Studies on Urinary Tract Infections among HIV – Seropositive Individuals with Particular Reference to Antiretroviral Drug Usage.

BY

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UNIZIK/PG/PhD/2012487010P

A DISSERTATION SUBMITTED TO THE DEPARTMENT OF APPLIED MICROBIOLOGY AND BREWING, FACULTY OF BIOSCIENCES, IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF DOCTOR OF PHILOSOPHY (PhD) IN MEDICAL MICROBIOLOGY (VIROLOGY) OF NNAMDI AZIKIWE UNIVERSITY, AWKA.

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OCTOBER, 2018

CERTIFICATION

This is to certify that this dissertation titled “Studies on Urinary Tract Infections among HIV - Seropositive Individuals with Particular Reference to Antiretroviral Drug Usage and Host Factors” was carried out by Oghotuama Chiagorom Nnenna, with registration number, 2012487010P, under supervision. The work is original and has not been submitted in part or in full for any other diploma or degree of this, or any other university.

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APPROVAL PAGE

This dissertation titled "Studies on Urinary Tract Infections among HIV – Seropositive Individuals with Particular Reference to Antiretroviral Drug Usage and Host Factors", carried out by Oghotuama Chiagorom Nnenna, with registration number, 2012487010P, has been approved for the award of the degree of Doctor of Philosophy (PhD) in Medical Microbiology (Virology), in the Department of Applied Microbiology and Brewing, Faculty of Biosciences, Nnamdi Azikiwe University, Awka.

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DEDICATION

This research is dedicated to every person living with HIV/AIDS in resource poor countries of the world, especially in Africa.

ACKNOWLEDGEMENTS

My top billing goes to my supervisor, the amiable Professor Chris Anyamene, supervisor par excellence, an epitome of fatherhood and encouragement, for all the ways you have positively impacted me throughout the duration of this research work, I salute you. I am praying for long life and prosperity for you and your family.

I stay forever indebted to my Department and lecturers: Prof. C. A. Oyeka, Prof. R.A.U Nwobu, Prof. F.J.C. Odibo, Prof. F.C Ogbo, Prof. (Dame) E.I. Chukwurah, Dr. E. J Archibong, Prof. I. Okoli, Dr. E.L Okoye and Dr. C.C Ekwealor. I will not write my academic story without a mention of your contributions. You have been my inspiration. I salute all you academic giants. I will not forget in a hurry, the sound contributions of Prof. I.M Ezeonu and Prof. C.A Ekwunife for your invaluable inputs which, in no little way, have made this research work better in terms of its content quality. Thank you very much!

To my family and in - laws, thank you for the family support system I was privileged to access. To my husband, Mr. Peter Oghotuama, thank you for your unflinching support. To my dear father, Bar. M.O Ani (Mbanabaragu), it was you who spurred me into academic pursuit by buying me my first post graduate form on completion of my Bachelors' degree. Thank you sir! I am not ungrateful to my mother, Princess C.C Ani (Ogbarummankiti), for all the times you had to baby sit the kids so I can have time for my studies, I am eternally grateful. You will definitely reap the fruit of your labor.

My gratitude also goes out to the tireless phlebotomists and Medical Laboratory Scientists in ESUT Teaching Hospital, Parklane, Enugu; Chief M.O Ani, Mrs. G.I

Okeke, Mrs. P.U Asogwa as well as all Medical Laboratory Interns who assisted in this work in one way or another, may Almighty God bless you all tremendously!

To my fellow course mates, especially Dr. V. Nnachetam, it has been a pleasure knowing you all. The Lord blesses all your future endeavors!

To all the respondents that volunteered and the laboratory scientists and technicians involved in the course of this research work; I thank you all immensely!

Not forgetting Seizure Support Foundation family, for giving me a sense of purpose and an opportunity to impact my generation, may your light never go out, and may you wax stronger, Amen!

Finally, I end by expressing my profound gratitude to the children of my youth: Debby, Dorey and Davey. You guys inspire me in ways that are beyond description. I love you guys!

ABSTRACT

Urinary Tract Infections are major cause of morbidity in people living with HIV. The advent of anti retroviral drug usage has been shown to have indirect but long lasting preventive effect against opportunistic infections; and has improved considerably the health and life expectancy of people living with HIV/AIDS by boosting CD_4+ counts. However, the complexities, side effects and the possibility of drug treatment complications associated with antiretroviral usage may carry serious potential consequences on HIV positive patients. Studies were carried out on urinary tract infections among HIV individuals with particular reference to antiretroviral drug usage and host factors. Prevalence rates of UTI were compared between HIV positive ART users and HIV negative non ART users. A comparative, hospital – based, cross – sectional study was carried out at three different tertiary healthcare facilities in Enugu State, South East Nigeria. Two hundred and eighty five (285) patients were enrolled. Of these, one hundred and eighty five were HIV positive, ART users while one hundred were HIV negative, non ART users. Patient distribution was categorized according to the various host factors: CD_4+ values, 17.5% of individuals had <200 cells/µl, 34.4% had 200 – 499 cells/µl while 48.1% had >500 cells/µl. Gender, 68.4% of the subjects, were females, while 31.6% males. Age groups, 34.7% of the subjects were within 18 – 38 years, 36.8% were within 39 – 59 years; while 28.5% were within 60 – 80 years. Previous history of urinary tract infections, 53.3% of individuals has had at least one previous episode of UTI, while 46.7% have had no previous history of urinary tract infection. Length of ART use, 6.5% of individuals were under one year of ART usage, 44.3% were within 1 – 3 years of ART usage; 41.1% were within 4 – 6 years of ART usage, while 8.1% had been on ART usage for over 6 years. Mid – stream urine and venous blood specimens were collected from subjects into sterile universal and EDTA bottles respectively. Validated questionnaires were also administered to each patient to elicit responses concerning patients' host factors. Overall prevalence of UTI was 50.2%. Prevalence of UTIs was higher in HIV positive patients, 71.9% than in HIV negative patients, 28.1%. Prevalence of UTI was highest in patients with >500 cells/µl CD_4+ values, 24.6%. Prevalence of UTI by gender was higher in females, 42.1% than in males; 10.8%. Prevalence of UTI by age was highest in the 18 – 30 years age groups, 18.9%. Prevalence of UTI by of length of ART usage was highest in those on ART between 1 – 3 years, 31.4%. Prevalence of UTI by previous history of UTI was higher in patients with previous history of UTI, 65.9%. Nine organisms were implicated as the cause of urinary tract infections in HIV positive individuals on antiretroviral therapy. *Escherichia coli* had the highest prevalence of 34.3%. Other implicated etiologic agents include *Staphylococcus aureus, Klebsiella pneumonia*, *Proteus mirabilis*, *Streptococcus faecalis*, *Pseudomonas aeruginosa, Streptococcus pyogenes* and *Candida albicans*. There was no direct relationship between ART usage (P = 0.780) and CD_4+ values (P = 0.655) on the prevalence of UTI in patients. Other host factors like age (P = 0.157), gender (P = 0.199), previous history of urinary tract infections (P = 0.968) and length of anti retroviral drug

usage (P = 0.124) had no significant impact in the prevalence of UTI in patients. In conclusion, study showed that there was high prevalence of urinary tract infections among HIV – infected patients on antiretroviral drugs. Although ART boosted CD_4+ counts, it did not directly translate to reduced prevalence of urinary tract infections. High CD_4+ counts and prevalence of opportunistic infections may not be directly related though a cofounding factor related to both might be responsible for the relationship, if any. There is strong possibility of drug usage/treatment failure, non – compliance and non – adherence to ART in patients. This will help extend our attention and understanding of possible treatment gaps, drug failures, behavioral/attitudinal factors that can sabotage therapy and host immunity. Consequently, a health strategy that focuses on these rationales will improve the rate of compliance and of therapy success, thereby drastically reducing urinary tract infection prevalence in HIV patients on antiretroviral therapy. UTI is therefore not a potent bacteriologic marker in monitoring HIV infection in HIV positive individuals on antiretroviral drugs.

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ABBREVIATIONS

ADC: AIDS Dementia Complex

AIDS: Acquired Immunodeficiency Syndrome

ALT: Alanine amino Transferase

ART: Antiretroviral Therapy

ASB: Asymptomatic Bacteuria

AZT: Azidothymidine

CDC: United States Centers for Disease Control and Prevention

CD_4+: T-lymphocyte bearing CD4 receptor

CFU: Colony Forming Units

CMV: Cytomegalovirus

CNS: Central Nervous System

CT: Computerized Tomography

DNA: Deoxyribonucleic Acid

EIA: Enzyme Immunoassay

ELISA: Enzyme-Linked Immunosorbent Assay

HAART: Highly Active Anti Retroviral Therapy

HEAP: HIV Emergency Action Plan

HIV: Human Immunodeficiency Virus

HHV-8: Human Herpes Virus Complex

HSV: Herpes Simplex Virus

HTC: HIV Testing and Counseling

ICS: Immunochromatographic Strip

KS: Kaposi Sarcoma

LACA: Local government Action Committee on AIDS

LMIC: Low and Middle Income Countries

MAC: *Mycobacterium avium* Complex

MDG: Millennium Development Goals

MOH: Ministry of Health

MRI: Magnetic Resonance Imaging

MTCT: Mother to Child Transmission

NACA: National Action Committee on AIDS

NHL: Non Hodgkin Lymphoma

NRTI: Nucleoside Reverse Transcriptase Inhibitor

NSF: National Science Foundation

OIs: *Opportunistic Infections*

OVC: Over the Counter

PCA: Presidential Council on AIDS

PCP: *Pneumocystis jiroveci* Pneumonia

PCR: Polymerase Chain Reaction

PEPFAR: The U.S President's Emergency Plan for AIDS Relief

PLHIV: People Living with HIV

PMTCT: Prevention of Mother to Child Transmission (of HIV)

RNA: Ribonucleic Acid

SACA: State Action Committee on AIDS

SDG: Sustainable Development Goals

SIV: Simian Immunodeficiency Virus

S/R Test: Simple or Rapid HIV antibody test

STI: Sexually Transmitted Infections

TB: Tuberculosis

UNAIDS: Joint United Nations Programme on HIV/AIDS

UNGASS: United Nations General Assembly Special Session

UTI: Urinary Tract Infections.

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CHAPTER 1

INTRODUCTION

1.1 Background of Study

Acquired Immunodeficiency Syndrome (AIDS) continues to be a serious health issue for most parts of the world (Kemajou *et al*, 2016). Worldwide, there are about 2.1 million new cases of HIV infections in 2015. About 36.7 million people are living with HIV around the world and as of June, 2016; 17 million people living with HIV are receiving anti retroviral usage (ART). An estimated 1.1 million people died from AIDS related illnesses in 2015. Sub – Saharan Africa, which bears the heaviest burden of HIV/AIDS worldwide, accounts for 65% of all new HIV infections. Other regions significantly affected by HIV/AIDS include Asia and the Pacific, Latin America and the Caribbean, Eastern Europe and Central Asia (Centers for Disease Control and Prevention, 2017). Nigeria has the second largest HIV epidemic in the world (UNAIDS, 2016). Although HIV prevalence among adults in Nigeria is remarkably small (3.1%), compared to other sub – Saharan African countries such as South Africa (25%) (UNAIDS, 2016). The size of Nigeria's population means 3.5 million people were living with HIV in 2015. An estimated 60% of new HIV infections in western and central Africa in 2015 occurred in Nigeria. Together with South Africa and Uganda, the country accounts for almost half of all new HIV infections in sub – Saharan Africa each year. This is despite achieving 3.5% reduction in new infections between 2005 and 2013. HIV prevalence is highest in Nigeria's southern states, known as the South South zone, and stands at 5.5%. It is lowest in the South East zone, where there is a prevalence of 1.8%. There are higher rates of HIV in the rural areas (4%) than in the urban areas (3%). Approximately 160,000 people died from AIDS – related illnesses in

Nigeria in 2015. Since 2005, the reduction in the number of annual AIDS – related deaths has been minimal, indicative of the fact that only half (51%) of those living with HIV in Nigeria are accessing anti retroviral ART users (ART) (Centers for Disease Control and Prevention, 2017).

Human immunodeficiency virus (HIV) is a lentivirus that causes immunodeficiency syndrome (Kemajou *et al,* 2016). This is a condition in humans in which progressive failure of the immune system allows life threatening opportunistic infections to thrive. Acquired Immuno – deficiency Syndrome has changed from a rapidly deteriorating illness, to a complex chronic disease, with increasing incidences of co morbidities. Most untreated people infected with HIV eventually develop AIDS. These individuals usually die of opportunistic infections or malignancies associated with progressive failure of their immune system. HIV infects vital cells in the immune system such as the T helper cells, macrophages and dendritic cells. HIV infections lead to low levels of CD_4+T cells through three main mechanisms. First, direct viral killing of the infected cells; secondly, increased rate of apoptosis in infected cells; and third, killing of infected CD_4+ cells by CD_8 cytotoxic lymphocytes that recognize infected cells. When CD_4+ cells number decline below a critical level, cell mediated immunity is lost and the body becomes progressively more susceptible to opportunistic infections. Once a patients' CD_4+ T cell count falls below 200cells/µl, the individual is then at risk of a variety of opportunistic infections.

