represent people in other regions including Dar es Salaam city. There appears to be no evidence of any study done in Dar es Salaam that assessed UTI among people living with HIV/AIDS.

#### **1.1.1.2. Aetiology of UTI**

Many microorganisms can infect the urinary tract, but the most common agents are gram-negative bacilli. E.coli causes 80% of acute infections (both cystitis and pyelonephritis)<sup>(14)</sup> in patients without catheters, urologic abnormalities or calculi. Other negative rods, especially proteus and Klebsiella spp and occasionally Enterobacter spp account for a smaller proportion of uncomplicated infections.

Urinary Tract Infection can also be caused by fungi. Funguria, a fungal UTI, are mostly caused by Candida species. Other causative agents are Cryptococcus neoformans, Aspergillus species, and endemic mycoses. Candiduria presents as a common nosocomial infection, which can involve all parts of the urinary tract, resulting in a spectrum of diseases varying from asymptomatic Candiduria to clinical sepsis.

The predisposing factors to UTI are low socioeconomic status, increasing age, urinary tract anomalies, previous treatment for UTI, other medical conditions like diabetes, multiple sclerosis and immune-compromised conditions like HIV/AIDS and spinal cord injuries<sup>(15-17)</sup>.

### **1.1.1.3. Pathophysiology of Urinary Tract Infection.**

In Urinary Tract Infections caused by bacteria, invade the urinary epithelium cells leading to irritation and inflammation of these cells. The infection can start in the urethra and can progress to the bladder, ureters or kidneys. Once they infect the epithelial mucosal lining some bacteria (e.g., *E.coli*) are believed to attach themselves to the bladder wall, and form a biofilm that resists the body's immune response. Some other bacteria (e.g., *Proteus mirabilis*) are associated with urinary stones. Yet in some other cases, gram-positive isolates (e.g., *Enterococcus spp.*, *Staphylococcus spp.*) have been found.

Urine is an excellent culture medium for bacteria, in addition, the urothelium of susceptible persons may have more receptors to which virulent strains of *E.coli* become adherent. Bacteria adhere to and colonize the mucosal lining of the urethra and bladder. Factors such as bacterial virulence factors (e.g., fimbriae) and host factors (e.g., Urinary tract abnormalities, catheter use) influence this process.

In women, the ascent of organisms into the bladder is easier than in men, here the urethra is shorter than a man's urethra and thus bacteria reach the bladder more easily. Moreover, women's urethral opening is closer to the anus making it easier for bacteria to migrate from the anus to the urethra. Other women are at more risk of contracting UTI because of their genes. Other conditions that increase the risk include hormonal changes, multiple sclerosis and anything that affects urine flow e.g., kidney stones, stroke and spinal cord injury

Sexual intercourse may cause minor urethral trauma and transfer bacteria from the perineum into the bladder. Instrumentation of the bladder may also introduce organisms. Two main factors contribute to the development of UTI i.e., the ability of the specific pathogen to produce infection and the strength of an individual's defence mechanisms against the specific pathogen<sup>(18,19)</sup>

#### **1.1.1.4. Clinical features of Urinary Tract Infection.**

Urinary tract infection presents with abrupt onset of increased frequency of micturition and urgency, pain in the urethra during micturition (dysuria), suprapubic pain during and after voiding, intense desire to pass more urine after micturition due to spasm of the inflamed bladder wall, urine may appear cloudy and have an unpleasant odour, microscopic or visible haematuria <sup>(20)</sup>. In other cases, the presence of pain during micturition is associated with an urge towards frequent micturition in the absence of vaginal discharge (in females).

#### **1.1.1.5. Diagnosis of UTI.**

##### **(i) Urinalysis;**

***Dipstick test***, rapid screening for leukocyte esterase (indicating pyuria), nitrites (suggesting bacterial presence) and glucose.

Nitrites are a by-product of bacterial metabolism, specifically by nitrate-reducing bacteria like E. Coli and K. pneumoniae. A positive nitrite test indicates the presence of these bacteria, making it highly specific for detecting gram-negative infections. However, gram-positive bacteria, such as S. Saprophyticus, do not reduce nitrates, leading to potential false negatives. Leucocyte esterase suggests an inflammatory response to infection. However, its sensitivity can be reduced in cases of dilute urine or diseases that do not produce significant pyuria.

While dipstick tests are convenient for screening, they are not definitive.

***Microscopic examination***, assessment of urine sediment for White Blood Cells, Red Blood Cells, bacteria and casts.

##### **(ii) Urine culture;**

Midstream clean-catch urine; the gold standard for diagnosing Urinary Tract Infection, involves quantitative culture to identify and quantify the causative pathogen<sup>7</sup>.

### **(iii)Imaging studies;**

Ultrasound; is useful for detecting structural abnormalities, obstructions or renal abscesses.

A computed Tomography scan or Magnetic Resonance Imaging is performed to evaluate for complications such as renal abscesses or structural abnormalities contributing to UTI.

Cystoscopy; If there is a continuous haematuria or other suspicion of bladder lesion.

### **(iv)Special tests;**

Antibiotic sensitive testing; Determines the susceptibility of the isolated pathogen to various antibiotics, guiding appropriate therapy.

#### **1.1.1.6. Management of UTI.**

For acute uncomplicated UTI, the Infectious Diseases Society of America (IDSA) advocates the use of nitrofurantoin, trimethoprim-sulfamethoxazole (TMP-SMX), or Fosfomycin for 3–5 days<sup>(12,18)</sup>. Follow-up urinary culture and urological evaluation are usually unneeded for patients who respond to first-line treatment of an uncomplicated UTI. <sup>(21,22)</sup> If a patient does not respond to first-line antimicrobials prescribed, many causes must be considered. The causes for the inability to eradicate a simple UTI are (1) initial or acquired bacterial resistance, (2) different bacterial species infecting the urothelium, (3) azotaemia, and (4) urologic structural abnormalities<sup>(23)</sup>. The most common cause, however, is bacterial resistance. In these cases, clinicians can obtain a second urine culture and might consider quinolones or cephalosporins<sup>(22,24)</sup>. Recently, extended-spectrum  $\beta$ -lactamase (ESBL)-producing bacteria have been emerging even in the ambulatory setting, with up to 7% of community-acquired UTIs due to ESBL-producing bacteria. In this situation, antibiotics must be tailored according to the urinary culture antibiogram, with the utilization of carbapenems in certain situations<sup>(25)</sup>. In complicated UTIs, Patients typically receive a broad-spectrum antibiotic while awaiting the results of urine culture, after which they ideally receive a narrow-spectrum antibiotic tailored to the specific etiologic organism<sup>(26)</sup>.

Examples of broad-spectrum antibiotics used here include penicillin or beta-lactams, cephalosporins, fluoroquinolones, and carbapenems<sup>(27,28)</sup>. Improved clinical symptoms indicate treatment response and should occur within 48 to 72 hours<sup>(29)</sup>. The typical treatment duration for complicated UTI is 10 to 14 days<sup>(16)</sup>

According to the Tanzania Standard Treatment Guideline (STG), first-line empirical treatment for uncomplicated UTI includes Nitrofurantoin and Trimethoprim-sulfamethoxazole. However, in cases of drug resistance, especially in People Living with HIV, culture and sensitivity testing are recommended to guide antibiotic choice, with Ciprofloxacin and Ceftriaxone used in complicated cases.

### **1.1.2. Human Immunodeficiency virus**

The HIV is an enveloped retrovirus that contains 2 copies of a single-stranded RNA genome. It causes AIDS which is the last stage of HIV disease<sup>(15,30)</sup>. Two to four weeks after HIV enters the body, the patient may complain of symptoms of primary infection<sup>(31)</sup>. After that, a long chronic HIV infection occurs, which can last for decades<sup>(32)</sup>. AIDS is mainly characterized by Opportunistic Infections and tumours, which are usually fatal without treatment<sup>(33,34)</sup>. The cause of this infectious disease is HIV, which can be classified into HIV-1 and HIV-2. HIV-1 is more globally expanded and virulent<sup>(35)</sup>.

### **1.1.3. Urinary Tract Infection in Human Immunodeficiency Virus-infected individuals.**

Globally, Prevalence of UTI in HIV/AIDS patients has increased from 6.3%-41% worldwide<sup>(14,36,37)</sup>. In Sub-Saharan Africa; Prevalence varies from 15-22%, with higher rates in those with advanced Immunosuppression (CD4< 200 cells/ul) and high viral load. In Tanzania, the prevalence ranges between 12%-27%. In PLHIV, almost every part of the genitourinary system is affected by different diseases<sup>(36,38,39)</sup>. In addition, such people are more vulnerable

to different bacterial infections including UTI because of the high viral load and low CD4+ lymphocyte count of the infected individuals<sup>(36,37,40)</sup>.

The incidence of UTI in the HIV population is related to infection and immune function, determined by CD4+ lymphocyte count<sup>(14,39,41)</sup>. As confirmed by observational studies the incidence of various bacterial infections in HIV-infected patients, including UTI, is inversely correlated with CD4+ lymphocyte count<sup>(12,42,43)</sup>

Antiretroviral therapy (ART), however, improves the health of people infected with HIV/AIDS by decreasing the progression of the infection, restoring the immunity of the patient, decreasing the viral load, and reducing the OIs<sup>(39,44-46)</sup>

Urinary tract infections in HIV patients are generally caused by the same gram-negative bacterial uropathogen that causes infections in healthy hosts, with E.coli being the predominant pathogen isolated. Enterococcus spp., Aeruginosa, Klebsiella Acinetobacter, Proteus spp., Salmonella spp. Candida are also found among HIV-infected patients<sup>(19,26,42)</sup>.

The clinical presentations of UTI in patients with HIV/AIDS infection are not different from those described in the general population; the infection would be expected to be more severe in immunosuppressed patients and signs and symptoms of UTI may be mild because there is no inflammatory response to infection. The health consequences of UTI among HIV- infected patients can be severe, resulting in acute and chronic kidney diseases, infertility, cancer, sepsis and neurologic complications which lead to urinary stasis<sup>(7,21-23)</sup>.

#### **1.1.3.1. Treatment of UTI in HIV-infected patients.**

The treatment of UTI which is the same as that of the general population, should be individualised, but it's more aggressive i.e., longer durations, careful monitoring for drug interactions, follow-up cultures and a proactive approach to preventing and managing recurrent infections. In patients with AIDS, a culture-specific treatment is advised. To select a specific treatment, it is recommended to use the recently revised international treatment

guidelines<sup>(13,19)</sup> according to how the epidemiology of UTI and resistance evolve in specific populations. Despite clear guidelines, practice patterns vary widely with numerous studies showing substantial discrepancies between clinical practice guidelines and antibiotic-prescribing practices<sup>(27,47)</sup>

## **1.2. PROBLEM STATEMENT.**

Urinary tract infections (UTI) are among the most common bacterial infections worldwide, with an especially high burden in immunocompromised populations such as people living with HIV (PLHIV). PLHIV are at increased risk of recurrent and severe UTIs due to their weakened immune systems, particularly those with low CD4+ counts and high viral loads. In these patients, UTIs not only occur more frequently but are also associated with greater morbidity, leading to complications like kidney disease, sepsis, and an increased risk of mortality <sup>(48)</sup>.

In resource-limited settings such as sub-Saharan Africa, the management of UTIs in PLHIV is complicated by limited access to diagnostic tools, frequent delays in seeking healthcare, and the emergence of multidrug-resistant (MDR) bacterial strains. Studies have shown that *Escherichia coli* and *Klebsiella pneumoniae* are the most common pathogens causing UTIs in PLHIV. Still, their resistance to commonly used antibiotics, including ampicillin and cotrimoxazole, is rising. This growing antibiotic resistance highlights the need for updated guidelines on empirical treatment and routine susceptibility testing to ensure effective management <sup>(2)</sup>.

Despite the prevalence of HIV in regions like Tanzania, there is limited data on the specific burden of UTIs in PLHIV, particularly in urban areas such as Dar es Salaam. Studies from neighbouring regions suggest that as many as 20-40% of PLHIV may develop UTIs, but local data on bacterial aetiology and resistance patterns are scarce.

Without this information, clinicians are often forced to rely on empirical treatment regimens, which may be inadequate given the rising rates of antibiotic resistance <sup>(3)</sup>.

Therefore, this study aims to fill the gap in understanding the prevalence, risk factors, and antibiotic resistance patterns of UTIs in HIV-positive individuals attending Care and Treatment Clinics (CTCs) in Dar es Salaam. By generating local data on UTI aetiology and resistance, this research will support targeted treatment strategies, reduce UTI-related complications, and develop more effective guidelines for managing UTIs in PLHIV <sup>(49)</sup>.

### **1.3. RATIONALE.**

Urinary tract infections (UTI) are a significant cause of morbidity among people living with HIV (PLHIV), particularly in resource-limited settings where access to timely and effective treatment is often constrained <sup>(2)</sup>. PLHIV are at an increased risk for UTIs due to their compromised immune systems, particularly those with low CD4+ cell counts, which reduce the body's ability to mount an effective immune response against infections <sup>(48)</sup>. Moreover, high viral loads and the use of antiretroviral therapy (ART) can complicate the management of UTIs, as interactions between antibiotics and ART drugs may limit treatment options <sup>(2)</sup>.

In sub-Saharan Africa, where the prevalence of HIV is highest, studies indicate a growing problem with antimicrobial resistance (AMR), particularly among common UTI pathogens such as *Escherichia coli* and *Klebsiella pneumoniae* <sup>(3)</sup>. This resistance complicates the empirical treatment of UTIs, which is often necessary in resource-limited settings due to the lack of routine laboratory testing for bacterial cultures and sensitivity profiles <sup>(50)</sup>. Additionally, inadequate surveillance and reporting of resistance patterns have led to an overreliance on outdated treatment guidelines that may no longer be effective, thus increasing the risk of treatment failure and recurrent infections <sup>(50)</sup>.

Despite the significant burden of HIV in regions like Tanzania, there remains a scarcity of local data on UTI prevalence, microbial aetiology, and resistance patterns among PLHIV. This lack of data makes it difficult to develop effective guidelines for managing UTIs in HIV-positive populations and increases the risk of complications, such as kidney damage and sepsis. Local studies are critical to understanding the specific challenges faced by PLHIV, such as the prevalence of multidrug-resistant organisms and the impact of immune suppression on infection risk and severity <sup>(51)</sup>.

By researching UTIs in HIV-positive individuals in Dar es Salaam, this study will provide locally relevant data that can inform treatment strategies, improve patient outcomes, and guide public health policies. Understanding the bacterial profile and resistance patterns in this population will help clinicians make better-informed decisions regarding empirical antibiotic therapy and reduce the risk of inappropriate treatment <sup>(52)</sup>. This study is crucial for optimizing care for PLHIV and reducing the burden of UTIs in Tanzania, where the HIV epidemic continues to pose a major public health challenge <sup>(3)</sup>.

#### **1.4. RESEARCH QUESTIONS.**

1. What is the magnitude of Urinary Tract Infection among PLHIV attending CTCs in Dar es Salaam?
2. What are the factors associated with Urinary Tract Infection among PLHIV?
3. Which organisms are resistant to commonly used antibiotics in UTI among PLHIV?

## **1.5. OBJECTIVES.**

### **1.5.1. Broad Objectives.**

To determine the prevalence of UTI, and the associated risk factors among HIV patients attending Care and Treatment Centers in Dar-es-salaam.

### **1.5.2. Specific Objectives.**

1. To determine the distribution of social demographic characteristics among PLHIV attending CTC in Dar es Salaam.
2. To determine the prevalence of UTI among PLHIV by age, gender, and marital status attending CTCs in Dar es Salaam.
3. To determine the distribution of the CD4+ lymphocyte count and viral load among adults living with HIV/AIDS suffering from UTI.
4. To determine the common bacterial etiologies of UTI among HIV/AIDS patients on ARTs by age, and gender attending Care and Treatment Centers in Dar-es-salaam.
5. To determine the susceptibility patterns of commonly used UTI antibiotics to the common isolated bacteria.

## CHAPTER TWO

### 2.0 LITERATURE REVIEW.

#### Introduction

Urinary Tract Infections (UTIs) are a significant cause of morbidity among people living with HIV (PLHIV) due to their compromised immune systems, which make them more susceptible to infections. This review synthesizes existing research on the prevalence of UTI in PLHIV, associated risk factors, bacterial etiologies, and antibiotic susceptibility patterns. This chapter also highlights gaps in the research and the relevance of this study in addressing those gaps, focusing on urban settings in Tanzania.

#### Prevalence of UTI Among PLHIV

The prevalence of UTI among PLHIV varies considerably depending on geographic location, population characteristics, and levels of immunosuppression. Globally, studies report UTI prevalence rates ranging from 6.3% to 41%, with Sub-Saharan Africa showing higher rates due to limited access to healthcare and suboptimal ART coverage <sup>(5)</sup>. In Ethiopia, Beyene et al. (2016) found a prevalence of 10.3% among PLHIV, with a higher prevalence in those with CD4+ counts below 200 cells/mm<sup>3</sup> <sup>(53)</sup>. Similarly, in Nigeria, Ezeigbo et al. (2016) reported a UTI prevalence of 27% in HIV-positive patients, with a higher prevalence among women <sup>(54)</sup>.

A study conducted at Kilimanjaro Christian Medical Centre (KCMC) in Tanzania found a prevalence of 25.3% among PLHIV <sup>(55)</sup>. This study also highlighted that low CD4+ counts, female gender, and older age were significant predictors of UTI in this population. More recently, a study conducted in Mwanza in 2021 observed bacteriuria in 364 PLHIV, from whom 412 urinary pathogens were isolated <sup>(56)</sup>. Another study from Bagamoyo reported that out of 270 individuals, 104 had a positive urine culture, and 119 putative pathogens were identified <sup>(57)</sup>. These findings suggest a high burden of UTI in Tanzanian PLHIV, especially in populations with advanced immunosuppression.