Urinary tract infections (UTI) refer to the presence of microbial pathogens within the human urinary tract and are usually classified by the site of infection: bladder (cystitis), kidneys (pyelonephritis). UTI can also be defined as the microbial invasion of any of the tissues of the urinary tract extending from the renal cortex to the urethral meatus (Ogbukagu *et al.,* 2016). Urinary tract infections are one of the

significant illnesses that cause disease burden in HIV infection. It is the most common nosocomial infection, but an important source of morbidity as well. Urinary tract infections are one of the most common bacterial infections and cause of morbidity and hospitalization in HIV positive individuals (Kemajou *et al*, 2016). Urinary tract infections always require the presence of bacteria in the urine (bacteuria) but can be both asymptomatic and symptomatic, and are characterized by a wide spectrum of symptoms ranging from mild, irritating voiding to bacteremia, sepsis, or even death. HIV infection is associated with a variety of renal syndromes; patients with low CD_4+ counts are at risk of urological complications which can lead to urinary stasis and ultimately, infection. Untreated UTIs account for 7 – 60% of opportunistic infections and could be a source for ascending urinary tract infection and septicemia in immunocompromised hosts (Centers for Disease Control and Prevention, 2017). Among opportunistic infections, UTI account for 60% of AIDS defining illnesses (Kemajou *et al*, 2016). Urinary tract infections usually start when organisms, usually bacteria from the digestive tract, cling to the opening of the urethra and begin to multiply. More than 90% of UTIs are due to enteric Gram negative bacteria including *Escherichia coli, Proteus mirabilis, Klebsiella pneumonia, Pseudomonas aeruginosa and Staphylococcus aureus.* According to Kemajou *et al*., the most predominant causative organisms causing UTI in HIV positive individuals are encapsulated bacteria, notably *Streptococcus pneumonia* and *Haemophilius influenza*, fungi, protozoa and viruses. But, non – typhoidal Salmonella, *Staphylococcius aureus* and *Pseudomonas aeruginosa* have been implicated. Bacterial UTIs are more common in HIV positive individuals than in HIV negative patients (Omoregie *et al*., 2009). The prevalence of data on the frequency of UTIs in HIV infected patients is scanty and not updated in Nigeria (Kemajou *et al*, 2016). Signs and symptoms of UTI vary depending on sex, age, immune status and the area of the

urinary tract that is infected; some unique symptoms develop depending on the infecting agent. Females have a higher risk of UTIs than males, probably because of their anatomy. Other risk factors for UTIs include any condition that may impede urine flow (like enlarged prostate, congenital urinary tract abnormalities and inflammation). The introduction of anti retroviral usage has (ART) has drastically reduced morbidity related with urinary tract infections in most patients with HIV/AIDS (Debalke, 2014). Anti retroviral usage improves the health of people infected through decreasing the progression of infection, restoration of the immunity of the patient, decreasing the viral load and reducing the opportunistic infections (Kemajou *et al*, 2016). Studies on the evaluation of the effect of retroviral usage show that ART has a significant impact on reduction of the prevalence of bacterial infections including bacteremia, bacterial pneumonia, and urinary tract infections that occur in HIV patients (Debalke, 2014).

People living with human immunodeficiency virus (HIV) are more prone to opportunistic infections including urinary tract infections (UTI). Studies on the prevalence of urinary tract infections among HIV patients in Aba, Abia State showed a high prevalence of UTI among HIV patients in Aba metropolis (Kanu *et al*., 2016).This is due to progressive immune dysfunction caused by the virus. In people living with HIV/AIDS, almost every part of the genitourinary is potentially affected with different diseases. High rates of renal diseases, neoplasm, voiding and erectile dysfunctions, haematuria, opportunistic genitourinary infections and epididymo – orchitis are found in HIV infected individuals (Abderrazzack *et al*., 2015). In high income countries, the following opportunistic infections; esophageal *Candidiasis, Cryptococcal meningitis, Cytomegalovirus retinitis, Toxoplasma encephalitis, Cryptosporidium* diarrhea, Herpes *and Kaposi sarcoma;* are mostly encountered (Bertozzi *et al.,* 2010). Anyamene, in 2006, characterized a spectrum

of bacterial infections associated with a cohort of HIV positive persons in South East, Nigeria. According to him, the most frequent bacterial infections common in HIV positive individuals were tuberculosis, followed by bacterial pneumonia, bacteraemia, urinary tract infections, and typhoid fever. The vulnerabilities of HIV positive individuals in lower income settings are mostly due to different bacterial infections including urinary tract infections. This is because of low CD_4+ count of these infected patients. The introduction of anti retroviral usage (ART) has dramatically reduced morbidity related with bacterial infections including urinary tract infections (UTI) among patients living with HIV/AIDS. The advent of anti retroviral usage has shown to have indirect (immune restoration) but long lasting preventive effect against opportunistic infections. This has improved considerably the health and life expectancy of people living with HIV/AIDS. Anti retroviral drug administration has been shown to be an independent factor that contributed to a two – fold decrease in the prevalence of bacterial infections (Inyang – Etoh *et al*., 2009). However, a study by Omoregie *et al.,* 2009, revealed a two – to three fold higher risk of acquiring urinary tract infections in HIV positive individuals on ART and increased prevalence of urinary tract infections in HIV positive patients on long term anti retroviral usage (Omoregie *et al.,* 2009). A study at the London Royal Hospital, London revealed urinary tract infections to be more common in elderly patients compared to younger patients with HIV infection. Another study revealed HIV/AIDS to be a predisposing factor for increased urinary tract infections in the young (Iroha, 2013). Studies on the evaluation of the effects of antiretroviral usage, show that ART has a significant impact on the reduction of the incidence of bacterial infections including bacteraemia, bacterial pneumonia, and urinary tract infections (UTI) that occur in HIV infected persons (De Gaetano *et al.,* 2003). Although several reports have linked patients on antiretroviral drug usage with high prevalence rate of urinary tract infections (Iroezindu *et al*., 2013).

A review of related studies showed an increased prevalence rate of urinary tract infections (UTI) in HIV/AIDS patients on ART. Since 2015, routine guideline recommends antiretroviral usage for HIV positive individuals at any CD_4+ count (Centers for Disease Control and Prevention, 2017).

CD_4+ count measures the rate of immunosuppression in HIV positive patients. It is also used in deciding when to commence anti retroviral usage, in staging of the disease, and in determining ART user's failure. Men infected with HIV and presenting with a CD_4+ count of 200cells/µl, have shown an increased risk of acquiring bacteriuria while women of CD_4+ count below 200cells/µl, have a higher prevalence rate of urinary tract infections. Although in 2009, Omoregie *et. al.*, researched on the impact of human immunodeficiency virus (HIV) infection and CD_4+ count on the prevalence of urinary tract infections in order to determine the prevalence of UTI among HIV and non- HIV infected subjects. He and his team found out that CD_4+ count values lower than 200cells/µl was not associated with asymptomatic urinary tract infection (Omoregie *et al*., 2009). Men with a history of AIDS – defining illnesses or below 200cells/µl counts have an increased risk of moderate to severe lower urinary tract symptoms than HIV positive men with higher CD_4+ counts (Graham, 2011). In addition to HIV, there are other factors which can affect CD_4+ cell count. Among demographic variables, older ages are predictors to lower CD_4+ count response to ART. With regards to sex, females experienced better CD_4+ count response to ART compared to males (Gezie, 2016). A study on '*The incidence of symptomatic urinary tract infections in HIV seronegative patients and the use of cotrimoxazoleas prophylaxis against PCP'* showed that UTI are more common in patients with advanced compared with early HIV infection (Evans *et al.*, 2015).

In people living with HIV/AIDS, different urinary tract pathogens have been implicated as the cause of urinary tract infections in different parts of the world. Schonwald *et. al*. 1999, implicated *Enterococci* as the most frequent cause of urinary tract infections in patients with HIV disease in Germany. *Anyamene* in 2006 implicated *Streptococcus pyogenes* as the most common etiologic agent responsible for UTI in HIV positive individuals in Anambra state, Nigeria. In 2009, Omoregie *et. al.*, implicated *Staphylococcus aureus* as the most implicated etiologic agent responsible for UTI in HIV individuals in Benin City, Nigeria. According to Debalke, *Staphylococcus aureus* was the predominant bacteria – causing urinary tract infections among ART user patients in Ethiopia. Following in order of prevalence were: *Escherichia coli*, *Enterococcus species*, *Pseudomonas aeruginosa*, *klebsiella species*, *Acetobacter*, *Proteus species*, *Candida species*, and *Salmonella species*. (Debalke *et. al.*, 2014). Enzyme and electrolyte abnormalities have been observed with antiretroviral usage and drugs used to treat opportunistic infections in HIV positive individuals (Salifu, 2015). Opportunistic infections and drugs used in the ART of HIV and its complications and malignancies associated with advanced immunosuppression may contribute to renal and liver diseases in HIV infected individuals (bmcpedtr.biomedcentral.com). Enzyme and electrolyte imbalance can either result from a direct kidney infect ion with HIV, urinary tract infection or adverse effects of antiretroviral drugs.

Laboratory analysis used in monitoring management in HIV positive patients are HIV – RNA (viral load) and CD_4+ count. The former is the gold standard. Its use is however, limited because of its cost and technology. Several studies have shown that CD_4+ count is a stronger predictor of disease progression and survival (Omoregie *et al.*, 2009). The cost of CD_4+ count is cheaper and becoming increasingly affordable in resource – poor counties of the world. CD_4+ counts

measures the degree of immunosuppression in HIV positive patients. There is an inverse relationship between CD_4+ counts and degree of immunosuppression. Thus, CD_4+ count is used to monitor the progression of the disease, in deciding commencement of usage, staging of disease, risk of disease transmission and ART users failure. The US Center for Disease Control and the prevention (CDC) 2017, used CD_4+ count as a tool to stage HIV into categories A, B and C based on whether the CD_4+ count is >500 cells/µl, between 200 – 499 cells/ µl or <200 cells/ µl.

1.2 Statement of Problem

The complexities, side effects and the possibility of drug treatment failures associated with antiretroviral usage carry serious potential consequences on HIV positive patients; from the development of viral resistance because of no adherence to the drug regimen or suboptimal levels of antiretroviral agents, to the failure in boosting patient immune system (CD_4+ counts). Consequently increasing the risk of opportunistic infections, attendant complications and hospital visits among HIV positive patients, despite ART drug usage.

1.3 Justification of Study

Recently, there has been increased frequency of hospital visits by HIV positive patients as regards urinary tract infections despite impressive CD_4+ count values, in tertiary health care facilities in Enugu State. Several studies have suggested that host associated co morbidities still persist in HIV infected patients on antiretroviral therapy usage compared to HIV – uninfected patients. This project was undertaken to find out implicating host factors, alongside CD_4+ values, responsible for increased hospital visits with a view to contributing to the existing knowledge base regarding changes in treatments, management and health care needs among HIV

positive patients. Consequently, significantly reducing hospital visits caused by urinary tract infections in the cohort.

1.4 Research Questions

1. Does ART use have any impact in increasing or decreasing the prevalence of urinary tract infections in HIV positive individuals?
2. Do CD_4+ count values have any impact in increasing or decreasing the prevalence of urinary tract infections in HIV positive individuals?
3. Do host socio demographic factors like age, gender, previous history of urinary tract infections, and length of anti retroviral usage have any impact in the prevalence of urinary tract infection in a cohort of HIV positive individuals?
4. Are etiologic agents responsible for urinary tract infections in this cohort same agents implicated in similar investigations in other parts of the world?

1.5 Scope of Study

For the purpose of this study, only HIV positive patients in Enugu State were considered for study. HIV negative patients were used as control population. By age, patients between 18 years and 80 years of age were considered. By length of antiretroviral usage, HIV positive patients who have been on ART regimen for at least 6 months and above, prior to study, were recruited. By previous history of urinary tract infections, patients with or without prior history of urinary tract infections, were considered. Isolation of organisms was also limited to aerobic organisms only.

1.6 Aim of Study

"To carry out studies on Urinary Tract Infections among HIV – seropositive individuals with particular reference to antiretroviral drug usage"

1.7 Specific Objectives

To determine and compare:

1. The overall prevalence of urinary tract infections among HIV positive ART users and non ART users in Enugu State metropolis.
2. Prevalence of urinary tract infections according CD_4+ values.
3. Prevalence of urinary tract infections according to gender.
4. Prevalence of urinary tract infections according to age.
5. Prevalence of urinary tract infections according to length of period on ART.
6. Prevalence of urinary tract infections according to previous history of UTI.
7. The etiological agents causing urinary tract infections among HIV positive ART users and non ART users.
8. To confirm if urinary tract infections should serve as a marker in HIV disease monitoring.

CHAPTER 2

LITERATURE REVIEW

2.1 Urinary Tract Infections

Urinary tract infections represent one of the most frequent reasons for hospitalization (Bigwan *et al*., 2015). Urinary tract infections remain the most under investigated yet most important problem among HIV positive patients (Banu *et al*, 2013). As a result of their prevalence, from community – based origins as well as those which develop in hospital settings, this constellation of infections, represents a tremendous burden to the global health care system.

2.11 DEFINITION

By definition, urinary tract infection is the presence of pathogenic microorganisms in specified amounts in human urinary tract (Bigwan *et al*., 2015). It is also defined as the microbial invasion of any of the tissues the urinary tract extending from the renal cortex to the urethral meatus (Akadri, *et al*, 2014). And occurs in all age groups and in both genders (Murugesh, 2015).They are the most frequent community – acquired infections in the world. Specific groups of people are at increased risk of urinary tract infections. People living with HIV are likely to be more predisposed to urinary tract infections due to suppression of their immunity and women in this category tend to get them more often due to the nature of their human anatomy (Banu *et al*, 2013).