## **Implications and Gaps**

Although several studies have examined UTI prevalence among PLHIV in Tanzania, much of the research has focused on rural or peri-urban areas, with limited data from urban centres like Dar es Salaam. Additionally, there is insufficient exploration of how ART adherence and viral suppression affect UTI risk. This study aims to fill these gaps by focusing on PLHIV attending Care and Treatment Clinics (CTCs) in Dar es Salaam, specifically examining the impact of viral suppression on UTI prevalence.

## **Risk Factors for UTI Among PLHIV**

The most significant risk factor for UTI in PLHIV is a low CD4+ lymphocyte count, which weakens the immune system and increases susceptibility to infections. Johnson et al. (2017) reported that PLHIV with CD4+ counts below 200 cells/mm<sup>3</sup> were three times more likely to develop UTI compared to those with higher counts <sup>(56)</sup>. Beyene et al. (2016) also found a strong association between low CD4+ count and UTI in Ethiopia <sup>(53)</sup>. Viral load is another important factor, with studies showing that individuals with unsuppressed viral loads have a higher risk of developing UTIs. Adefurin et al. (2018) found that unsuppressed viral load was associated with a 1.5-fold increased risk of UTI in Nigerian PLHIV <sup>(57)</sup>.

Behavioural factors such as alcohol consumption and smoking also contribute to UTI risk. Beyene et al. (2016) found that PLHIV who consumed alcohol were twice as likely to develop UTIs compared to non-drinkers <sup>(53)</sup>. Women are particularly vulnerable to UTIs due to anatomical differences that facilitate bacterial migration into the urinary tract. Nguetack et al. (2017) in Cameroon found that UTI prevalence was higher among females than males due to the shorter urethra and proximity to the anus, making it easier for bacteria to ascend into the bladder <sup>(58)</sup>.

## **Implications and Gaps**

While the association between immunosuppression (low CD4+ count) and UTI risk has been well-documented, there is limited research on how viral load suppression through ART influences UTI risk in Tanzania. Additionally, few studies have explored the impact of behavioural factors such as alcohol use and smoking on UTI risk in Tanzanian PLHIV. This study assessed the combined effects of viral suppression, CD4+ count, and behavioural factors such as alcohol consumption on UTI risk in urban PLHIV.

## **Common Bacterial Etiologies of UTI Among PLHIV**

Escherichia coli (E. coli) is the most frequently isolated pathogen in UTI cases, both in PLHIV and the general population. In PLHIV, Gram-negative bacteria such as E. coli and Klebsiella pneumoniae are the predominant causes of UTI. Omoregie et al. (2018) found that E. coli was responsible for 68.18% of UTI cases in Nigerian HIV-positive patients <sup>(8)</sup>. Similarly, in Cameroon reported that E. coli accounted for 52.3% of UTI cases in PLHIV <sup>(58)</sup>.

Recent studies from Tanzania have identified similar bacterial etiologies. The Mwanza study found that among the 412 pathogens isolated from PLHIV, E. coli and Klebsiella pneumoniae were the most common bacteria <sup>(59)</sup>. The Bagamoyo study reported similar findings, with E. coli and Proteus mirabilis among the top pathogens identified in the 119 putative isolates <sup>(6)</sup>. Fungal infections, particularly Candida species, are also known to cause UTI in PLHIV, especially in individuals with advanced immunosuppression. Lewis et al. (2019) reported an increase in fungal UTIs in South African PLHIV, particularly among those with indwelling catheters or extended hospital stays <sup>(60)</sup>.

## **Implications and Gaps**

Although several studies have identified E. coli and Klebsiella pneumoniae as the primary UTI pathogens in PLHIV, limited data exists on the specific bacterial etiologies in urban

Tanzanian populations. This study will contribute to filling this gap by determining the bacterial and fungal causes of UTI in PLHIV in Dar es Salaam.

### **Antibiotic Susceptibility Patterns in UTI Pathogens.**

Antibiotic resistance is a significant challenge in the treatment of UTI, particularly in PLHIV who may experience recurrent infections. Hooton et al. (2016) reported that *E. coli* isolates from PLHIV in Kenya exhibited high levels of resistance to ampicillin and cotrimoxazole <sup>(10)</sup>. Similarly, Moges et al. (2017) found that over 60% of *E. coli* isolates from Ethiopian PLHIV were resistant to first-line antibiotics, necessitating the use of second-line treatments such as ciprofloxacin and nitrofurantoin <sup>(61)</sup>.

The emergence of Extended-Spectrum Beta-Lactamase (ESBL)-producing bacteria further complicates UTI management. Aiyegoro et al. (2018) reported that 7% of community-acquired UTI cases in Nigerian PLHIV were caused by ESBL-producing bacteria, which are resistant to beta-lactam antibiotics, requiring more potent treatments such as carbapenems <sup>(62)</sup>.

### **Implications and Gaps**

There is limited data on antibiotic susceptibility patterns in UTI pathogens isolated from Tanzanian PLHIV, especially in urban centres. This study addressed this gap by evaluating the antibiotic susceptibility patterns of UTI pathogens in PLHIV in Dar es Salaam, providing critical data to inform local empirical treatment guidelines.

## **Conclusion**

The literature highlights a significant burden of UTI among PLHIV, with low CD4+ counts, unsuppressed viral loads, and behavioural factors such as alcohol consumption emerging as major risk factors. E. coli remains the predominant pathogen, but the increasing prevalence of multidrug-resistant bacteria, particularly ESBL producers, complicates treatment. However, significant gaps remain in understanding UTI prevalence and bacterial resistance patterns in urban Tanzanian populations. This study aimed to address these gaps by investigating UTI prevalence, bacterial etiologies, and antibiotic resistance patterns in PLHIV in Dar es Salaam, while also examining the role of ART in reducing UTI risk.

## CHAPTER THREE

### 3.0. METHODOLOGY.

#### 3.1. Study Design.

A hospital-based, cross-sectional study was conducted on HIV patients receiving CTC in Dar es Salaam.

#### 3.2. Study Area.

The study was carried out in Dar-Es-Salaam, a city with five administrative municipalities (Kinondoni, Ilala, Temeke, Ubungo, and Kigamboni). According to the Tanzania National Census of 2022, 5,383,728 people were living in the city: 2,600,018 men and 2,783,710 women <sup>(63)</sup>.

It comprises five districts with a municipal level which include Kinondoni Ubungo, Temeke, Ilala and Kigamboni in which each district has one public district hospital which conducts CTC clinic. According to the 2022 Tanzania National Census results, Dar es Salaam has a total population of approximately 5 million people. It's a commercial city with a lot of different social interactions.

Mwananyamala is a regional referral hospital located in the Kinondoni neighbourhood of Dar es Salaam. The hospital has ARTS clinics which are run by two medical officials and two nurses who are trained in PVIH management. In a week the clinic receives an average of 100 to 300 people participating each Monday and Tuesday (Ministry of Health, United Republic of Tanzania)<sup>(32),32)</sup>.

Situated in the Ilala urban district of Dar es Salaam, Amana is a regional referral hospital. The hospital has a capacity of 600 beds in total, the hospital can accommodate about 350,598 patients annually. The hospital has ARTS clinics, which are run by two medical officials and two nurses who are trained in PVIH management. In a week, the clinic receives an average

of 100 to 300 people participating each Monday and Tuesday (Ministry of Health, United Republic of Tanzania)<sup>(32),32)</sup>.

The regional referral hospital, Temeke Regional Referral Hospital, is in Dar es Salaam's Temeke area. The hospital has a capacity of 700 beds in total; the hospital can accommodate about 320,598 patients annually. (Republic of Tanzania, Ministry of Health) <sup>(32),32)</sup>. It possesses an ART clinic which works 2 days a week and has three medical officers, three nurses and two social workers trained in the management of PLVIH. The ART clinic receives an average of 150 to 250 patients a week (Ministry of Health, United Republic of Tanzania)<sup>(32),32)</sup>.

### **3.1. Study Duration.**

A total of three months were spent doing the study.

### **3.3. Population**

#### **3.3.1. General population**

Everyone living with HIV in Dar es Salaam.

#### **3.3.2. Target population.**

All HIV patients attending Care and Treatment Clinics in Dar es Salaam.

#### **3.3.3. Study population.**

Individuals who agreed to participate in the study and were CTC patients in Dar es Salaam.

### **3.4. Sampling procedure.**

Multi-stage cluster sampling was used to select hospitals (Private and Public hospitals), and then by simple random sampling, one cluster was picked (Public Hospitals). All the public hospitals were listed down depending on their levels (Tertiary hospital/MNH, RRH, District hospitals and dispensaries) and by simple random selection one cluster was picked (RRH), hence the study was done in the CTCs in all three RRH in Dar-es-salaam namely; Temeke,

Amana and Mwananyamala hospitals. Lastly, a random sample technique was used to choose study participants from the designated hospitals.

### **3.4.1. Inclusion Criteria**

i. Every adult HIV-positive who visited CTC between the ages of 18 and over during the study period.

### **3.4.2. Exclusion Criteria.**

i. Patients with pre-existing renal disease.

iii. Those who had received antibiotic treatment during the two weeks before data collection.

### **3.5. Sample Size Estimation.**

Was calculated using the Kish and Leslie formula as used in the previous study.