Normally, the urinary tract proximal to the distal urethra is sterile, but it is constantly challenged by infectious pathogens fighting to gain access. Urinary tract infections, strictly speaking, occur when an infectious agent is present within this sterile system; however, a more appropriate clinical definition is that UTI occurs when the infectious agent is not only present, but is also causing illness. This distinction underscores the inherent clinical difficulty of managing patients with UTI. In practice, a diagnosis of UTI is presumed when irritating urinary tract symptoms occur simultaneously with a positive test for infectious agents, such as bacteria, fungi, viruses, or parasites, in the urinary tract. Because other factors can cause similar symptoms, the presence of symptoms in the absence of a positive culture has historically been considered inadequate for diagnosis. Likewise, the presence of leukocytes in the urine is not proof of infection. Asymptomatic bacteriuria may represent colonization or contamination and should be differentiated from UTI. Thus, for clinical purposes, the definition of a UTI requires a combination of symptoms and laboratory findings. Both the infectious agent and the anatomic location typically define the UTI. The urinary tract is commonly divided into the upper tract (kidneys and ureters) and the lower tract (bladder and urethra). In the male, infections such as prostatitis, epididymitis, and orchitis are frequently included as UTIs but are more accurately considered genital infections; they have a separate epidemiology and natural history. UTIs are also categorized as complicated or uncomplicated. Complicated UTIs are infections in which there is a comorbidity that predisposes a child either to infection or to greater morbidity due to the infection. Comorbidities include the presence of stones, neurological impairment affecting urinary tract functioning, and anatomic abnormalities such as obstruction, reflux, or enterovesical fistula. UTI is a frequent complication of medical care, especially hospitalization. Unfortunately, the datasets analyzed for this chapter preclude distinguishing nosocomial from

community-acquired infections. In this compendium, children are defined as persons less than 18 years of age. Where possible, they are further subdivided into infants (under 3 years of age), older children (3 to 10), and adolescents (11 to 17). Most of the datasets analyzed for this chapter do not distinguish the site of the UTI, with the notable exception of data from the Healthcare Cost and Utilization Project (HCUP) and MarketScan, in which pyelonephritis and orchitis, respectively, are distinguished from UTIs in other sites. The method by which the site of UTI is determined in these datasets is based on diagnostic coding and likely varies across the population. The vast majority of UTIs are caused by bacterial agents, the most important of which are the *Enterobacteriaciae,* a family of gram-negative bacilli. *Escherichia coli* accounts for more than 80% of acute UTIs in children. The rest of the cases are distributed primarily among *Proteus mirabilis, Klebsiella pneumonia,* and *Pseudomonsa aeruginosa*. Less common infectious agents include gram – positive cocci, such as *Enterococcus* and *Staphylococcus.* Fungal infections, particularly *Candida,* are usually seen in nosocomial infections, complicated UTIs, or catheter-associated UTIs. Viral infections are under-recognized because of difficulties with culture and identification, but they have clearly been associated with infectious bladder symptoms. Cytomegalovirus is frequently seen in immunocompromised patients, particularly following organ transplantation. Urinary tract infections (UTIs) are considered to be the most common bacterial infections (Foxman, 2003). They are usually bacterial in origin, might be complicated by frequent recurrences, and may also present as more severe manifestations such as pyelonephritis and sepsis especially in individuals at risk. Urinary Tract Infection (UTI) means infection in the urinary tract; types are named for the part of the tract involved, such as urethritis, cystitis, ureteritis, pyelonephritis, and glomerulonephritis. It is more common in women than in men because of the relative shortness of the female urethra. Men over the age of 50 are

more susceptible because of enlargement of the prostrate and urinary stasis. Symptoms include dysuria, malaise, nausea, urinary frequency and urgency, and nocturia. There also may be a feeling of suprapubic fullness not relieved by urination. If the infection is higher in the urinary tract, in the ureters or kidney, there can be lower back pain or genital pain. Factors that contribute to infection of the urinary tract include structural defects and systemic disorders that interfere with the free flow of urine. Examples include congenital disorders, neuromuscular disease or spinal cord injury, and renal stones. Infectious agents that cause sexually transmitted diseases can also invade the urinary tract. Moreover, urinary tract infection is a constant threat and a major cause of morbidity in patients living with HIV. Urinary tract infections are microbial infections, usually bacterial, of any part of the urinary tract; may involve the parenchyma of the kidney, the renal pelvis, the ureter, the bladder, the urethra or combinations of these organs. Often, the entire urinary tract is affected; the most common organism causing such infection is *Escherichia coli.* Urinary tract infections are infections of one or more structures in the urinary system. Most UTIs are caused by gram-negative bacteria, most commonly *Escherichia coli* or species of *Klebsiella*, *Proteus, Pseudomonas*, or *Enterobacter*, although other strains, such as *Staphlyococcus* and *Serratia*, are emerging. The condition is more common in women than in men. UTI may be asymptomatic but is usually characterized by urinary frequency, burning pain with voiding, and, if the infection is severe, visible blood and pus in the urine. Fever and back pain often accompany kidney infections. Diagnosis of the cause and location of the infection is made by microscopic examination and bacteriologic culture of a urine specimen, physical examination of the patient, and, if necessary, various radiologic techniques such as retrograde pyelography or cystoscopy. Treatment includes antibacterial, analgesic, and urinary antiseptic drugs and increased fluid intake up to 3L/day, unless contraindicated. Teaching the patient about increased

fluid intake, frequent voiding, and good perineal hygiene is also helpful. Kinds of urinary tract infections include cystitis, pyelonephritis, and urethritis (Mosby's Medical Dictionary, 2009) UTIs are infections of the kidney, ureter, bladder, or urethra. Affects young women with acute uncomplicated pyelonephritis or cystitis, or recurrent cystitis, and adults with asymptomatic bacteruria or with complicated UTI. Epidemiology Common in young, sexually active women, often associated with sexual intercourse, use of a diaphragm with a spermicide (McGraw-Hill Concise Dictionary of Modern Medicine, 2002). UTIs are microbial infections, usually bacterial, of any part of the urinary tract. Nevertheless, it is difficult to accurately assess the prevalence of UTIs, because they are not reportable diseases in Nigeria. This situation is further complicated by the fact that accurate diagnosis depends on both the presence of symptoms and a positive urine culture, although in most outpatient settings this diagnosis is made without the benefit of culture. Women are significantly more likely to experience UTI than men Nearly 1 in 3 women will have had at least 1 episode of UTI requiring antimicrobial therapy by the age of 24 years (Banu, 2014). Almost half of all women will experience 1 UTI during their lifetime. Specific subpopulations at increased risk of UTI include infants, pregnant women, the elderly, patients with spinal cord injuries and/or catheters, patients with diabetes or multiple sclerosis, patients with acquired immunodeficiency disease syndrome/human immunodeficiency virus, and patients with underlying urologic abnormalities.

2.12 NATURAL HISTORY

The natural history of uncomplicated acute urinary tract infections is generally benign and free of significant long- term morbidity. The course is typically

characterized by discomfort and irritative voiding symptoms with rapid resolution following the initiation of appropriate antimicrobials. The primary risk is that of recurrence or persistence. Children with constipation or voiding dysfunction are particularly prone to recurrence; 10% of these children develop a rapid recurrence following the completion of a course of antimicrobials. However, most recurrences do not progress to severe infections in the absence of anatomic abnormalities, and recurrent childhood UTIs tend to disappear in adolescence. The natural history of pyelonephritis carries greater potential for long-term morbidity. Pyelonephritis can result in irreversible scarring of the renal parenchyma due to interstitial inflammation and virulence factors from the pathogen. Renal scarring is frequently, although not exclusively, associated with the simultaneous presence of reflux and infection. The likelihood of scarring increases with the number of infectious episodes, but significant renal damage can occur after a single infection. Renal scarring can lead to renal insufficiency and subsequent hypertension. The actual incidence of renal insufficiency due to scarring is unknown, in part because of changing definitions of reflux nephropathy and changing clinical presentations that have resulted from the widespread use of prenatal ultrasound. Historically, reflux nephropathy was considered responsible for 3% to 25% of the ESRD cases in children.

2.13 INCIDENCE

It is difficult to estimate accurately the incidence of UTI in the pediatric population. Contributing questions include whether the determination of infection is based on symptoms, positive culture, or both; how accurate the method of specimen collection is; how accurate the history is, especially in young children;

whether evaluation is focused on a specific age group or gender; whether the data are prospective or retrospective; whether or not the infections are associated with fever; and what the baseline rate of circumcision is in the population. Frequently quoted estimates place the incidence of UTI in infants at approximately 1% during the first year of life (boys and girls), cumulative incidence at approximately 2% at two years of life (boys and girls), and cumulative childhood risk at 2% for boys and 8% for girls. Beyond the age of 2, UTIs in boys are not common enough to alter the childhood incidence through age 17. Boys are at the greatest risk for UTI in the first months of life, but the risk decreases significantly

2.14 RISK FACTORS

Socio – demographic/ host factors have been shown to play roles in the prevalence and spectrum of bacterial pathogens implicated as causative agents of urinary tract infections in HIV positive patients. The urinary tract is challenged by the ubiquitous presence of pathogens in close proximity. Any factors that enhance bacterial virulence or detract from host defense can predispose to UTI. Bacterial virulence factors include adhesins, K-antigen, hemosysins, and colicin. Bacterial colonization of the perineum typically precedes acute infection in the susceptible host. Adhesins are specialized structures that enable the bacteria to adhere to specific receptors on the uroepithelium. Such attachment leads to ascension into the urinary tract and promotes tissue invasion, inflammation, and tissue injury. Adhesins may also help promote intestinal carriage of more virulent bacteria, leading to perineal colonization. K-antigen helps prevent phagocytosis of bacteria; hemosysins.

Damage renal tubular cells; and colocin helps kill competing bacteria near the colocin-producing cell. Successful host defense depends on the proper functioning of the urinary system. A primary function of the urinary tract is the frequent and complete emptying of urine in a low-pressure environment. This effectively flushes out bacteria prior to their establishment of clinical infection. Any breakdown in this process can tip the balance toward the pathogen and result in UTI. Host risk factors are thought to include vesicoureteral reflux, dysfunctional voiding, constipation, obstruction, and gender-specific anatomy (the short urethra in females and the prepuce in males). Vesicoureteral reflux is a frequent finding in children presenting with febrile infections. Present in approximately 1% of the asymptomatic population and 35% of those with UTI, reflux increases the risk of infection, in part by increasing post-void residual. Reflux also bypasses one of the host defense mechanisms against upper tract invasion by allowing less virulent strains of bacteria to reach the kidney. Obstruction at the ureteropelvic junction, ureterovesical junction, or urethra is an infrequent but important host risk factor that can contribute to increased morbidity, persistence, and recurrence. Obstruction is present in fewer than 1% of children with UTI. Dysfunctional voiding and dysfunctional elimination (constipation or functional fecal retention) are increasingly recognized as important host risk factors for UTI, particularly recurrent infections in anatomically normal children. Dysfunctional voiding refers to a learned pattern of behavior surrounding voiding that frequently begins with voluntary holding. It can present clinically with irritative symptoms such as urgency, frequency, urge incontinence, pelvic pain, and signs of holding such as squatting. Alternatively, it can present as an atonic bladder with infrequent voiding and high post-void residuals. In both patterns, elevated intravesical pressure, infrequent voiding, and poor emptying enhance the risk of UTI. Frequently, dysfunctional voiding can be compounded by chronic constipation.

The exact mechanism by which constipation exerts its influence on voiding is unclear, but it frequently coexists in children with recurrent UTIs, and its resolution is often associated with resolution of the UTIs.

The relatively short length of the female urethra has traditionally been blamed for the increased risk of UTIs in girls. In the past, there was concern that a tight ring narrowed the urethra, often prompting urethral dilation in girls with UTI. Current evidence indicates that urethral constriction is not a reproducible finding, nor does it cause infection. Urethral dilation should play no role in the contemporary management of UTI in girls. In boys, the most widely discussed host risk factor for UTI is the presence of the prepuce. It is clear that male infants with an intact prepuce are at a significantly higher risk of UTI during their first year of life. Colonization of bacteria on the inner preputial mucosa occurs, but it is not clear whether this is the etiology of infection. Circumcision is protective against UTI, but it carries its own risks. Uncircumcised boys have an overall 12-fold increased risk of urinary infection during their first 6 months compared with circumcised boys, in addition to a significantly higher probability of hospital admission for UTI (7.02 of 1,000) as compared with circumcised boys (1.88 of 1,000; $P<0.0001$). A fuller discussion of this controversial subject is beyond the scope of this chapter. The important predisposing factors for urinary tract infections in females are age, sex, pregnancy, sexual intercourse, menopause, use of birth control devices, catheterization, surgery, diabetes, use of calcium supplements, immunosuppression, renal transplantation and spinal cord injury (Kanu, 2016). Urinary tract infections are also the most frequent medical complications in patients with neurological bladder dysfunction leading to high morbidity, poor quality of life and limited life expectancy. Moreover, severe protein malnutrition, poor fluid intake and poor hygiene resulting in decrease immunity are also

associated with urinary tract infections. A number of predisposing factors render individuals susceptible to urinary tract infections. Any obstruction in normal flow of of urine or complete emptying of bladder facilitates the access of organisms to the bladder and, in turn, predisposes an individual to infections (Debalke *et al*, 2014). There are numerous possible structural abnormalities of urinary tract that are associated with 'residual urine' which increases the chances of infection and may become associated with repeated attacks of UTI. Some of these are renal calculi, tumors, and urethral stricture. An important predisposing factor for UTI is the sex of patient. It is evident from the substantial research that UTIs are more common in women as compared to men (Fenta, 2016). Most infections in women are uncomplicated, whereas in men, complicated infections predominate (Kanu, 2016). Women are especially prone to UTIs probably because of the shortness of urethra and closeness of urethra to opening of genital and intestinal tract. The shorter the length of the female urethra allows uropathogens easier access to the bladder. Men are less prone to get UTI, possibly because of their longer urethra and the presence of antibacterial substances in the prostatic fluid. The relationship between sex and the incidence of urinary tract infections has been confirmed by establishing females at significant increased risk as compared to males (Murugesh, 2015). The incidence of urinary tract infections in females tend to increase with increasing age. Symptomatic and asymptomatic urinary tract infections are extremely common in the elderly population. The prevalence of bacteruria in women is about 205 between ages 65 and 75, increasing to between 20 – 25% over the age of 80 years (Debalke *et al*, 2014). Whereas a significant number of infections occur in men only after the age of 50 years when prostatic hypertrophy or other urinary tract abnormalities occur. Urinary tract infections in young men are unusual and require further investigations (Fenta, 2016). The prevalence in men is 3% at age 65 – 70 years and about 20% at ages over 80 years. The geriatric