**As follows:**

$$n = \frac{(Z(\alpha/2))^2 * p(1-p)}{(d)^2}$$

N-represents the initial sample size

Z  $\alpha/2$  -represents the standardized normal distribution value for the 95% CI=1.96(16)

p- represents the population proportion from the previous study 25.3% from a study done in KCMC, Moshi, Tanzania<sup>(16)</sup>

d- Represents the margin of error of 0.05

Therefore, the minimum sample was;

$$n = (1.96)^2 * 0.253(1-0.253) / (0.05)^2 = 290$$

The estimated minimum sample size was approximately **290**.

### **Justification of formula.**

The proportional prevalence reference used in this analysis was from a 2020 study named "Prevalence of Multidrug-Resistant UTI among People Living with HIV in Northern Tanzania".

This is because the study's design and the geographic area in which it was conducted were identical. As a result, using the same sample size calculation reduced bias and guaranteed the validity of the results.

### **3.6. Sample collection.**

A urine sample was collected (by the participants themselves) after adequate explanation/information that was provided by attending laboratory professionals. Participants were instructed to collect about 30mls of midstream urine (MSU) for microbiological examination by giving a sterile, dry, wide-necked, leak-proof container. Urine samples were processed immediately at the Microbiology laboratory. If there was a delay the samples were stored in the refrigerator at 2-8<sup>0</sup>c.

### **3.7. Variables of the study.**

**Dependent Variable:** Urinary Tract Infection; that was determined by leucocyte 3+ or positive Nitrites or both.

**Independent Variable:** Age, gender, marital status, level of education, occupation, CD4+ lymphocyte cell count, History of alcohol use, history of smoking.

### **3.8. Data collection.**

Data collection comprised of clinical and laboratory variables.

### **3.8.1. Clinical variables**

(i) Sociodemographic and clinical data.

Two days of training were provided to data collectors about every aspect of the instrument, including how to use the extraction tool to gather data before collecting data from patients and their medical records. To gather relevant data, the principal investigator with the assistance of two nurses working in CTCs in selected hospitals or at least who have worked in an outpatient clinic in the past.

In addition, the P. I used a structured questionnaire to collect sociodemographic which included age, gender, history of alcohol consumption, history of cigarette smoking and occupation. For clinical data; Duration of HIV/AIDS, use of ARTs and its duration, History of Diabetes, presence of any UTI symptoms, i.e., increased frequency in micturition, painful micturition, low abdominal pain and fever.

The participants' current CD4+ lymphocyte cell value and viral load were taken from their medical records by the principal investigator and her assistants.

### **3.8.2. Laboratory data.**

Two mid-stream clean-catch urine samples (each not less than 5ml) from all eligible study participants were collected using two wide-mouth screw-capped leakproof sterile containers by taking all precautions to avoid contamination.

One specimen in each patient was cultured on blood agar (HiMedia laboratory Pvt Ltd, Mumbai, India) and cysteine lactulose electrolyte deficient (CLED) agar (HiMedia laboratory Pvt Ltd, Mumbai, India). One -microliter disposable loop was used for nucleation on culture media plates then the plates were incubated at 37<sup>o</sup>c for 24 hours.

Gram-negative bacteria identification test was performed by using the conventional method of identification which includes Kligler Iron Agar (HiMedia laboratory Pvt Ltd, Mumbai, India), Sulphur indole motility (SIM) (HiMedia laboratory Pvt Ltd, Mumbai, India), Sulphur Indole

Motility, Citrate (HiMedia laboratory Pvt Ltd, Mumbai, India), Urea(HiMedia laboratory Pvt Ltd, Mumbai, India) and Oxidase(Remel Europe Ltd, Dartford, UK), Coagulase(Remel Europe Ltd, Dartford, UK) for staphylococcus spp. And Bile esculin test (HiMedia laboratory Pvt Ltd, Mumbai, India) for enterococcus spp. Bacitracin and optochin (all from Oxoid Ltd, Basingstoke, England) test was used for the identification of streptococcus spp.

Antimicrobial susceptibility tests were done for commonly prescribed antibiotics in our set and zones of inhibition were interpreted using the Clinical Laboratory Standard Institute guideline of year 2020(CLSI).

Leucocyte and nitrite counts were measured and documented for the second urine sample using Cybow urinalysis test strips. The questionnaire included the findings from the urinalysis and urine culture.

### **3.9. Data entry and analysis.**

Before data cleaning, data was stored using a pre-designed template, followed by data entry performed at the end of each business day by the principal investigator herself. A data cleaning exercise was followed, and mainly, the data was checked for potential missing data during entry/recording as well as the accuracy of information fed into the template. SPSS version 23, the statistical package for social sciences, was used for analysis.

Continuous variables like duration of smoking and age among other variables were represented as the interquartile range, standard deviations, means, and medians. The SPSS 25 series for Windows was used to compute proportions, percentages, and frequencies for categorical data, such as gender and place of residence. The prevalence of UTI by age, gender and marital status among PLHIV was computed as a percentage of PLHIV with UTI by age, gender and marital status to all PLHIV who attended CTCs in Dar es Salaam. The distribution of CD4+ lymphocyte count, and viral loads among PLHIV with UTI was expressed in frequency and percentage and the chi-square test was used to compare different categories with

respective OR at a corresponding 95% confidence interval (CI). Sociodemographic factors associated with UTI were computer at both bivariate and multivariate regression with corresponding odds ratios. Subsequently, the percentage of common isolated bacteria to all isolated bacteria in HIV/AIDS was calculated to determine the rate of common bacterial etiologies among HIV/AIDS participants with UTI. Eventually, different isolated bacteria species summarized the susceptibility pattern, which was then displayed in a table with panels denoting sensitivity(S), resistance (R), and intermediate (I).

## **CHAPTER FOUR**

### **4.0 ETHICAL APPROVAL**

#### **4.1 Ethical clearance**

Before starting the study, IREC(Ref. No. HKMU/IREC/27.10/436), the Dar es Salaam Regional Medical Officer, the medical officer in charge of the selected hospitals, and the Research Committee of Hubert Kairuki Memorial University (HKMU) granted ethical clearance and permission to conduct the study.

#### **4.2 Ethical consideration**

The participants received an explanation of the study's objectives and methods. An informed consent form was signed in Swahili by all participants. In the case of illiterate patients, the form was read to them and their index finger fingerprint was used instead of a signature. The HIV patients were allowed to make their own decisions regarding participating in the study and their healthcare choices. Information that was obtained during this study was treated with confidentiality. Any potential harm or discomfort to participants was minimised by ensuring proper handling of the samples and referring them for appropriate medical care for any UTI identified during the study. All investigation results were communicated back to the patients. Approval from Institutional Research Ethics Committee (IREC) with Ref. No. HKMU/IREC/27.10/436 was obtained to ensure that the study meets ethical standards and complies with relevant regulations and guidelines. Following completion of the study, HKMU and the Ministry of Health will receive the information and findings, which will then be publicized.

## CHAPTER FIVE

### 5.0 RESULTS

#### 5.1. Study participants.

During the period of data collection, 327 HIV-positive patients visited CTC at the Regional referral hospitals in Temeke, Mwananyamala and Amana. Following eligibility screening, 37 participants were not included because 8 had pre-existing renal diseases and 29 of them had been on antibiotics two weeks before data collection. After being contacted, eligible subjects were progressively enrolled in the study until the desired sample size of 290 participants was attained.

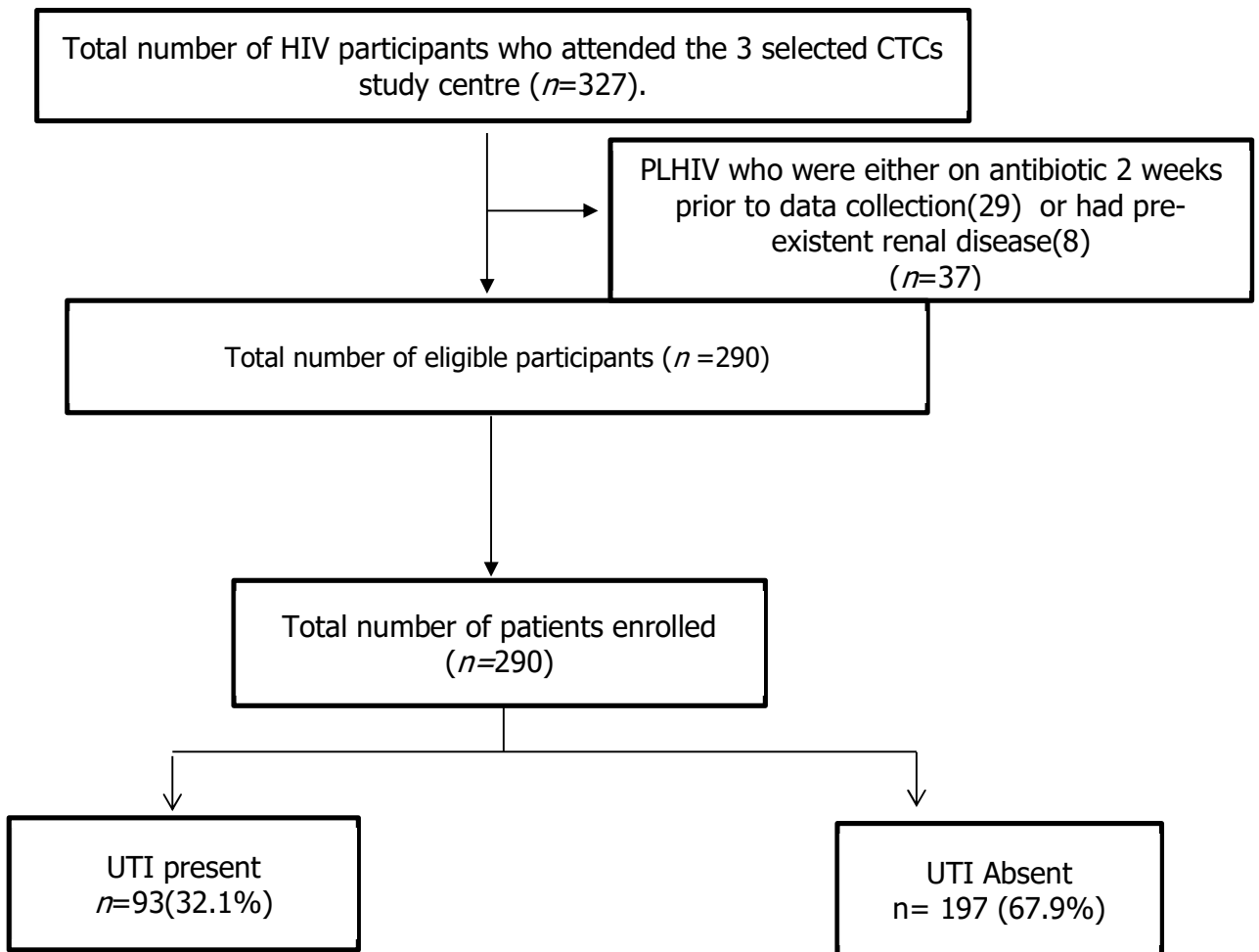


Figure 1. Study flow chart of PLHIV who attended CTC clinics at the regional referral hospitals in Temeke, Mwananyamala, and Amana.

## 5.2. Sociodemographic Characteristics of HIV Patients Attending Care and Treatment Clinics in Dar-es-salaam.

In this study, the majority of participants (37%) were between the ages of 35 and 44 (108), and the majority were females (65.2%). Furthermore, the majority of participants were not smokers (87.2%) or taking alcohol (74.8%). Married participants accounted for 77.2% and 13.1% were single.

**Table 1. Sociodemographic Characteristics of HIV Patients attending Care and Treatment Clinics in Dar-es-salaam.(n=290)**

Population Characteristics		Frequency (n=290)	Percent %
<b>Age (years)</b>	<i>&lt;25</i>	13	4.5
	<i>25-34</i>	38	13.1
	<i>35-44</i>	108	37.2
	<i>45-54</i>	73	25.2
	<i>&gt;55</i>	58	20.0
<b>Gender</b>	<i>Male</i>	101	34.8
	<i>Female</i>	189	65.2
<b>Occupation</b>	<i>Non employed</i>	58	20
	<i>Self employed</i>	183	63.1
	<i>Employed</i>	46	15.9
	<i>Student</i>	3	1.0
<b>Education Level</b>	<i>Primary</i>	136	46.9
	<i>Secondary</i>	112	38.6
	<i>College</i>	35	12
	<i>Illiterate</i>	7	2.4
<b>Marital Status</b>	<i>Single</i>	38	13.1
	<i>Married</i>	224	77.2
	<i>Divorced</i>	4	1.4
	<i>Widow</i>	24	8.3
<b>Alcohol intake</b>	<i>No</i>	217	74.8
	<i>Yes</i>	73	25.2
<b>Smoking</b>	<i>No</i>	253	87.2
	<i>Yes</i>	37	12.8

### 5.3. Prevalence of UTI among People Living with HIV by age, gender, and marital status attending Care and Treatment Clinics in Dar es Salaam.

In this study, the overall prevalence of UTI was 30.6 % (positive culture).

UTI was most common in participants aged between 35 to 44 years accounting for 37 % of cases. With a rate of 69.5 per cent, Women were the gender most afflicted, with a rate of 69.5%, and Married people were affected the most (78.5%).

**Table 2. Prevalence of UTI among People Living with HIV by age, gender, and marital status attending Care and Treatment Clinics in Dar es Salaam. (n=290)**

Population Characteristics		Urinary tract Infection	
		Absent Frequency (%)	Present Frequency(%)
<b>Age (years)</b>	<i>&lt;25</i>	9(69.2)	4(30.8)
	<i>25-34</i>	25(65.8)	13(34.2)
	<i>35-44</i>	68(63)	41(37)
	<i>45-54</i>	54(74)	19(26)
	<i>&gt;55</i>	46(79.3)	12(20.7)
<b>Gender</b>	<i>Female</i>	124(65.6)	65(34.4)
	<i>Male</i>	73(72.3)	28(27.7)
<b>Marital status</b>	<i>Single</i>	25(65.8)	13(34.2)
	<i>Married</i>	151(67.4)	73(32.6)
	<i>Divorced</i>	2(50)	2(50)
	<i>idow/widower</i>	19(79.1)	5(20.9)

**5.4. Distribution of the CD4+ lymphocyte count, and viral load among adults living with HIV/AIDS attending Care and Treatment Clinics in Dar es Salaam.**

Participants in this study who had undetectable viral loads had a low chance of developing a UTI (OR=0.1,95% CI:0.05-0.2) P value=0.01)). The likelihood of presenting with a UTI was 1.3 times higher in those with an unsuppressed viral load, (OR=1.3,95% CI:1.2-1.3) P value 0.03). In contrast, participants with a CD4+ lymphocyte count >500 were less likely than those with a CD4+ lymphocyte count <500 to present with a UTI(OR= 0.20, 95%CI:0.11-0.3) p-value 0.01), (95% CI=2.0-5.7; OR=3.4) respectively.

**Table 3. Distribution of the CD4+ lymphocyte count, and viral load among adults living with HIV/AIDS attending Care and Treatment Clinics in Dar es Salaam city.(n=290)**

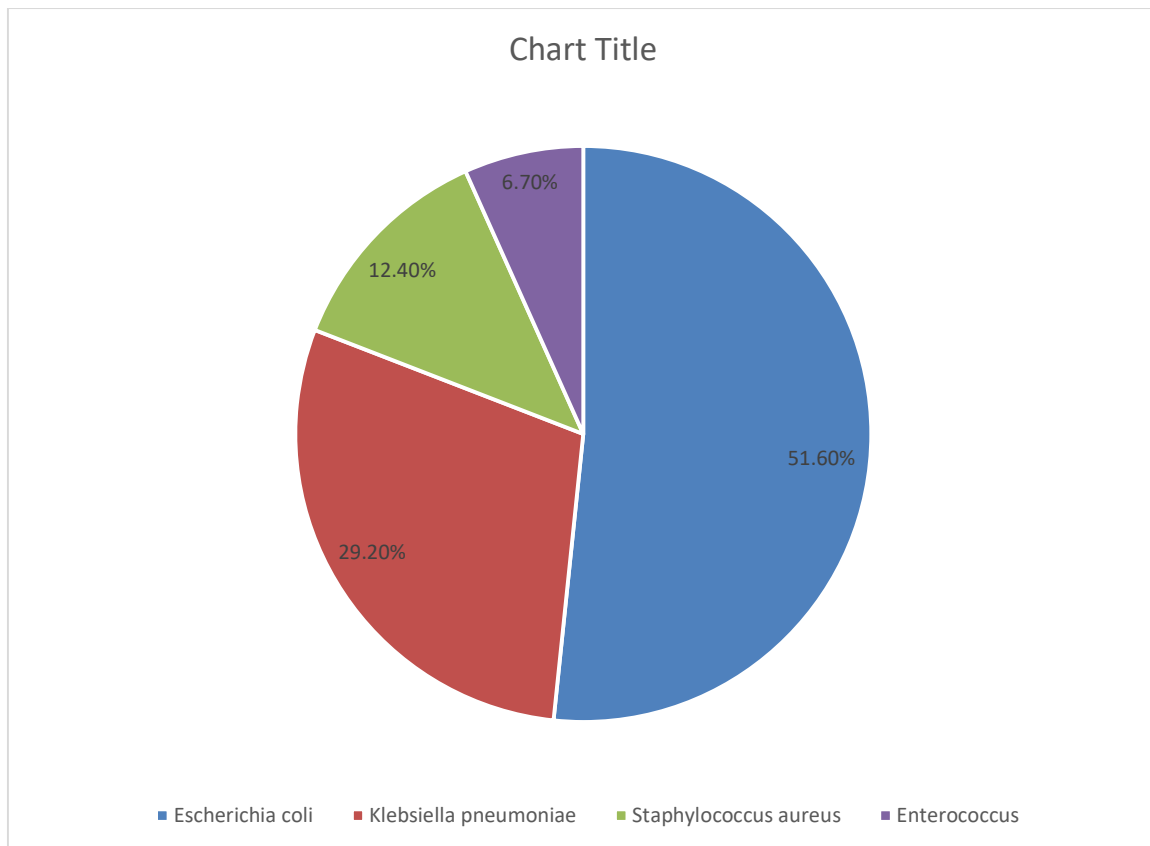
Population Characteristics		Urinary tract Infection					
		Absent Freq n=197(%)	Present Freq n=93(%)	Odds (95%CI)	$\chi^2$	P Value	
<b>Viral load</b>	<i>Undetected</i>	105 (94.6)	6(5.4)	0.1(0.05-0.2)	10.4	0.01	
	<i>suppression</i>	91(52.3)	83(47.7%)	0.2(0.09-0.3)			0.07
	<i>Unsuppressed</i>	0(0.0)	3(100)	1.3(1.2-1.3)			0.03
	<i>Unknown</i>	1(50)	1(50)				
<b>CD4+ lymphocyte count.</b>	<i>&gt;500</i>	137(90.7)	14(9.3)	0.2(0.11-0.3)	8.7	0.01	
	<i>&lt;500</i>	60(43.1)	79(56.8)	3.4(2.0-5.7)			0.01