community is frequently affected by urinary tract infections but these infections are usually asymptomatic. Approximately 25% of all infections in the elderly are urinary tract infections (Kemajou *et al*, 2016). In a study, it was documented that 50% of elderly women are affected by asymptomatic urinary tract infections. In many cases, bladder catheterization is a contributing factor and cause s increasing incidence of urinary tract infections in elderly populations. Urinary tract infections were found in 14.8% of the overall individuals of 80 years of age. Of those, 19% were women and 5.8% were men. A woman over 80 years with urinary incontinence and needing support to walk has 50% risk of asymptomatic urinary tract infections. The majority of symptomatic urinary tract infections occur in females after the age of 50 years. In another related study, prevalence of symptomatic and asymptomatic urinary tract infections was evaluated in women between 57 – 97 years of age. It was found that symptomatic urinary tract infection occurred in 54% women and asymptomatic urinary tract infections occurred in 10% of women. From these results, it was concluded that asymptomatic urinary tract infections was common in elderly women while only a small percentage of women have symptomatic urinary tract infections. In another study, an increased prevalence of urinary tract infection among women aged 18 – 30 years was found associated with sexual intercourse and pregnancy. It has been reported that complicated urinary tract infections were found most frequent among females aged between 40 – 59 years while in other age groups, uncomplicated urinary tract infections were most frequent (Essien, 2015). It has also been noted that the isolation frequency of *Escherichia coli* gradually decreases with increasing age and with both complicated and uncomplicated urinary tract infections. Urinary tract infections are generally asymptomatic among apparently healthy, sexually active young women. In contrast, urinary tract infections are more complicated among elderly individuals, infants and young children. UTIs in children younger than two

years have been associated with significant morbidity and long term medical consequences (Schonwald, *et al*, 2009). Dunn, D.T. (1992) the bladder instability in children with recurrent urinary tract infections. It was found that the most common disturbance of lower urinary tract functioning in the children with children with recurrent UTIs was instability of the dtrusor muscles which occurred more often in children with vesicoureteral reflux. The incidence of nosocomial urinary tract infections has been found to be higher in age group of 53.6± 20 years than the patients in age group 39.7±22.2 years. However, all the urinary tract infections are usually asymptomatic and develop in catheterized individuals. In contrast, Abdulrazak *et al*., (2015) observed that the risk of urinary tract infections decrease with age. Another predisposing factor, sexual imtercourse, is also a common cause of urinary tract infections among women because of sexual intercourse, bacteria in the vaginal area could be massaged into the urethra. This problem could be abated by urinating immediately after sexual intercourse. Women with multiple sexual partners may experience more frequent bladder infections (Palladino *et al*., 2012). In a study, independent risk factors for recurrent urinary tract infections in young women included recent one month intercourse frequency 'odds ratio' (OR), 5.8; 95% confidence interval (CI), 3.1 – 10.6 for 4 – 8 episodes, twelve month spermicide use (OR, 1.8; 95% CI, 1.1 – 2.9), while new sex partner change the past year (OR,1.9; 95% CI, 1.2 – 3.2). Several studies have shown that women who use diaphragms are more likely to develop urinary tract infections than women who use other forms of birth controls (Debalke *et al*, 2014). More recently, investigators have demonstrated that women whose life partners use condom with spermicidal foam also tend to have growth of *Escherichia coli* in the vagina (Bigwan *et al*., 2015). Women with urinary tract infections are 2.7 times more likely to be current users of intrauterine devices (IUCD)/ condoms (95% CI, 1.3 – 5.6) and 1.6 times more likely to be house wives by occupation (95% CI, 1.0

– 3.0) as compared to women who did not have urinary tract infections. UTI among IUCD/condom users may reflect existence of unhygienic conditions during application of procedure or spread of infection by the thread of IUCD. Urinary tract infections in these women may have serious consequences of developing renal damage (Palladino *et al*., 2012). Pregnancy also acts as a risk factor for urinary tract infections as it causes anatomic and hormonal changes which favours development. A history of current urinary tract infections, diabetes mellitus, analgesic nephropathy, hyperuricaemia and Fanconi's syndrome are predisposing factors for UTI during pregnancy (Fauci *et al*., 2011). Dietary habits seem to be an important risk factor for urinary tract infections recurrence in fertile women, and dietary guidance could be a first step towards prevention. The physiological changes associated with pregnancy are the relaxation of ureter under the effect of hormones and increased urinary output. The chemical composition of urine is also affected and results in increased urinary substances like glucose and amino acids, which may facilitate bacterial growth. Pregnant women with kidney infections have a greater chance of delivering their babies prematurely with low weight (Palladino *et al*., 2012). Sometimes it results in fetal and maternal morbidity (Murugesh, 2015). Recently, the relationship of maternal urinary tract infections in pregnancy with the rate of pre term birth was evaluated (Bigwan *et al*., 2015). It was found that 38,151 newborn infants, 5.7% had mothers with urinary tract infections with pregnancy. pregnant women also had somewhat shorter gestational age and higher proportion of preterm birth. This preterm inducing effect of maternal UTI was preventable by antimicrobial therapy. In this connection, Abdulrazak *et al*., (2015) evaluated the frequency of asymptomatic urinary tract infections in pregnant women, one thousand one hundred apparently healthy pregnant women were screened for significant bacteriuria. The prevalence of asymptomatic urinary tract infection was found to be 6.1%. However

asymptomatic urinary tract infections had no relationship with gestational age, parity, level of education, and body mass index. In another study, 500 pregnant women were screened for asymptomatic urinary tract infections in their first and second trimester. Out of them 8.4% were positive for culture. A control group of non pregnant women were also screened for asymptomatic urinary tract infections. The control group yielded 3% positive cultures. The frequency of urinary tract infections in pregnant women was observed, 30% of the women suffered from UTI. Of these infected women, 53.7% were in the age group of 15 – 24 years and 48.8% were in the third trimester. Primagravida had highest percent culture positivity of 66.6%. The incidence was higher (71.42%) in those less than 20 years of age. The incidence of prematurity was 75% and that of low birth weight is 50% in untreated patients (Bigwan *et al*., 2015). In a related study, it was observed that out of 1000 pregnant women, 42.6% complained of one or more symptom of urinary tract infections. The urine culture of symptomatic patients showed growth in only 8.69% cases. In another study, 542 women were screened for urinary tract infections. Out of them, 9.04% had UTI. Of these, 35% had asymptomatic while 65% had symptomatic urinary tract infections. By age, incidence of urinary tract infections in pregnancy was observed in age groups less than 25 years, 25 – 29 years and greater than 30 years as 5.26%, 10.36% and 12.43% respectively. Moreover, third trimester was associated with highest number of urinary tract infection cases (11.9%), followed by second trimester (7.5%) and third trimester (5.7%). Prevalence of asymptomatic urinary tract infection was 6.2% in pregnant women and 2.85% in non – pregnant women. During pregnancy, symptomatic and asymptomatic urinary tract infections can trigger the development of serious complications affecting both the mother and the fetus. Thus, proper screening and treatment of bacteriuria is necessary to prevent complications during pregnancy. All women should be screened for bacteriuria in the first trimester. Women with

history of recurrent urinary tract infections should have repeated screening for bacteriuria during pregnancy (Bigwan *et al*., 2015). Posts menopausal are also susceptible to urinary tract infections due to lack of estrogen which plays an important role in pathogenesis (Abdulrazak *et al*., 2015). The protective effect of estrogen replacement on ascending urinary tract infections is controversial. A study was designed using an experimental model of UTI. In that study, surgically menopausal mice were supplemented estrogen and the susceptibility of urinary tract infections was evaluated after experimental Escherichia coli infection. Surprisingly despite the hypotheses that estrogen would protect mice from infection, estrogen treatment significantly increased the susceptibility of mice to ascending urinary tract infections (Kanu, 2016). In post menopausal women, sexual activity, history of urinary tract infections, treated diabetes and urinary incontinence are associated with high risk of urinary tract infections. However, therapeutic role of estrogen remains uncertain. Another common source of infection is catheter. The use of vesicle catheter over five days is the cause of urinary tract infections. Bacteria on the outside of the catheter can climb up the device into the bladder and cause infection (Bigwan *et al*., 2015). UTI associated with an indwelling catheter is a representative type of biofilm infection occurring in the urinary tract. More than 90% of urinary tract infections in catheterized individuals are asymptomatic. These infections are rarely symptomatic and infrequently cause blood stream infections. Catheter associated urinary tract infections accounts for 40% of all nosocomial infections and is the most common source of gram negative bacteremia in hospitalized patients. The risk of bacteriuria is approximately 5% per day in 10 – 20% of hospitalized patients who receive an in dwelling catheter. With long term catheterization, bacteriuria is inevitable (Kanu, 2016). For example, the impact of urinary catheterization on 294 elderly (>65 years) in patients with community acquired UTIs was studied. Of 294

patients, 144 subjects had urinary catheterization. Patients with urinary catheterization were found with significantly more advanced age, female predominance, frequent admission in hospital, longer hospital stay and higher pathogen isolation after culture than subjects without urinary catheterization (Akadri *et al*, 2014). It is evident from literature that diabetic subjects are also at high risk of urinary tract infections (Olowe *et al*, 2013). The prevalence of urinary tract infections in diabetic patients were found to be higher when compared with non diabetic subjects (9% vs 0.78%) (Fenta, 2016). Symptomatic and asymptomatic urinary tract infections occur more frequently in patients with diabetes mellitus than in patients without diabetes mellitus (Auvert *et al*., 2005). Women with diabetes mellitus who require pharmacological treatment have approximately twice as high risk of cystitis as non – diabetic women. However, gestational diabetes was not associated with increased risk of urinary tract infections (Bigwan *et al*., 2015). Although asymptomatic bacteriuria is not associated with serious health outcomes in healthy persons, further research needs to be undertaken regarding the impact of asymptomatic bacteriuria in patients with diabetes (Abdulrazak *et al*., 2015). In another study, the characteristics associated with the development of urinary tract infections among diabetic patients were evaluated. It was found that 14% of women with type 1 diabetes developed asymptomatic urinary tract infections. The most important risk factors of those women were sexual intercourse during the week before the study (44% without vs 53% with sexual intercourse). 23% women with type 2 diabetes developed symptomatic urinary tract infections. The most important risk factor for those women was the presence of asymptomatic urinary tract infections at baseline (25% without vs. 42% with asymptomatic UTI). The risk of symptomatic and asymptomatic urinary tract infections among diabetic and non – diabetic women were recorded as 12.2% and 6.7% respectively. Whereas the incidence of

asymptomatic urinary tract infections was 6.7% for diabetic women and 3% for non – diabetic women. It was concluded that the increased urinary tract infection risk occurred mainly in diabetic women taking insulin and women with a longer diabetic duration (> 10 years) compared with non – diabetic women. The presence or absence of blood group determinants on the surface of uroepithelial cells may influence an individual's susceptibility to urinary tract infections (Abdulrazak *et al*., 2015). Blood groups AB or B, constitute independent risk factors in some but not all studies. Studies have shown a concordance between urinary tract infections and blood group A Rh positive. Infectious microorganisms interfere with specific molecules on epithelial cells. These specific molecules are antigens of the P and ABO system. Antigen structures on uroepithelial cells, for example, the glycolipids of the P – antigen serves as receptors for adhesion of microorganisms. The proportion of persons with B phenotype was 23% and P1 antigen was found in 76% of patients suffering from chronic urinary tract infections. In comparison with P1 negative individuals, P1 positive individuals had a longer disease history and more frequently suffered from symptomatic urinary tract infection as well as destructive renal changes. The use of calcium supplements also increases the risk of urinary tract infections. Since calcium ions significantly increase bacterial adherence to uroepithelial cells. Studies demonstrated in vitro that as the concentration of calcium was increased to levels higher than normally found in urine, there was a significant increase in bacterial adherence. It was also discovered that if diet was supplemented with calcium, there was an increase in the excretion of calcium in the urine and a corresponding increase in bacterial adherence when bacteria and uroepithelial cells were incubated in the urine. Any surgery on the urinary tract increases the chances of urinary tract infections. Urological complications after renal transplantation are also frequently associated with urinary tract infections (Abdulrazak *et al*., 2015). Urinary tract infections are

also the most common bacterial infections occurring in renal transplant recipients, particularly anatomic abnormalities of the native or transplanted kidneys and possible rejection and immunesuppresion. The major risk factors for urinary tract infections in renal transplant recipients include indwelling bladder catheters, trauma to the kidney and ureter during surgery (Bigwan *et al*., 2015). Steroids or cytotoxic drugs, as given to renal transplant recepients, greatly increase the chances of recurrent urinary tract infections and infections of the kidney in the first few months of post transplant (Fenta, 2016). In a study, it was observed that 13.3% episodes of urinary tract infections occurred in the first to sixth month and 72% after the sixth month of transplantation. The most commonly isolated organism was *Escherichia coli* (Kanu, *et al.,* 2016). Frequent meat consumption appeared to be the predisposing factor for urinary tract infections. UTI were found significantly more common among the people consuming meat more frequently than once a week but not daily (Debalke *et al*, 2014). Certain diseases most certainly are predisposing factors to urinary tract infections. HIV patients are susceptible to acquiring urinary tract infections. Schonwald *et al*., (1999) performed a study to determine the relationship between urinary tract infections and AIDS. The analysis showed that patients with HIV had UTI more frequently than those who were HIV negative (control patients). Besides the difference in the frequency, it was also observed that *Enterococci* were the frequent isolates in patients with HIV disease, whereas *Escherichia coli* were most frequently isolated organism from control subjects. Cancer patients are also at high risk of urinary tract infections (Abdulrazak *et al*., 2015). In related studies, the prevalence of urinary tract infections in children with cancer was studied. The prevalence of urinary tract infections was 8.1%. Out of 15, only 5 patients were symptomatic, the remaining three were asymptomatic. *Escherichia coli* and *Klebsiella* species were responsible for 93.4% of the infections.

2.15 HOST FACTORS IN THE PREVALENCE OF UTI IN HIV INFECTION

Urinary tract infections, both symptomatic and asymptomatic, are serious public healthcare problems that ultimately decrease the quality of life of HIV positive patients, specific groups of HIV positive individuals are at increased risk of urinary tract infections. Studies have indicated that HIV infection is associated with a higher risk of lower urinary tract symptoms in men, regardless of age and other risk factors. The chances of severe urinary tract problems are greatest in HIV – positive men with a history of AIDS (Bigwan *et al*., 2015). Urinary tract infections are common in aging men. Possible risk factors for lower urinary tract problems in HIV – positive men include chronic urinary tract infections, use of highly active retroviral therapy (HAART), opportunistic infections and direct effects of HIV on the nervous and excretory systems. Although evidence suggests HIV is linked with lower urinary tract symptoms and bladder function problems, previous studies have been small and took place before the advent of HAART. HIV positive men with were twice as likely to report severe urinary tract symptoms as men without HIV, even after accounting for other risk factors. HIV – positive men with a history of AIDS – defining illness or CD_4+ counts less than 200 cells per micro liter are 2.5 times more likely to report severe urinary tract infections (Murugesh, 2015). Men with a history of AIDS – defining illness or low CD_4+ counts also have an increased risk of moderate to severe lower urinary tract symptoms than HIV – positive men with no history of AIDS – defining illnesses (Debalke *et al*, 2014). Risk factors for moderate urinary tract symptoms include older age, depression, diabetes, and history of urinary tract infections, prostratitis, or gonorrhea. Risk for severe symptoms includes older age, depression, high blood cholesterol/triglyceride levels.

2.16 ASYMPTOMATIC BACTERIURIA

Asymptomatic bacteriuria or asymptomatic urinary infection is the isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen obtained from a person without symptoms or signs referable to urinary infection (Murugesh, 2015). Asymptomatic bacteriuria is a microbiological diagnosis wherein the usual quantitative definition is more than or equal to 10^5 CFU/ml in 2 consecutive urine specimens. In human immunodeficiency virus (HIV) infection, co-morbidity with other organisms is common. Some studies have indicated that the risk of bacteriuria and urinary tract infections (UTI) may be increased in HIV-infected patients and is inversely related to CD_4+ lymphocyte counts (Banu *et al*, 2013)

Asymptomatic bacteriuria refers to persistent, actively multiplying bacteria within the urinary tract without symptoms of urinary tract infections. Significant bacteriuria is generally defined as the presence of at least 100,000 bacterial colonies of a single pathogen per milliliter (ml) of freshly voided urine collected by the mid-stream clean-catch technique (Akadri *et al*., 2014). Asymptomatic bacteriuria (ASB), the presence of a significant quantity of bacteria, of $\geq 10^5$ colony-forming units per milliliter (CFUs/ml), in the urine of a patient without symptoms or signs of a UTI, has been said to be associated with increased risk of symptomatic urinary tract infection. With the number of people living with HIV/AIDS (PLWHA) in Nigeria, there is no data regarding the occurrence of asymptomatic bacteriuria among this group in our country. Since NACO guidelines advocate the use of cotrimoxazole prophylaxis for all HIV positive cases, it is difficult for the physicians to treat urinary symptoms (Olowe *et al*, 2013).

2.17 ETIOLOGY: Traditional and emerging pathogens

The microbial etiology of urinary tract infections has been regarded as well as established and reasonably consistent (Bigwan *et al*., 2015). Urinary tract infections are caused by various microorganisms such as bacteria, fungi, parasites. Recent studies revealed a broad range of bacteria – causing UTIs in HIV infected patients, including common uropathogens like *Escherichia coli, Proteus spp*., and *Klebsiella spp.* Nosocomial organisms such as *Pseudomonas aeruginosa,Streptococcus spp., Staphylococcus aureus* and unusual microorganisms including *Candida spp. Salmonella spp., Acinetobacter spp.,* and *Cytomegalovirus* (Banu *et al*, 2013). More than 90% of UTIs are due to enteric gram negative organisms of which *Escherichia coli*, *Enterobacter*, *Proteus* and *Klebsiella* are most commonly implicated. Murugesh, 2015 stated that *Escherichia coli* remains the predominant uropathogen (80%) isolated in acute community – acquired uncomplicated infections, followed by *Staphylococcus saprophyticus* (10% - 15%). Klebsiella, Enterobacter, Enterococci and Proteus species infrequently causes uncomplicated cystitis and pyelonephritis. The pathogens traditionally associated with urinary tract infections are changing many of their features, particularly because of antimicrobial resistance. The etiology of urinary tract infections is also affected by underlying host factors that complicate UTI, such as age, diabetes, spinal cord injuries, or catheterization. Consequently, complicated UTI has a more diverse etiology than uncomplicated UTI, and organisms that rarely cause disease in healthy patients can cause significant disease in hosts with anatomic, metabolic or immunologic underlying disease. The majority of community acquired symptomatic UTIs in elderly women are caused by *Escherichia coli*. However, gram positive organisms are common and poly microbial infections account for up to 1 in 3 infections in the elderly. In

comparison, the most organisms isolated in children with uncomplicated UTI are *Enterobacteriaceae.* Etiologic pathogens associated with UTI among patients with diabetes include Klebsiella spp., group B Streptococci, Enterococcus spp., as well as E. coli. Patients with spinal cord injuries commonly have E. coli infections. Other common uropathogens include Pseudomonas and *Proteus mirabilis*. Almost all the causative organisms of UTIs originate from faecal materials or the periurethral environment (Grulich *et al*., 1999). UTI s also account for a large proportion of antibacterial drug consumption (Schönwald, 1999). Due to the fact that majority of the treatments are done factually, it is necessary to have a good knowledge of the causative organisms as well as their epidemiological characteristics.

2.18 EPIDEMIOLOGY

The magnitude of the epidemiology of urinary tract infections can be considered from two perspectives: catheter – associated (nosocomial) and non – catheter associated (community – acquired) infections. In both groups urinary tract infections can both be symptomatic or asymptomatic. Community – acquired urinary tract infections results in more hospital visits. It is quite difficult to accurately access the rate of occurrence of urinary tract infections especially in Nigeria. This is because they are not reportable diseases in most parts of the world. Women are significantly more likely to experience urinary tract infections than men. Early 1 in 3 women would have had at least one episode of UTI requiring antimicrobial therapy by the age of 24 years. Almost half of all women would experience one UTI in their lifetime. Specific subpopulations at increased risk of UTI include infants, pregnant women, the elderly, catheterized patients, diabetic

patients, spinal cord injury patients, patients with underlying urologic abnormalities and patients with acquired immuno deficiency syndrome. The risk of urinary tract infections increases with increasing duration of catheterization. In the non pregnant female adult, acute uncomplicated UTI is believed to be a benign illness with no long – term medical consequence. However, UTI increases the risk of pyelonephritis, premature delivery and foetal mortality among pregnant women. Urinary tract infections are also associated with impaired renal function and end stage renal disease among paediatric patients.

2.19 PATHOGENESIS

Urinary tract infections usually spread to the urinary tract through an ascending route of fecal flora, from the fecal reservoir through the urethra into the bladder, particularly in patients with intermittent or in dwelling catheter. In women, colonization of the mucosa of the vaginal introitus is an essential step in the pathogenesis of urinary tract infections. Once the introitus is colonized, sexual intercourse or urethral manipulation can force bacteria into the female bladder. The ascending route of bacterial infection has been proved in animal experiments after unilateral ureteral ligation. Only the unligated kidney develops pyelonephritis once bacterial cystitis ensues (Bigwan *et al*., 2015). Hematogenous dissemination secondary to organisms in the blood stream is another possible route to the development of urinary tract infections specifically pyelonephritis. Experimental pyelonephritis can be produced by intravenous infection of several species of bacteria and *Candida*. However, the production of pyelonephritis via this method with gram negative bacilli rarely occurs by the hematogenous route. Direct extension from adjacent organs via the lymphatic system, as in the case of

retroperitoneal abscesses or severe bowel obstruction has been proposed as a third mechanism for urinary tract infection pathogenesis. However, evidence of this pathogenesis is unimpressive and consists of demonstrating lymphatic connections between ureters and kidneys in animals (Murugesh, 2015). Furthermore, increased pressure in the bladder can cause lymphatic flow to be directed towards the kidneys.

2.110 DIAGNOSIS

The clinical diagnosis of UTI is usually based on a combination of symptoms, physical and radiographic findings, and laboratory results. Diagnostic methods vary markedly and depend on presentation, clinical suspicion, medical history, and local practice patterns. Children pose a unique challenge in the diagnosis of UTI, because they often are unable to provide an accurate history or description of symptoms. Obtaining adequate specimens may also be difficult, and clinical signs such as fever and leukocytosis may be unreliable in the very young. A lower tract infection is typically suspected in the presence of dysuria, urgency, frequency, and, less commonly, suprapubic pain. Upper tract involvement is typically heralded by fever, flank pain, nausea, vomiting, and lethargy. In the young child, there can be significant overlap in the clinical presentations of upper and lower tract infections. Symptoms may not be verbalized, and the diaper may conceal the voiding pattern. Fever is frequently the presenting sign, although lethargy may be the sole indicator of significant infection in infants. Parents' perception of an odor is an unreliable sign of infection. Hence, the clinician must have a high index of suspicion to make an accurate diagnosis of UTI. Diagnosis is further hindered by the difficulty of obtaining adequate samples for laboratory testing. Urinalysis, the standard initial

screening test for UTI, ideally requires a midstream, clean catch of urine, but this may be impossible in the very young. Alternatively, urine can be obtained by sterile catheterization or suprapubic needle aspiration. However, both of these techniques are invasive and frequently met with parental disapproval. Urine may be obtained by the adherence of a sterile collection bag to the perineum, but this method has a high rate of contamination, limiting its reliability. Once obtained, urine is examined with a reagent dipstick for the presence of nitrates and leukocyte esterase. A finding that the urine is crystal clear to visual inspection has a 97% negative predictive value for UTI. The urine can also be microscopically examined after gram- stain, as well as cultured for the presence of bacteria or fungi. Other adjunctive laboratory tests include serum white blood cell count and C-reactive protein level. Imaging studies can assist in diagnosis, but they play a more prominent role in elucidating underlying co morbid conditions that may increase the risk or morbidity of infection. Ultrasound, the most common imaging study employed in cases of pediatric UTI, is used to evaluate for the presence of obstruction or stones, which can greatly increase the severity and sequelae of infection. The ultrasonographic appearance of the kidney can also be altered by the presence of acute infection. Ultrasound can assist in localizing the site of infection in the presence of renal abscess, parenchymal edema (lobar nephronia), or pyonephrosis. Despite the many advantages of ultrasound (it has no ionizing radiation and is non- invasive, well-tolerated, relatively low-cost, and readily available), its usefulness for identifying acute UTI has recently been questioned, given its relatively low yield in an era of widespread prenatal screening. Indeed, significant controversy has arisen over the timing of imaging studies and their implications for therapy recommendations in children with UTIs. The nuclear renal scan with dimercaptosuccinic acid (DMSA) has been proposed as the most sensitive means for documenting renal involvement in UTI. It has been reported to

be the best method for confirming acute pyelonephritis and later for assessing the presence of scarring. Many advocate basing further evaluation and follow-up care on the results of the DMSA scan. Computed tomography (CT) can also be useful for identifying anatomic anomalies, stones, and intrarenal abscess, as well as for documenting renal involvement in UTIs. CT is often used to exclude alternate diagnoses, such as appendicitis, in the presence of fever and abdominal pain or hematuria. Intravenous pyelography (IVP) is rarely used in the evaluation of pediatric UTI, particularly in young children, in whom renal visualization is limited by poor renal concentrating ability and increased small bowel air. Voiding cystourethrography (VCUG) has no role in the diagnosis of acute UTI, although it is nearly universally recommended for identifying vesicoureteral reflux or other anatomic abnormalities that may contribute to future infection risk.

2.111 DISTRIBUTION AND STATISTICS

Urinary tract infections are some of the most common bacterial infections, affecting 150 million people each year, worldwide (Olowe *et al*, 2013). In Nigeria, limited information is available on the prevalence and prevalence of urinary tract infections in people living with HIV/AIDS. There is, however, limited data especially in this environment, on the occurrence of ASB in the general population of HIV-positive individuals. Nigeria has a high burden of HIV infection with the 2013 prevalence estimate as 3.2% (Akadri, 2014) and considering its large population size, this constitutes a significant population of individuals who are at risk of UTI and other complications following ASB. The prevalence of asymptomatic bacteriuria in HIV-positive individuals varies depending on the population studied. De Pinho *et al*., for example, reported a prevalence of 3% in

asymptomatic HIV-positive individuals and 13% in those with AIDS. Although the current recommendation is not to screen for or treat ASB in this population, many reports have indicated an increased risk of bacteriuria and UTI in HIV. Catheter – associated UTI is the most common nosocomial infection accounting for less than one million cases in hospitals and nursing homes worldwide (Olowe *et al*, 2013).

2.112 ECONOMIC IMPORTANCE

Results of a urine culture are often interpreted in conjunction with the results of a urinalysis and with regard to how the sample was collected and whether symptoms are present. Since some urine samples have the potential to be contaminated with normal flora from the skin, care must be taken with interpreting some culture results. Typically, the presence of a single type of bacteria growing at high colony counts is considered a positive urine culture. For clean catch samples that have been properly collected, cultures with greater than 100,000 colony forming units (CFU)/mL of one type of bacteria usually indicate infection. In some cases, however, there may not be a significantly high number of bacteria even though an infection is present. Sometimes lower numbers (1,000 up to 100,000 CFU/mL) may indicate infection, especially if symptoms are present. Likewise, for samples collected using a technique that minimizes contamination, such as a sample collected with a catheter, results of 1,000 to 100,000 CFU/mL may be considered significant. A culture that is reported as "no growth in 24 or 48 hours" usually indicates that there is no infection. If the symptoms persist, however, a urine culture may be repeated on another sample to look for the presence of bacteria at lower colony counts or other microorganisms that may cause these symptoms. The presence of white blood cells and low numbers of microorganisms in the urine of a

symptomatic person is a condition known as acute urethral syndrome. If a culture shows growth of several different types of bacteria, then it is likely that the growth is due to contamination. This is especially true in voided urine samples if the organisms present include *Lactobacillus* and/or other common nonpathogenic vaginal bacteria in women. If the symptoms persist, the doctor may request a repeat culture on a sample that is more carefully collected. However, if one type of bacteria is present in significantly higher colony counts than the others, for example, 100,000 CFUs/mL versus 1,000 CFUs/mL, then additional testing may be done to identify the predominant bacteria. If a culture is positive, susceptibility testing is typically performed to guide antimicrobial treatment. Any bacterial infection may be serious and can spread to other areas of the body if not treated. Pain is often the first indicator of an infection. Prompt treatment, usually with antibiotics, will help to alleviate the pain.