$\chi^2$  chi square test

**5.5. Common bacterial aetiologies of UTI among HIV/AIDS patients on ARTs attending Care and Treatment Centres in Dar-es-salaam.**

In this study, the total number of microbes isolated was 89. E.coli was the most isolated microbe, with a rate of 46(51.6%), followed by Klebsiella pneumonia accounting for 26 microbes (29.2%). This was then followed by S.aureus and Enterococcus with rates of 11(12.4%) and 6(6.7%) respectively.

Figure 2: Pie chart Figure 4: pie chart showing the distribution of different isolated bacteria among PLHIV at the regional referral hospitals in Temeke, Mwananyamala, and Amana.



**5.5.1 Common bacterial aetiologies of UTI among HIV/AIDS patients on ARTs by age, and gender attending Care and Treatment Centres in Dar-es-salaam.**

All of the isolated bacteria in this study were common in participants between the ages of 35 and 44, with rates of 39.1% for E. coli, 50% for Klebsiella, 33.3% for streptococcus aureus and 83.3% for Enterococcus.

However, isolated microbian was common in both genders, with females being most impacted and E. Coli and Klebsiella being the most common microbian.

**Table 4. Common bacterial aetiologies of UTI among HIV/AIDS patients on ARTs by age, gender attending Care and Treatment Centres in Dar-es-salaam. (n=87)**

Population		Bacteria			
Characteristics		<b>E. COLI</b> (n=46) Frequency (%)	<b>K.</b> <b>Pneumoniae</b> (n=26) Frequency (%)	<b>Staph.</b> <b>Aureus</b> (n=11) Frequency (%)	<b>Enterococcus</b> (n=6) Frequency (%)
<b>Age</b>	<25	2(4.3)	2(7.7)	0(0.0)	0(0.0)
<b>(years)</b>	25 - 34	6(13.0)	7(26.9)	1(9.1)	0(0.0)
	35- 44	18(39.1)	8(50.0)	3(33.3)	5(83.3)
	45-54	13(28.3)	3(11.5)	2(18.2)	1(16.7)
	>55	7(15.2)	1(3.8)	3(33.3)	0(0.0)
<b>Gender</b>	<i>Male</i>	16(34.8)	9(34.6)	1(11.1)	2(33.2)
	<i>Female</i>	30(65.2)	17(65.4)	8(88.9)	4(66.7)

**5.6. Susceptibility patterns of commonly used UTI antibiotics to the common isolated bacteria.**

Ciprofloxacin and Nitrofurantoin were the most active drugs against isolated macrobian, with rates of 63% and 53% respectively Moreover they were both sensitive to gram-positive and negative microbes. The least effective treatment was ampicillin, which showed high resistance at 66.3 % and sensitivity at 5.6% in all isolated.

**Table 5. Susceptibility patterns of commonly used UTI antibiotics to the common isolated bacteria by age, gender and duration of ART use. (n=89)**

Antibiotic sensitivity	E. Coli n=46		Klepsiela pneumonia n=26		Staph. Aureus n=11		Enterococc us. n=6		Growth Total (%)	Non growth Total (%)	
	S	%	n	%	n	%	n	%			
<b>Ciprofloxacin</b>	S	31	67	17	50	8	73	0	0.0	<b>56(63)</b>	26(29)
	R	0	0.0	2	23	0	0.0	5	83.3	7(7)	
<b>Nitrofurantoin</b>	S	21	46	15	57	5	45.4	6	100	<b>47(53)</b>	41(46)
	R	1	0.3	0	0.0	0	0.0	0	0.0	1(1)	
<b>ceftriaxone</b>	S	15	63	09	46	0	0.0	0	0.0	24(27)	40(44.9)
	R	14	0.0	7	15	0	0.0	4	67	25(28)	
<b>Gentamicin</b>	S	20	44	0	0.0	3	27.3	0	0.0	23(26)	33(37)
	R	15	32	14	54	0	0.0	4	67	33(37)	
<b>Cotrimoxazole</b>	S	15	32	16	62	0	0.0	0	0.0	31(35)	16(17.9)
	R	26	57	7	27	9	82	0	0.0	42(47.1)	
<b>Ampicillin</b>	S	0	0.0	0	0.0	0	0.0	5	83.3	<b>5(5.6)</b>	25(28)
	R	34	73	16	62	9	82	0	0.0	<b>59(66.3)</b>	
<b>Nalidixic acid</b>	S	1	2.1	0	0.0	0	0.0	0	0.0	1(1)	67(75)
	R	17	37	4	15	0	0.0	0	0.0	21(24)	
<b>Clindamicin</b>	S	0	0.0	0	0.0	6	55	0	0.0	6(6.7)	83(93)
	R	0	0.0	0	0.0	0	0.0	0	0.0	0(0.0)	
<b>Tetracycline</b>	S	0	0.0	0	0.0	0	0.0	3	50	3(3.3)	86(96.6)
	R	0	0.0	0	0.0	0	0.0	0	0.0	0(0.0)	

**5.7. Sociodemographic factors associated with the occurrence of UTI among adults living with HIV/AIDS attending Care and Treatment Clinics in Dar es Salaam.**

**Table 6. Sociodemographic factors associated with the occurrence of UTI among adults living with HIV/AIDS attending Care and Treatment Clinics in Dar es Salaam. (n= 290)**

Populations Characteristics	Absence UTI N=197	Presence UTI N=93	Bivariate		Multivariate	
			COR (95%CI)	Sig	AOR (95%CI)	Sig
<b>Age</b>						
<25	9(69.2)	4(30.8)	Reff			
25-34	25(65.8)	13(34.2)	0.6(0.03-14)	0.7		
35-44	68(63)	41(37)	0.3(0.02-6.7)	0.5		
45-54	54(74)	19(26)	0.4(0.02-7.7)	0.6		
>55	46(79.3)	12(20.7)	0.7(0.3-1.1)	0.4		
<b>Gender</b>						
Male	73(73.0)	28(27.0)	Reff			
Female	124(65.6)	65(34.4)	0.7(0.4-1.2)	0.5		
<b>Occupation</b>						
Non employed	39(67.2)	19(32.8)	Reff			
Self employed	124(67.8)	59(32.2)	0.9(0.5-1.8)	0.9		
Employed	32(69.6)	14(30.4)	0.8(0.3-2.0)	0.6		
Student	2(75.0)	1(25.0)	2(0.1-34)	0.6		
<b>Education level</b>						
Primary	92(67.6)	44(32.4)	Reff			
Secondary	74(66.7)	37(33.3)	1(0.6-1.7)	0.8		
College	0(0.0)	1(100)				
University	26(75.8)	8(24.2)	0.6(0.2-1.6)	0.3		
Illiterate	5(71.4)	2(28.6)	0.4(0.2-1.4)	0.4		

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<b>Marital status</b>						
<i>Single</i>	151(67.4)	73(32.4)	1.8(0.6-5.1)	0.2		
<i>Married</i>	25(65.8)	13(34.2)	1.9(0.6-6.5)	0.2		
<i>Divorced</i>	2(50.0)	2(50.0)	3(0.4-34)	0.2		
<i>widow</i>	19(79.2)	5(20.8)	reff			
<b>Alcohol intake</b>						
Yes	40(54.8)	33(45.2)	0.4(0.2-0.8)	<b>0.006</b>	2(1.1-3.5)	0.012
No	157(72.)	60(27.6)	reff			
<b>Smoking</b>						
Yes	21(56.8)	16(43.2)	0.5(0.2-0.9)	<b>0.12</b>	1.4(0.7-3)	0.2
No	21(56.8)	16(43.2)	reff			
<b>Number of sexual patterned</b>						
None	9(64.3)	5(35.7)				
1	173(71.8)	68(28.2)	0.7(0.2-2.1)	0.5		
>2	15(53.6)	20(46.4)	1.5(0.4-5.8)	0.5		

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In this study at binary regression, participants with a history of alcohol intake and smoking had significant ( $P < 0.2$ ) odds of presenting with UTI compared to those who didn't hence they were taken for multivariate to control the confounders. However, at multivariate regression, only participants who had a history of alcohol intake had significantly ( $P < 0.05$ ) 2-fold time to present with UTI. UTI was also more common in older ( $> 35$  years), male, self-employed, primary school-educated and single participants. However, this difference was not statistically significant. Moreover, there was a trend of participants with more than two sexual partners presenting with UTI compared to those with a single sexual partner.