2.2 Opportunistic infections (OIs)

People with advanced HIV infection are vulnerable to infections or malignancies that are called "opportunistic" because they take advantage of the opportunity offered by a weakened immune system. People with healthy immune systems can be exposed to certain viruses, bacteria, or parasites and have no reaction to them—but people living with HIV/AIDS can face serious health threats from what are known as "*opportunistic" infections* (OIs). These infections are called "opportunistic" because they take advantage of your weakened immune system, and they can cause devastating illnesses. OIs are signs of a declining immune system. Most life-threatening OIs occur when your CD_4+ count is below 200 cells/mm^3. OIs are the most common cause of death for people with HIV/AIDS.

The CDC developed a list of more than 20 OIs that are considered *AIDS-defining conditions.* Various treatments and prophylaxis—some simple and low-cost, others highly complex and expensive—exist to counter the most common opportunistic diseases, but delivery systems and funding are insufficient in many parts of the world to ensure their universal use. Opportunistic diseases in a person with HIV are the products of two things: the person's lack of immune defenses caused by the virus, and the presence of microbes and other pathogens in our everyday environment. A partial list of the world's most common opportunistic diseases and diseases includes:

• Bacterial diseases such as tuberculosis (TB, caused by *Mycobacterium tuberculosis*), *Mycobacterium avium* complex disease (MAC), bacterial pneumonia and septicemia ("blood poisoning")

• Protozoan diseases such as *Pneumocystis carinii* Pneumonia (PCP), Toxoplasmosis, Microsporidiosis, Cryptosporidiosis, Isosporiasis and Leishmaniasis.

• Fungal diseases such as Candidiasis, Cryptococcosis (Cryptococcal

Meningitis (CRM)) and Penicilliosis.

• Viral diseases such as those caused by Cytomegalovirus (CMV), Herpes Simplex and Herpes Zoster virus.

• HIV-associated malignancies such as Kaposi Sarcoma, Lymphoma and Squamous Cell Carcinoma.

2.21 DEFINITION

Opportunistic infections are caused by pathogens (bacteria, viruses, fungi or protozoa) that take advantage of an opportunity not normally available, such as a host with a weakened immune system, an altered microbiota (such as disrupted gastrointestinal flora), or breached integumentary barriers. Many of these pathogens do not cause disease in a healthy individual that has a normal immune system. However, a compromised immune system, a penetrating injury, or a lack of competition from normal commensals presents an opportunity for the pathogen to infect. Since opportunistic infections can cause severe disease, much emphasis is placed on measures to prevent infection. Such strategy usually includes restoration of the immune system as soon as possible, avoiding exposures to infectious agents, and using antimicrobial agents directed against specific infections. In patients with HIV infection, starting antiretroviral therapy is especially important for restoration of the immune system and reduces the prevalence of opportunistic infections. In patients undergoing chemotherapy, completion of and recovery from treatment is the primary method for immune system restoration.

2.22 PRIMARY PROPHYLAXIS FOR OPPORTUNISTIC INFECTIONS

Before the advent of antiretroviral therapy, the use of prophylaxis to decrease the risk of acquiring opportunistic infections was the only intervention available to delay the onset of life-threatening infections. With the development of antiretroviral therapy in the 1990s, the prevalence of many opportunistic infections has been greatly reduced, and the use of prophylaxis has decreased correspondingly (Palella *et al*., 2003). Nevertheless, prophylaxis for opportunistic infections remains necessary in patients who lack access to antiretroviral therapy,

in extremely immunosuppressed patients until the therapy takes effect, in patients who do not wish to or who cannot take antiretroviral therapy, in patients for whom such therapy fails, and in the small group of patients who are unable to recover sufficient CD_4+ cells despite good inhibition of viral replication (Berenguer *et al*., 2004).

2.23 SECONDARY PROPHYLAXIS/TREATMENTS OF OPPORTUNISTIC INFECTIONS

Even as the availability of antiretroviral therapy increases in many developing countries, appropriate diagnosis and management of life-threatening opportunistic infections, including HIV-associated cancers, remain the most important aspects of the care of patients with HIV disease. Opportunistic infections usually begin five to seven years after infection and occur progressively as uncontrolled HIV replication destroys the immune system. Opportunistic infections are typically caused by organisms that exist in the environment of the body (on the skin, in the lungs and gastrointestinal system) and remain latent until HIV has impaired the immune system.

2.24 MANAGEMENT OF OPPORTUNISTIC INFECTIONS

The three components of effective management of opportunistic infections are diagnosis, treatment, and secondary prophylaxis. As immune function continues to deteriorate, secondary prophylaxis is required to prevent recurrence of the treated infection. Some of the most common infections, such as PCP, can be diagnosed with a reasonable degree of confidence by clinical history and treated empirically (Kaplan *et al*., 2001). Less frequently occurring infections often require sophisticated diagnostic equipment and skilled clinicians to confirm a diagnosis

from a wide range of pathogenic possibilities before starting complex and expensive treatment. For example, toxoplasmosis can be accurately diagnosed only by a lumbar puncture and CT brain scan (and in some cases an MRI), and cryptosporidium diagnosis requires specialized laboratory techniques. The full spectrum of options for treating opportunistic infections in developing countries has not been systematically evaluated for cost-effectiveness. Because of the effect of anti-retroviral therapy on both the efficacy of treatment of individual infections and on life expectancy (and therefore on potential DALYs gained from treating a life-threatening infection), the limited economic evaluations conducted are already out of date. In particular, chronic infections such as *Mycobacterium avium* complex and cytomegalovirus may be more effectively treated over the medium term by reversing immunosuppression with antiretroviral therapy than by directly treating the infectious agent. Other treatment regimens for opportunistic infections that was marginally cost-effective before antiretroviral therapy may now become substantially more cost-effective if the patient can begin the therapy following treatment of the infection, thereby extending life expectancy

2.25 ROLE OF ANTIRETROVIRAL THERAPY IN MANAGING OPPORTUNISTIC INFECTIONS

Antiretroviral therapy is effective in reducing viral load and partially enabling immune restoration, thereby preventing the onset and recurrence of opportunistic infections. If taken strictly according to directions, antiretroviral therapy can induce a sustained recovery of CD_4+ cell reactivity against opportunistic pathogens in severely immunosuppressed patients. The effectiveness of antiretroviral therapy is determined by its ability to rapidly reduce viral load and to sustain low values of

viral activity. This viral activity is what has an independent effect on increasing or decreasing susceptibility to opportunistic infections (Kaplan *et al*., 2001). Initiating antiretroviral therapy can also have detrimental effects by causing complications from latent or undiagnosed opportunistic infections, especially in resource-poor settings. One of the challenges in initiating antiretroviral therapy in resource-limited settings is that patients tend to present late in their illness, usually when they have an opportunistic infection that prompts them to seek medical care or in the case of countries with lax pharmaceutical policy, when they buy anti-retroviral therapy from a private pharmacy. It is well documented that initiating antiretroviral therapy in severely immunosuppressed patients can result in illnesses associated with reconstitution of the immune system. These illnesses can occur with all presenting opportunistic infections and may be more serious than the infection itself. The major problem with care of patients in this situation is that they may believe the illness is a side effect of their antiretroviral therapy and refrain from medicating. Training clinicians to recognize and treat immune reconstitution disease is therefore essential.

2.26 PREVALENCE OF AIDS – DEFINING OPPORTUNISTIC INFECTIONS

Opportunistic infections remain the single main cause of ill health and death among HIV/AIDS patients in resource poor countries (Hira *et al*., 2003). Opportunistic infections lower the quality of life of HIV infected individuals, speeds up the rate of progression to fully blown AIDS, reduce patient's response to antiretroviral treatment especially when co infected with tuberculosis, increases stigma and limits one's ability to work and are usually associated with high medical care costs. OI s have therefore greatly contributed to poverty among those

affected and infected by HIV/AIDS hence an impediment to the attainment of the millennium development goals (MDGs) on health and poverty eradication in resource poor countries. Although the natural history of AIDS tends to be similar in most patients, the patterns of opportunistic infections that largely define the symptomatic and clinical manifestation of AIDS tend to vary in different regions of the world (Grulich *et al*., 1999). Thus, while HIV patients in developed countries rarely suffer from bacterial and protozoan infections, they are a major cause of morbidity and mortality in resource poor countries. However, with increasing availability of highly active antiretroviral therapy (HAART) and other highly potent prophylactic and therapeutic drugs to eligible HIV patients. The risk of suffering from an opportunistic infection has been substantially reduced. However, HIV positive patients in sub Saharan Africa have a problem of late enrolment HAART and adherence problems while on antiretroviral drug usage. This is sometimes as a result of drug side effects thereby increasing the risks of opportunistic infections, morbidity and death (Banu *et al*, 2013). HIV positive patients in resource poor settings also suffer because of the high risk of exposure to potential pathogens which are endemic in these settings and most patients suffer from nutritional deficiency resulting from poor prognostic outcomes while on antiretroviral therapy (Palella *et al*., 2003). Sub Sahara Africa where the access to HAART is still limited cotrimoxazole prophylaxis still remains the most viable alternative and has greatly increased the chances of survival for HIV – infected individuals who are eligible but cannot access HAART. UNAIDS recommends cotrimoxazole prophylaxis for life to all persons living with HIV/AIDS regardless of their immunological status. The unique pathogenesis of the HIV virus causing a decrease in the CD_4+ cells, signals the emergence of opportunistic infections

2.27 PREVALENCE OF AIDS – DEFINING OPPORTUNISTIC INFECTIONS IN NIGERIA

The hallmark of HIV infection is immunosuppression which predisposes to opportunistic infections (OIs) and malignancies. Opportunistic infections constitute a major cause of morbidity and mortality in PLHIV. This is even more critical in sub-Saharan Africa (SSA) where the standard of living is generally poor and access to ART is still inadequate. A striking feature of the reported clinical spectra of OIs in HIV/AIDS has been the contrasting findings from divergent socio-economic settings. In developed regions such as North America, Europe, and Australia, *Pneumocystis carinii* pneumonia (PCP), Kaposi's sarcoma (KS), oesophageal candidiasis, cytomegalovirus (CMV)- related disease and disseminated *Mycobacterium avium* complex (MAC) infection were the prevalent OIs in PLHIV in the pre-ART era (Anyamene, 2006). In developing regions such as SSA and South East Asia, where an estimated 90% of PLHIV reside, the predominant HIV-associated OIs in the pre-ART era were Tuberculosis (TB), Candidiasis, Infective diarrhea, meningitis, dermatitis and recurrent *Herpes simplex* infection.

Since the introduction of Highly Active Anti-retroviral Therapy (HAART), a significant decline in OIs and AIDS progression has been observed. However, significant differences still exist in the burden of OIs between high income and resource-limited settings. Most of the evidence for decline in OIs has come from high-income settings with relatively less burden of OIs in the pre-HAART era, early and widespread access to ART and sophisticated diagnostic tools (Iroezindu, *et al*., 2013). According to Iroezindu et.al, 2013, their research carried out in Nigeria, as a resource limited country setting; The most frequent conditions were *Candidiasis* (8.6%); TB (7.7%); Dermatitis (5.6%); Chronic diarrhea, (1.5%); and

Sepsis (1.5%). Bacterial pneumonia (0.9%), *Cryptococcal meningitis*, *Herpes zoster*, genital herpes, and genital warts (0.6%) each; *Kaposi's sarcoma* (0.3%). In relative terms, *Candidiasis*, TB and dermatitis, constituted 38.2%, 34.2%, and 25% of the OIs respectively. According to Anyamene, TB accounted for 64%, followed by bacterial pneumonia (33%), bacteraemia (29%), UTI (28%), and typhoid fever (28%). There were a total of 96 opportunistic infections diagnosed in the 76 patients. Fifty five (16.2%) patients had single OI, 20 (5.9%) had dual OIs while 1 (0.3%) had triple OIs. The most frequent conditions were candidiasis, 29 (8.6%); TB, 26 (7.7%); dermatitis 19 (5.6%); chronic diarrhea, 5 (1.5%); and sepsis 5 (1.5%). Bacterial pneumonia was diagnosed in 3 (0.9%) patients, cryptococcal meningitis, herpes zoster, genital herpes, and genital warts were each diagnosed in 2 (0.6%) patients while only 1 (0.3%) patient had Kaposi's sarcoma. In relative terms, candidiasis, TB and dermatitis, constituted 38.2%, 34.2%, and 25% of the OIs respectively.

2.28 AIDS – DEFINING CONDITIONS

AIDS – defining clinical conditions (AIDS – defining illnesses or AIDS-defining diseases) is the list of diseases published by the Centers for Disease Control and Prevention (CDC) that are associated with AIDS, and used worldwide as a guideline for AIDS diagnosis. According to the CDC definition, a patient has AIDS if he or she is infected with HIV and has either: a CD_4+ T-cell count below 200 cells/μL, a CD_4+ T-cell percentage of total lymphocytes of less than 15%, or one of the defining illnesses. A patient presenting one of the above conditions but with laboratory evidence against HIV infection is not normally considered to have AIDS, but an AIDS diagnosis may be given if the patient has had *Pneumocystis jiroveci* pneumonia, and has either: Not undergone high-dose corticoid therapy or

other immunosuppressive/cytotoxic therapy in the three months before the onset of the indicator disease; Been diagnosed with Hodgkin's disease, Non-Hodgkin's lymphoma, lymphocytic leukemia, multiple myeloma, or any cancer of lymphoreticular or histiocytic tissue, or angioimmunoblastic lymphoadenopathy; Or been diagnosed with a genetic immunodeficiency syndrome atypical of HIV infection, such as one involving hypogamma globulinemia . Also, patient that has one of more of the illnesses listed below:

- Candidiasis of bronchi, esophagus, trachea or lungs
- Cervical cancer that is invasive
- Coccidioidomycosis that has spread
- Cryptococcosis that is affecting the body outside the lungs
- Cryptosporidiosis affecting the intestines and lasting more than a month
- Cytomegalovirus disease outside of the liver, spleen or lymph nodes
- Cytomegalovirus retinitis that occurs with vision loss
- Encephalopathy that is HIV-related
- Herpes simplex including ulcers lasting more than a month or bronchitis, pneumonitis or esophagitis
- Histoplasmosis that has spread
- Isosporiasis affecting the intestines and lasting more than a month
- Kaposi's sarcoma
- Lymphoma that is Burkitt type, immunoblastic or that is primary and affects the brain or central nervous system
- Mycobacterium avium complex or disease caused by M. kansasii
- Mycobacterium tuberculosis in or outside the lungs
- Other species of mycobacterium that has spread
- Pneumocystis jiroveci, formerly called carinii, pneumonia

- Pneumonia that is recurrent
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia that is recurrent
- Toxoplasmosis of the brain, also called encephalitis
- Wasting syndrome caused by HIV infection
- Symptoms also may include anxiety, dementia, depression and insomnia.

Encyclopedia of Life Sciences reported clinical spectrum of AIDS-defining illnesses in countries of North America, Europe, sub-Saharan Africa and the Asia–Pacific Region (Dore *et al*., 1997). These clinical spectra are derived predominantly from hospital-based clinic sites in each country, although some are based on routine AIDS surveillance data. The most obvious distinguishing feature within this spectrum is the division between industrialized and developing countries, with PCP (*Pneumocystis jiroveci* pneumonia,) the major AIDS-defining illness in the United States, Europe and Australia, in contrast to tuberculosis as the major AIDS-defining illness in Thailand and the Ivory Coast and in clinical series from several other developing countries in Asia and sub-Saharan Africa (Hira *et al*., 2003). Fungal infections, in particular Oral–esophageal *Candidiasis* and Cryptococcal disease, are relatively common in both industrialized and developing settings.

Tuberculosis

With more than 90% of global HIV infection occurring in the developing world, and a prevalence of tuberculosis of 30–50% in the AIDS clinical series of many developing countries, tuberculosis represents the most common AIDS-defining illness on a global scale. The impact of the HIV epidemic on the prevalence of tuberculosis has been clearly demonstrated in both sub-Saharan Africa and Asia,

where several countries have experienced a more than 2- fold increase in cases. In the United States and Europe, although tuberculosis occurs at a lower rate than in developing country settings among people with HIV infection, some groups are at particular risk. These include injecting drug users, the homeless, and people born in countries with high background rates of tuberculosis. The clinical features of AIDS-related tuberculosis differ somewhat from those of tuberculosis occurring among non-HIV-infected persons. These include a younger age distribution, a higher proportion of extra pulmonary tuberculosis, less cavitatory pulmonary disease, a higher proportion of smear-negative pulmonary disease, and a substantially greater 12-month mortality rate. A large proportion of HIV wasting (previously commonly known as 'slims' disease) in sub-Saharan African countries is now recognized as due to disseminated tuberculosis.

Pneumocystis Carinii Pneumonia

Although previously described in non-HIV-infected immunocompromised patients, PCP became a major opportunistic infection with the emergence of AIDS in the 1980s (Encyclopedia of Life Sciences, 2001). Since the initial descriptions of cases of PCP among homosexual men in San Francisco and New York, this almost exclusively pulmonary infection has remained the most common AIDS-defining illness in industrialized countries. The increasing use of co-trimoxazole and other agents as prophylaxis against PCP has led to a significant decline in the risk of PCP among people with HIV infection in the 1990s (Dore *et al*., 1997), but in those with undiagnosed HIV infection, in particular, PCP persists as a major cause of AIDS-related morbidity and mortality. The lower rate of reported PCP in clinical series from sub-Saharan Africa and Asia may reflect a lack of diagnostic

capability. However, even in autopsy series from sub-Saharan Africa, with specific staining for detection of P. carinii, the prevalence of PCP was considerably lower than in AIDS clinical series from industrialized countries (Lucas *et al*., 1993).

Fungal infections

Cryptococcosis appears to be an important AIDS-related illness in both industrialized and developing countries. In the United States, Europe and Australia, *Cryptococcosis*, the vast majority of which presents as cryptococcal meningitis, represents 3–5% of initial AIDS-defining illness, with a further 5% developing the disease subsequent to an AIDS diagnosis. *Cryptococcosis* appears to be particularly common in Southeast Asia, representing approximately 20% of initial AIDS-defining illnesses in Thailand. In people with HIV infection, *Cryptococcosis* is almost exclusively due to infection with Cryptococcus neoformans, which has been isolated from soil and pigeon excrement in various parts of the world. The other major strain, *C. neoformans* var. *gattii*, is seen only rarely among people with HIV infection, even in areas where it is commonly isolated from immunocompetent patients. Oropharyngeal candidiasis, a relatively early clinical manifestation of HIV infection, develops in the majority of people with HIV infection, and when present predicts more rapid progression to AIDS. Oesophageal candidiasis, an AIDS-defining illness, is associated with more severe immunodeficiency and, like *Cryptococcosis*, appears to be relatively common within industrialized and developing countries. Although a diagnosis can be made on presumptive grounds in a person with oral candidiasis and odonyphagia, a definitive diagnosis requires endoscopy. This may explain the relatively low rate of reported oesophageal candidiasis in some clinical series from developing countries. Disseminated infection with the fungus *Penicillium marneffei* (penicilliosis) has been reported from southern China, Thailand and other areas of Southeast Asia.

Although occasionally reported among people without HIV infection, penicilliosis has both a more rapid onset and more severe clinical picture when associated with HIV infection. The substantial geographical variation of this fungal infection is evidenced by the contrasting prevalence, even within Thailand. In the northern region of Thailand it is one of the major AIDS-defining illnesses; however, in Bangkok and other areas of Thailand it is relatively uncommon. Other AIDS-related fungal infections include *Aspergillosis, Histoplasmosis* and *Coccidioidomycosis.* Disseminated histoplasmosis is common among people with HIV infection in South America and areas of the United States. Thus, fungal infections constitute a considerable proportion of HIV-related morbidity in both industrialized and developing countries (Encyclopedia of Life Sciences, 2001).

Diseases of very advanced immune deficiency

Cytomegalovirus (CMV) disease and Mycobacterium avium complex (MAC) infection occur when immune deficiency is very advanced, with the majority of cases presenting subsequent to AIDS diagnosis and associated with a CD_4+ cell count of less than 50/mL (Dore *et al*., 1997). The most common presentation of CMV disease in people with HIV infection is retinitis, with other sites including gastrointestinal (oesophagitis, gastritis, colitis) and neurological (encephalitis, polyradiculopathy) involvement. MAC generally presents as a disseminated infection with diarrhoea, fevers and weight loss, although localized disease including pulmonary infection is seen. The relative absence of both these conditions in clinical series from developing countries may indicate either a lack of diagnostic services or a contrasting natural history of HIV disease. If people with HIV infection in developing countries are dying from other opportunistic infections, such as tuberculosis, before the development of very advanced immune deficiency, then conditions such as CMV disease and MAC infection will be

relatively uncommon. However, autopsy and specific diagnostic studies in developing countries demonstrate a much higher prevalence of both CMV disease and MAC infection than observed in clinical series, and would suggest that limited diagnostic capability may be the major factor for this apparent disparity.

HIV-related malignancies Kaposi's sarcoma and non Hodgkin lymphoma (NHL) are considerably more common among people with HIV infection than in the general population, with relative risks in the order of 70 000 and 100 respectively in industrialized countries. Although having a considerably lower relative risk, both Hodgkin disease and multiple myeloma are also more common among people with HIV infection (Grulich *et al*., 1999). In industrialized countries AIDS-associated KS has been seen predominantly among homosexual men, with a prevalence of 20–30% in some AIDS clinical series. The prevalence among other HIV exposure groups is considerably lowers. The only region where KS is relatively common among people with heterosexually acquired HIV infection is sub-Saharan Africa, where KS was present before the HIV epidemic (African endemic KS). In contrast, most developing countries of the Asia–Pacific Region have neither preexisting endemic KS nor a large male homosexual component of HIV infections, factors that almost certainly explain the low prevalence of KS in clinical series. Recent evidence has demonstrated a human herpes virus (HHV-8) as the probable causative agent for KS, with illustration of HHV-8in the vast majority of KS tissue specimens examined and serological evidence of infection strongly predicting subsequent development of KS. Approximately 5–10% of people with AIDS in industrialized countries develop NHL, with Burkitt lymphoma, large cell immunoblastic NHL and primary central nervous system (CNS) lymphomas described. The latter form of NHL is associated with more advanced immune deficiency, and carries the poorest prognosis. In contrast, NHL

has been relatively uncommon in clinical and autopsy series from developing countries in sub-Saharan Africa and Asia.

Neurological disease

In industrialized countries, AIDS dementia complex (ADC) is the initial AIDS illness in approximately 5% of AIDS cases, with a lifetime estimated risk of 10–20% (Encyclopedia of Life Sciences, 2001). ADC presents as a progressive cognitive and motor deficit, and, although supported by the presence of cerebral atrophy on cerebral imaging and/or an increase in cerebrospinal fluid markers (b2-microglobulin and neopterin), the diagnosis is made on clinical grounds. The apparent absence of ADC in many clinical series from developing countries may reflect either the lack of awareness of the diagnosis or again may be related to the relative lack of survival to very advanced immune deficiency; as with CMV and MAC, ADC generally presents when the CD_4+ cell count is less than 50/mL. Toxoplasmosis occurs in 5–20% of people with AIDS in developed countries, depending on the background prevalence of the causative protozoal agent *Toxoplasma gondii*, higher in European countries than in North America. Cerebral toxoplasmosis constitutes the vast majority of cases of AIDS-related toxoplasmosis, although retinal, pulmonary and cardiac cases are also seen. Based on autopsy series from sub-Saharan Africa, toxoplasmosis also appears to be a common AIDS illness in developing countries, with the absence of cerebral imaging techniques an explanation for under diagnosis in some clinical series. Other AIDS-defining CNS neurological conditions include *Cryptococcal meningitis*, primary CNS lymphoma, and progressive multifocal leucoencephalopathy. Although not AIDS-defining, peripheral neurological disorders such as myelopathy, polyradiculopathy and peripheral neuropathy are common disorders in advanced HIV disease. The latter may also occur at earlier

stages of HIV disease when the etiology is often related to nucleoside analogue antiretroviral therapy.

Gastrointestinal disease

AIDS – defining gastrointestinal disease includes CMV disease (oesophagitis, gastritis and colitis) and chronic cryptosporidiosis; however, several other organisms are responsible for gastrointestinal symptoms in people with HIV. These include protozoal agents such as Microsporidia, Isospora belli and Entamoeba histolytica. HIV-related cholangiopathy generally presents with right upper quadrant abdominal pain and is diagnosed by the presence of features including papillary stenosis, common bile duct dilatation and intrahepatic cholangitis on imaging of the biliary system. *Cryptosporidium spp*., are commonly isolated in association with HIV-related cholangiopathy, although microsporidia and CMV may also be etiological agents (Encyclopedia of Life Sciences, 2001).

Bacterial infections

Recurrent bacterial pneumonia was included in the CDC 1993 revised AIDS case surveillance definition (Centers for Disease Control, 1993). Although bacterial organisms such as *Streptococcus pneumoniae, Haemophilus influenza* and *Staphylococcus aureus*, which commonly cause pneumonia in immunocompetent patients, are also causative organisms for pneumonia in people with HIV, Gram negative organisms such as *Pseudomonas spp.* are often isolated from patients with HIV-related pneumonia. In addition to mixed bacterial flora, pneumonia in people with HIV often includes mixed pathology with fungal and *P. carinii* infections. Salmonella septicemia appears to be a common HIV related condition in developing countries, particularly among children with HIV infection. In contrast to the majority of HIV-related opportunistic infections, bacterial sepsis is common

at all values of immunodeficiency. Risk factors for HIV-related bacterial infection include neutropenia, hospitalization and injecting drug use.

2.29 AIDS DEFINING ILLNESSES VERSUS AIDS RELATED OPPORTUNISTIC INFECTIONS

AIDS – defining illnesses are those which the centers for disease control and prevention (CDC) has classified as being directly associated with advanced HIV infection, many of these diseases are seen outside the realm of HIV but are considered AIDS defining because they are more prevalent in HIV – positive individuals and are rarely seen outside of immune suppressive disorder (Schonwald *et al*, 1999). Although some AIDS – defining illnesses can occur in people who do not have HIV, they are only considered AIDS – defining in the presence of HIV infection. Although AIDS – defining illnesses can be classified as opportunistic infections, opportunistic infections cannot be classified as AIDS – defining illnesses. Opportunistic infections are those caused by otherwise common, harmless viruses, bacteria, fungi or parasite which can cause diseases when immune defenses have been compromised. Many opportunistic infections are not life threatening and can develop even when a person's CD_4+ count is high. AIDS – defining illnesses, by contrast, tend to appear during the later stage disease when the CD_4+ count has dropped significantly. Some opportunistic infections like herpes simplex are only considered to be AIDS – defining when they disseminate beyond the tissue or organ where they are typically seen.

2.3 Urinary Tract Infections and HIV Co infection

It is a known fact that HIV – positive patients are liable to acquire opportunistic infections. Although their liability to acquire other common infectious conditions is less frequently reported. Asymptomatic bacteriuria is one among the important causes of opportunistic infections in HIV positive (Schönwald, 1999). Urinary infections are one of the most common bacterial infections and the cause of morbidity and hospitalization in HIV positive individuals. HIV disease is associated with a variety of renal syndromes. In patients with low CD_4+ counts, bladder hyporeflexia are common neurologic complications, which lead to urinary stasis and ultimately infection (WHO, 2011). Persons living with HIV/AIDS (PLWHA) are prone to infection from non-pathogenic microbes in the environment than normal individuals; and this development has been greatly attributed to the weakened immune system of HIV infected patients which makes it difficult to protect the body against invading commensal organisms (American Journal of BioScience, 2013). In people living with HIV/AIDS, almost every part of the genitourinary system is affected with different diseases. In addition, such people are more vulnerable to different bacterial infections including urinary tract infection (UTI) because of high viral load and low CD_4+ count of the infected individuals Different researchers have shown an increased prevalence rate of UTI in HIV/AIDS patients: prevalence rate of 6.3%–41% was reported from various parts of the world (Murugesh, 2015). Low CD_4+ counts have been said to put HIV-positive patients at higher risk of bacteriuria. Untreated Urinary tract infections accounts for 7-60% of opportunistic infections in immunocompromised hosts (American Journal of BioScience, 2013). Conversely, according to research by Akadri *et al*, HIV/AIDS does not predispose an individual to increased prevalence of UTI. However, when it occurs, it is caused by the same organisms that usually

cause UTI in normal, healthy individuals. Physicians treating these patients should therefore consider asymptomatic bacteriuria as a possible source of infection and periodically monitor for the same (Akadri, 2014).