## CHAPTER SIX

### DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS.

#### 6.0. Discussions.

In this study, UTI has an overall prevalence of 30.6 %. Participants whose age range is between 35 to 44 years were the most affected in 37% of cases. Women had the highest rate of affliction with a rate of 69.5% among participants with UTI.

Several studies reported comparable findings. In Tanzania in a study conducted by Bartholomeo and colleagues, females had higher rates of UTI in a study of PLHIV visiting CTC at Kilimanjaro Christian Medical Centre hospital in Northern Tanzania<sup>(18)</sup>. However, the overall UTI prevalence was 12.3%, which was lower than in the current study. This may be explained by the fact that, in contrast to this study, where only 30% of individuals had a CD4 lymphocyte count level above 500 and were, therefore, more susceptible to UTI, the majority of participants (70%) in Bartholomeo and colleagues' study had a CD4 lymphocyte count above 500. Agata and colleagues in Poland reported comparable results, with females being the most affected by UTI in PLWHIV<sup>(19)</sup>. However, the findings of Agata and colleagues were from a retrospective review of the medical record of PLHIV attending CTC in Poland. Similar results were reported in India and by other authors<sup>(2,3)</sup>. The prevalence of UTI in female gender may be due to the proximity of the urethra to the vaginal and gastrointestinal tracts, which serve as reservoirs for the urogenital microorganisms that incriminate in UTI<sup>(22)</sup>.

Controversial results were observed in a study conducted by Olla Yigazaw and colleagues where the male gender was shown to be most afflicted by UTI<sup>(23)</sup>. This discrepancy could be explained by the fact that, in contrast to Olla and colleagues, who recruited more male participants than female participants, this study recruited more female participants.

On the other hand, UTI have affected different categories of age as observed in several literature. In this study, UTI was most observed in participants aged above 35 years and most

specifically in those age range between 35 and 44 years. This might be to the fact that majority of study participants in the present study were in this category of age . on the other side, the study did not find a scientific reason which could explain the predisposition of UTI in this range of population. Similar findings were reported also in Ethiopia by Dadi and colleagues and Tsgabu Kahsay et al, with participant's age ranging between 35 to 44 years being the most affected among HIV-positive patients who visited the Hiwot Fana Specialized University Hospital ART clinic and ART clinics at Mekelle General Hospital and Ayder Comprehensive Specialized Hospital<sup>(24)</sup>.

Urinary tract infection is common in patients living with HIV. Several literatures reported an association between the immunity system and the occurrence of different opportunistic infection, UTI included. In this study participants with undetectable viral load and those with CD4 lymphocyte counts above 500 had lower odds to present UTI. On the other side, those with CD4 counts less than 500 and unsuppressed viral load had high odds of presenting UTI. Comparable findings were reported by Moses and colleagues, in a study conducted among patients living with HIV attending Bamenda Regional Hospital in Cameroon, that a CD4 lymphocyte count of less than 300 was substantially associated with the prevalence of UTI, which is consistent with this study's findings <sup>(18)</sup>. In Ethiopia, Netsanet and colleagues reported similar findings with significant correlation between CD4 lymphocyte counts of less than 200 significantly associated with the occurrence of UTI patients attending the ARTS clinic in Hawasa Teaching Hospital <sup>(25)</sup>. Several other authors, in India and Poland observed comparable findings<sup>(8,2)</sup>. In addition, an increase in viral load was reported also in several literature as a risk factor of UTI as observed in a systematic review conducted by Newton and colleagues<sup>(27)</sup>.

There have been conflicting findings published by various authors who postulated that the tiny number of T lymphocytes in the urine mucosa prevents the urinary tract from being

affected by a decrease in CD4 lymphocyte count; consequently, the systemic decrease in TCD4 lymphocytes brought on by HIV infection would not have a major impact on local immunity. In Nigeria, Jamshidi Makiani and colleagues reported that patients with high CD4 lymphocyte counts exceeding 200/ml were the most affected by UTIs <sup>(28)</sup>. Similar results were found in the study conducted by Admasu et al. in Ethiopia and Hoepelman and colleagues in the Netherlands<sup>(8,9)</sup>.

This discrepancy may be explained by the difference in study population, and criteria used to select participants between studies.

In the present study, there was an association between the occurrence of UTI and participants who smoke and those who take alcohol. However, only participants who take alcohol had significant risk of presenting UTI. This may be explained by the fact that alcohol consumption was reported to impact adherence to ART treatment which could lead to reduced CD4 lymphocyte count and unsuppressed viral load, increasing the likelihood of opportunistic infection, UTI <sup>(12,13)</sup>. Alcohol use may also result in urine that is more acidic than usual, which irritates the lining of the bladder and speeds up the growth of E. Coli bacteria <sup>(13)</sup>.

Scarce studies were conducted to evaluate the impact of alcohol in the occurrence of UTI in HIV patients. Published data was not found in this field.

In this study, E. Coli followed by Klebsiella pneumonia and staphylococcus aureus were the most isolated bacterium with respectively rates 16%, 9% and 3.4%.

Comparable results were reported in Ethiopia by Tsabu et al, and Gondar and colleagues where the most isolated bacteria was E.coli followed also by Klebsiella pneumonia and Staphylococcus aureus<sup>(32)</sup>. In India, Kala and colleagues reported similar results, however Staphylococcus aureus was the second most prevalent<sup>(26)</sup>. The presence of a particular feature that aids in the bacteria's adhesion to uroepithelial cells and facilitates tissue invasion and

proliferation may be the cause of the preponderance of E. coli. In addition, E.coli is among the most prevalent bacteria in the vaginal and rectal areas

Controversy results were reported in Cameroon, where Staphylococcus aureus was reported as the most isolated microbe in the HIV/AIDS treatment centre of the Bamenda Regional Hospital in the North-West Region of Cameroon<sup>(20)</sup>. This could be explained by the difference in study population, as in the Cameroonian study, most participants had a CD4 lymphocyte count of less than 300<sup>(20)</sup>. The findings of Murugesh et al in India and Omoregie et al in Nigeria reported similar results with S.Aureus as the most frequently encountered bacteria<sup>(4,5)</sup>. In Croatia, S. Schoenwald and colleagues reported Enterococcus as the prevalent isolated bacteria among PLHIV<sup>(35)</sup>. The difference in study population and study design may explain this discrepancy in this study's findings.

In the present study, Ciprofloxacin and Nitrofurantoin were the most active drug, respectively, in 63 % and 53 % of all isolated macrobian. The least effective antibiotic agent was ampicillin which showed high resistance at 66.3 % and sensitivity in 5.6 % in all isolated bacteria. These findings are in line with Tanzania's standard treatment guideline of 2021, which recommends use of nitrofurantoin as first line in the management of UTI<sup>(1)</sup>. On the other side the resistance to ampicillin may be because the aminopenicillin group of antibiotics are the common self-medication antibiotic used in community pharmacies as reported in a study conducted by Bernard and colleagues among university students in Moshi Kilimanjaro<sup>(2)</sup>.

These findings are in line with a study conducted in the north of Tanzania by Bartholomeo and colleagues, where Nitrofurantoin and ceftriaxone were susceptible to gram-negative bacteria<sup>(18)</sup>. However, Bartholomeo and colleagues found resistance of gram-positive bacteria to ciprofloxacin. This discrepancy may arise from the fact that this study contained a low proportion of gram-positive bacteria compared to Bartholomeo and colleagues' study. Iroha and colleagues also observed comparable findings with ciprofloxacin, which showed activities against commonly isolated bacteria with high resistance to ampicillin<sup>(36)</sup>. In Ethiopia, Elias and

colleagues reported also comparable results with high resistance of gram-negative bacteria to ampicillin and cotrimoxazole <sup>(37)</sup>. In addition, Elias and colleagues found an approximate MDR(12%) to our findings(9%). This decreased susceptibility to uropathogens may be explained by the use of cotrimoxazole in prophylaxis against opportunistic infection in HIV patients.

Resistance to gram negative bacteria might be explained by the fact that their distinctive structure, are more resistant than Gram-positive bacteria. To reach their targets, most antibiotics need to cross the outer membrane. Hydrophilic antibiotics, such as  $\beta$ -lactams, can pass through porins, while hydrophobic medicines can pass by a diffusion channel. Resistance can result from any modification of the outer membrane by Gram-negative bacteria, such as modifications to the hydrophobic characteristics or changes in porins<sup>(38)</sup>. The absence of this crucial layer in Gram-positive bacteria results in increased antibiotic resistance in Gram-negative bacteria. Resistance to many different antibiotics is primarily caused by decreasing permeability of Gram-negative bacteria's outer membrane<sup>(39)</sup>.

Controversies results were reported in Nigeria, where, ceftriaxone and ciprofloxacin have shown increase resistance to both gram negative and positive with sensitivity to ampicillin<sup>(40)</sup>. Similar pattern of susceptibility were reported in South Africa and India<sup>(41)</sup>.The difference in study population, prevalence in common isolated macrobian between studies may explain this discrepancy.

### **6.1. Limitations and mitigations.**

This study sheds light on the prevalence and different susceptibility patterns of UTI among immune-competent patients living with HIV. Owing to the challenges of the unavailability of antibiotic discs, an equal number of tests for sensitivity conducted on all bacteria couldn't be conducted. However, effort was made to test the common empirical antibiotic used to manage UTI in PLHIV.

Another thing, in culture and sensitivity, morning midstream urine is used, because overnight urine has had time to accumulate in the bladder, which allows bacteria, if present, to multiply to detectable levels hence increasing the likelihood of identifying an infection if one exists. In this study, obtaining the morning midstream urine from the patients who attended the CTCs was difficult. Due to the logistics and practical constraints, patients often provided on-the-spot urine samples. Therefore, efforts were made to collect urine samples as early as possible during clinic visits. Moreover, patients were given detailed instructions on how to collect a clean catch urine sample, even when not providing a first-morning specimen. This aimed to reduce the likelihood of contamination in the on-the-spot samples.

### **6.2. Conclusions.**

The prevalence of UTI by age and gender among PLHIV attending CTC at Dar-es-salaam was relatively average compared to that reported in the literature. Participants with low CD4+ lymphocyte count <500 and those with unsuppressed viral load had a high risk of presenting UTI. On the other hand, gram-negative bacteria (*E. coli* and *Klebsiella pneumoniae*) were prevalent bacteria isolated. Nitrofurantoin, ciprofloxacin, and ceftriaxone were the most sensitive antibiotic agents, with ampicillin being the least sensitive to all isolated microbes.

### **6.3. Recommendations.**

The following are suggestions for this study:

Use of Nitrofurantoin, Ciprofloxacin, and Ceftriaxone as the empirical antibiotic agents in PLHIV with undetectable viral load.

Before administering ampicillin and cotrimoxazole for the treatment of UTI, patients should be selected based on their culture and sensitivity.

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## 8.0 APPENDICES

### APPENDIX 1: QUESTIONNAIRES

Serial No.....Date of interview..... Centre/Hospital.....

File Number.....

#### A: CLINICAL DATA

##### SOCIAL AND DEMOGRAPHIC CHARACTERISTICS

Gender 1. Female 2. Male

Age (date, Month, year ...../..... /..... )

Level of education..... 1. No formal education 2. Primary

3. Secondary 4. College 5. University

Occupation 1. formal employed 2. No 3. Self-employed

Family history of Diabetes ..... 1. Yes 2. No,

Prior history of diabetes 1. Yes 2. No

If yes when diagnosed?.....

History of alcohol intake ..... 1. Yes 2. No,

If yes how often do you take alcohol 1. stopped 2. daily 3. weekly

4. Occasionally

History of cigarettes smoking?.....

Duration of smoking?.....

Number of sexual partners.....

#### B: CLINICAL DATA

Presence of signs and symptoms of UTI

Painful micturition 1. Yes 2. No,

Frequency in urination 1. Yes 2. No,

Lower Abdominal pain. 1. Yes 2. No,

Hesitancy 1. Yes 2. No,

Urgency 1. Yes 2. No.

HIV status 1. Positive 2. Negative 3. Unknown

The use of anti-retro viral drugs, 1. Yes 2. No

When did you start using ARTs? Duration?.....

Method of UTI Diagnosis 1. urinalysis 2. culture

**C: LABORATORY DATA**

CD4 Cell count .....

Viral load.....

Urinalysis (pus cells, RBCs, .....

Urine culture .....

## **APPENDEX II: DODOSO**

Nambari ..... Tarehe ..... Kituo/Hospitali..... Nambari ya Faili.....

### **TAARIFA: TABIA ZA KIJAMII NA DEMOGRAFIA**

Jinsia: 1. ke 2. me

Umri .....

Kiwango chako cha elimu ..... 1. Sijasoma 2. Msingi 3. Sekondari

4. = Chuo cha Kati, 5. = Chuo Kikuyu

Kazi ..... 1. Ndio 2. Hapana

Kama ndio, kazi gani?

Je Kuna historia ya ugonjwa wa kisukari katika familia yenu ..... 1. Ndio, 2. Hapana

Je, wewe ni mgonjwa wa kisukari? 1.Ndiyo 2. Hapana

Kama Ndio, iligundulika lini? .....

unywaji pombe ..... 1. Ndiyo 2. Hapana

Kama ndio 1. umeacha 2. kila siku 3. kwa wiki mara moja 4. Mara chache

uvutaji sigara 1. Navuta 2. Nimeacha 3. Sijawahi

12. Je, umevuta kwa muda gani? .....

13. una wapenzi wa njei? 1. Ndio. 2. hapana.....

Kama ndio, wangapi?

### **TAARIFA ZA KLINIKALI: B**

Dalili zinazoashiria ugonjwa kwenye mfumo wa mkojo kwa maana ya: -

Kukojoa mara kwa mara mkojo mwingi 1. Ndiyo 2. Hapana

Kupata maumivu wakati wa kukojoa 1. Ndiyo 2. Hapana

Kujisikia kukojoa ila mkojo hautoki. 1. Ndiyo 2. Hapana

Kupata homa 1. Ndiyo 2. Hapana.

Umetumia dawa za kufubaza maambukizi kwa muda gani?.....

Historia ya kutumia mpira wa mkojo

Njia iliyotumika kugundua maambukizi kwenye mfumo wa mkojo:

1. Uchambuzi wa mkojo. 2. Utamaduni wa mkojo 3. nyinginezo (taja).....

### **TAARIFA ZA MAABARA**

Uchunguzi wa mkojo.....

Uotesho wa wadudu kwenye mkojo .....

Kiwango cha seli za CD4.....

wingi wa virusi.....

**APPENDIX III: CONSENT FORM (ENGLISH VERSION)**

Title: URINARY TRACT INFECTION AMONG PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION ATTENDING CLINICS IN DAR ES SALAAM.

I am Dr. Catherine Chacha, a resident in the Department of Internal Medicine. I would like to conduct the study above as a requirement for the fulfilment of my postgraduate studies.

This study requires your participation so that important information can be obtained regarding your health.

This study aims to determine the prevalence and risk factors of UTI among HIV patients attending CTCs in Dar es Salaam.

Patients who meet the inclusion criteria will be recruited into the study. They will be interviewed using a questionnaire, which will include their social demographic characteristics and other clinical parameters.

CD4 count and viral load will be taken from the participants' files.

Study findings will not be released to anybody except the researcher and the Subject him/herself.

The participant will not be asked for any fee during the study.

Person to contact in case of questions or problems:

Prof Y. Mgonda, Chairperson of Department, Internal Medicine, HKMU.

Dr Catherine Chacha, Post-graduate student, Department of Internal Medicine

Director of Postgraduate Studies and Research Institute, HKMU.

I, \_\_\_\_\_ have read/been told of the contents of this form and understood its meaning; hence, will participate in this study.

Signature \_\_\_\_\_ (Parent/guardian), Date \_\_\_\_\_

Signature \_\_\_\_\_ (Researcher), Date \_\_\_\_\_

## **APPENDIX IV: SWAHILI VERSION**

Title: URINARY TRACT INFECTION AMONG PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION ATTENDING CLINICS IN DAR ES SALAAM.

Jina langu ni Catherine Chacha, mwanafunzi wa shahada ya uzamili ya magonjwa ya ndani katika chuo kikuu cha Kumbukumbu ya Hubert Kairuki. Ninafanya utafiti kuhusiana na maambukizi ya mfumo wa mkojo kwa wagonjwa wanaoishi na virusi vya ukimwi kama ilivyoanishwa kwenye kichwa cha fomu hii.

Utafiti huu ni kati ya mahitaji muhimu kwa ajili ya kumaliza shahada hii. Hivyo basi unaombwa kuwa mmoja wa washiriki katika utafiti huu ili taarifa muhimu kuhusiana na afya yako ziweze patikana. Matokeo ya utafiti huu yatasaidia katika uboreshaji wa afya ya binadamu kwa kutoa mapendekezo yatakayolenga namna ya kuzuia magonjwa haya mapema. Watakaoshiriki katika utafiti huu; watajaza umri wao, watapimwa mkojo kama una maambukizi yoyote.

Matokeo ya utafiti huu hayatatolewa kwa mtu yeyote isipokuwa mtafiti mkuu na mshiriki tu.

Mshiriki atakuwa huru kujitoa kwenye utafiti muda wowote na hatatozwa gharama

Yoyote.

Watu wa kuuliza maswali yoyote kama yapo:

Dr. Catherine Chacha, Mwanafunzi wa shahada ya uzamilit, Idara ya Magonjwa ya

ndani, HKMU Prof Y. Mgonda, Mkuu wa idara, Magonjwa ya ndaini, HKMU

Mkurugenzi wa utafiti, HKMU

Mimi

\_\_\_\_\_ nimesoma na kuelewa maelezo

yaliyotolewa katika fomu hii, hivyo namruhusu mtoto wangu kushiriki katika utafi huu.

Sahihi ya mzazi/mlezi \_\_\_\_\_, Tarehe \_\_\_\_\_

Sahii ya mtafit mkuu \_\_\_\_\_, Tarehe \_\_\_\_\_