HIV infected people may present with co infections, comorbodities and side effects associated with antiretroviral drug usage. People living with Human Immunodeficiency Virus (HIV) are likely to be more predisposed to urinary tract infection due to the suppression of their immunity and women in this category tend to get them more often due to the nature of their anatomy (Akadri, *et al*. 2014). Bacterial infections are a common cause of morbidity and mortality in HIV positive individuals. Recent reports suggest that the incidence of urinary tract infection is increased in HIV positive patients (Banu *et al*, 2013). Furthermore, there is evidence that bacteriuria is more common as HIV disease progresses (Hira *et al*., 2003). UTIs are an important health problem in HIV-infected persons, where the incidence is between 5% and 20 % .Studies have shown that the incidence of UTIs is greater among men and women infected with HIV than among men and women who are sero-negative for HIV (Akadri *et al*, 2014). This increased risk of bacteriuria correlates with the degree of immunosuppression, as reflected by the CD_4+ count. Most studies have demonstrated increased susceptibility to UTIs in HIV-infected patients with CD_4+ count of <200 lymphocytes/mm3 (Kemajou, 2016). Some studies have indicated that the risk of bacteriuria and UTI may be increased in HIV-infected patients and is inversely related to CD_4+ lymphocyte counts (Akadri *et al*, 2014). UTI in HIV-positive patients tends to recur, requiring longer treatment and it is suggested that treatment should be culture-specific

2.31 COMMUNITY – ACQUIRED URINARY TRACT INFECTIONS

Community – acquired urinary tract infection is defined as an infection of the urinary tract that occurs in the community or within less than 48 hours of hospital admission and was not incubating at the time of admission. It is the most common infection caused by extended spectrum β – lactamase producing *Enterobacteriaceae*, but the clinical epidemiology of these infections in low prevalence countries is largely unknown. Community – acquired infections are defined by the types of organisms that affect the patients. Patients with community – acquired urinary tract infections have less co morbidities, and recurrent urinary tract infections, and have previously received antibiotics more often than patients with hospital – acquired or nosocomial urinary tract infections. *Escherichia coli* remain the predominant uropathogen isolated in uncomplicated community – acquired urinary tract infections. The management of community – acquired urinary tract infection entails the prompt use of antibiotics to eliminate the pathogens to eliminate the pathogen to avoid complications including, but not limited to scarring that could lead to hypertension and end – stage renal disease.

2.32 HOSPITAL – BASED URINARY TRACT INFECTIONS

Hospital – acquired Infections, also known as nosocomial infections or, to emphasize both hospital and non – hospital settings, it can sometimes also be called Healthcare – associated infections. It is usually the kind of urinary tract infection that occurs three days after a patient is admitted into the hospital or other health facilities. Hospital acquired infections can be caused by bacteria, viruses, fungi or parasites. These organisms may already be present in the patient's body or may come from the environment, contaminated hospital equipments, health care workers, or other patients. Depending on the causative agent involved, an infection

may start from any part of the body. A localized infection is limited to a specific part of the body and has local symptoms. For example, if a surgical wound in the abdomen becomes inflated, the area of the wound becomes red, inflamed and painful. A generalized infection is one that enters the bloodstream and causes general systemic symptoms such as fever, chills, low blood pressure, and mental confusion. Hospital acquired infections may develop from surgical procedures, catheters placed in the urinary tract or blood vessels, or from materials from the nose or mouth that is inhaled into the lungs. The most common types of hospital acquired infections include urinary tract infections, pneumonia and surgical wound infections.

All hospitalized patients are susceptible to contracting nosocomial infections. Some patients are at greater risk than others – young children, the elderly and persons with compromised immune systems like HIV infection, are most likely to get an infection. Other risk factors for getting hospital – acquired infections are prolonged hospital stay, the use of indwelling catheters, poor hand washing habits by both patients and healthcare workers and overuse of antibiotics. Urinary tract infections being the most common type of hospital – acquired infection happens after urinary catheterization. Catheterization is the placement of a catheter through the urethra into the urinary bladder. This procedure is done to empty urine from the bladder and relieves pressure in the bladder, measure urine in the bladder, put medicine in the bladder, or for any medical reasons. Other hospital procedures that put patients at risk for nosocomial infections are gastrointestinal procedure, obstetric procedures and kidney dialysis. Fever is often the first sign of infection. Other symptoms and signs of infection are rapid breathing, and high white blood cell count. An infection is suspected any time a hospitalized patient develops a fever that cannot be explained. A complete physical examination is conducted in

order to locate the signs and symptoms of infection. Hospital – acquired infections are serious illnesses that cause death in about 1% of cases.

2.4 Impact of Antiretroviral Therapy

There are several classes of antiretroviral agents that act on different stages of the HIV life-cycle. The first effective therapy against HIV was the nucleoside reverse transcriptase inhibitor (NRTI) *zidovudine* (AZT). It was approved by the US FDA in 1987. Subsequently, several more NRTIs were developed but even in combination were unable to suppress the virus for long periods of time and patients still inevitably died. To distinguish from this early anti-retroviral therapy (ART), the term highly active anti-retroviral therapy (HAART) was introduced. The use of multiple drugs that act on different viral targets is known as highly active antiretroviral therapy (HAART). HAART decreases the patient's total burden of HIV, maintains function of the immune system, and prevents opportunistic infections that often lead to death Antiretroviral therapy (ART), however, improves the health of people infected with HIV/AIDS through decreasing the progression of the infection, restoration of the immunity of the patient, decreasing the viral load, and reducing the opportunistic infections (Debalke, 2014). HIV treatment has been proven so successful that in many parts of the world HIV has become a chronic condition in which progression to AIDS has become increasingly rare.

2.41 CLASSES OF ART

Anti retroviral drugs are grouped into five drug classes according to their peculiar modes of action. The six drug classes are:

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIS)

These inhibit reverse transcriptase by binding to an allosteric site of the enzyme; NNRTIs act as non-competitive inhibitors of reverse transcriptase. NNRTIs affect the handling of substrate (nucleotides) by reverse transcriptase by binding near the active site. NNRTIs can be further classified into 1st generation and 2nd generation NNRTIs. 1st generation NNRTIs include *nevirapine* and *efavirenz*. 2nd generation NNRTIs are *etravirine* and *rilpivirine*. HIV-2 is naturally resistant to NNRTIs.

Nucleoside Reverse Transcriptase Inhibitors (NRTIS)

These are nucleoside and nucleotide analogues which inhibit reverse transcription. HIV is an RNA virus and hence unable to become integrated into the DNA in the nucleus of the human cell; it must be "reverse" transcribed into DNA. Since the conversion of RNA to DNA is not done in the mammalian cell it is performed by a viral protein which makes it a selective target for inhibition. NRTIs are chain terminators such that once incorporated, work by preventing other nucleosides from also being incorporated into the DNA chain because of the absence of a 3' OH group. Both act as competitive substrate inhibitors. Examples of currently used NRTIs include *zidovudine*, *abacavir*, *lamivudine*, *emtricitabine*, and *tenofovir*.

Protease Inhibitors (PIS)

These block the viral protease enzyme necessary to produce mature virions upon budding from the host membrane. Particularly, these drugs prevent the cleavage of *gag* and *gag/pol* precursor proteins. Virus particles produced in the presence of protease inhibitors are defective and mostly non-infectious. Examples of HIV protease inhibitors are *Lopinavir*, *Indinavir*, *Nelfinavir*, *Amprenavir* and *Ritonavir*. *Darunavir* and *atazanavir* are currently recommended as first line therapy choices. Maturation inhibitors have a similar effect by binding to *gag*, but development of two experimental drugs in this class, *Bevirimat* and *Vivecon*, was halted in 2010.

Resistance to some protease inhibitors is high. Second generation drugs have been developed that are effective against otherwise resistant HIV variants

CCR5 Antagonists (CCR5S) (Also called Entry Inhibitors/Fusion Inhibitors)

These interfere with binding, fusion and entry of HIV-1 to the host cell by blocking one of several targets. Caution should be used when administering this drug however due to a possible shift in tropism which allows HIV to target an alternative co-receptor such as CXCR4. In rare cases, individuals may have a mutation in the CCR5 delta gene which results in a nonfunctional CCR5 co-receptor and in turn, a means of resistance or slow progression of the disease. However, as mentioned previously, this can be overcome if an HIV variant that targets CXCR4 becomes dominant

Integrase Strand Transfer Inhibitors (INSTIS)

These inhibit the viral enzyme integrase, which is responsible for integration of viral DNA into the DNA of the infected cell. There are several integrase inhibitors currently under clinical trial, and *raltegravir* became the first to receive FDA approval in October 2007 *Raltegravir* has two metal binding groups that compete for substrate with two Mg^{2+} ions at the metal binding site of integrase. As of early 2014, two other clinically approved integrase inhibitors are *elvitegravir* and *dolutegravir*.

2.42 COMBINATION THERAPY

Combinations of antiretrovirals create multiple obstacles to HIV replication to keep the number of offspring low and reduce the possibility of a superior mutation. If a mutation that conveys resistance to one of the drugs being taken arises, the

other drugs continue to suppress reproduction of that mutation. With rare exceptions, no individual antiretroviral drug has been demonstrated to suppress an HIV infection for long; these agents must be taken in combinations in order to have a lasting effect. As a result, the standard of care is to use combinations of antiretroviral drugs. Combinations usually consist of three drugs from at least two different classes. This three drug combination is commonly known as a triple cocktail. Combinations of antiretrovirals are subject to positive and negative synergies, which limit the number of useful combinations.

2.43 INITIATION OF ART

Antiretroviral drug treatment guidelines have changed over time. Before 1987, no antiretroviral drugs were available and treatment consisted of treating complications from opportunistic infections and malignancies. After antiretroviral medications were introduced, most clinicians agreed that HIV positive patients with low CD_4+ counts should be treated, but no consensus formed as to whether to treat patients with high CD_4+ counts. A review of several cohort studies and guidelines shows a widespread view clinical staging and CD_4+ counts are the best primary markers and viral load the secondary marker for this decision. WHO recommends initiation of ART using clinical and immunological criteria that other variances (for example, concurrent illnesses). In case of a concurrent acute illness, CD_4+ cell count should be repeated only after the illness is cured. Therapy should not however be delayed if a patient is unwell or if the second count cannot readily be performed. If the CD_4+ count is not available, the decision to initiate ART can still be made on clinical grounds alone – with clinical stage 3 or 4 illness. Baseline CD_4+ count at the onset of ART (ideally determined when the patient is free from

any active major opportunistic infection) is a critical value in determining prognosis, response to ART and for monitoring the subsequent immunological response to ART

2.44 CONSIDERATIONS FOR DRUG RESISTANCE TEST

Prevalence of HIV drug resistance varies in different countries and is linked to several factors, including the duration of ART availability, history of treatment (mono- and dual therapy) and adherence. In Western Europe, multicentric studies showed a 10% overall prevalence of resistance in newly diagnosed HIV-infected individuals between 1996 and 2002. A study of 40 cities in the United States revealed a resistance rate of 14%. The highest results from these studies were 26% in Spain and 19% in San Francisco. In countries with a short or no history of ART, risk of HIV drug resistant virus transmission is significantly lower, and the first-line highly active antiretroviral treatment (HAART) regimen is effective for treatment of naïve patients. It is important to have population-based HIV drug resistance strategies in place to monitor for the appearance and spread of HIV drug resistance; and to act on the early warning indicators for drug resistance emergence in order to minimize its appearance and onward spread.

2.45 ADHERENCE TO ART

Optimal treatment benefits require strict adherence to ART. It is well recognized that when adherence is high, there is a dramatic reduction in HIV-associated morbidity and mortality, whereas low adherence leads to rapid development of drug resistance. Effective adherence values have not been fully defined for ART (there being differences between a number of regimens), but values lower than 95% have been associated with poor virological and immunological response,

while values of 100% seem to achieve even greater benefit than 95%. The most recent data show a correlation between drug resistance in various classes of ARVs and adherence. Low or insufficient adherence has consequences for patients, public health and national economies.

• Patients are in danger of developing significant viral resistance, treatment failure and disease progression. Changing to a new regimen after treatment failure results in most cases, in more difficult adherence (more pills, side-effects, dietary restrictions, toxicity and dosing complexity).

• The increase in resistant viruses is likely to result in their transmission to newly infected individuals.

• Economically, the presence of resistant strains will result in increased use of second-line and salvage regimens, which are in general more expensive than first-line regimens.

• Low adherence also means a higher risk of disease progression, resulting in higher costs for treating opportunistic infections

There has been a decrease in cases of many opportunistic infections among people living with HIV low – and middle – income countries due to the effect of antiretroviral drug usage. Investigators estimated that use of ART is averting over 161,000 opportunistic infections each year.

2.5 Studies on related research

A review of related studies showed urinary tract infections (UTI) prevalence rates of 6.3% to 41% in HIV/AIDS patients reported from various parts of the world (Debalke, 2014). Related reports on studies in other parts of Nigeria recorded varying prevalence rates of urinary tract infections in HIV positive patients.

Prevalence rate of 56.7% of urinary tract infections in HIV/AIDS patients under ART was recorded in Edo State (Inyamba *et al*., 2016). *Iyamba et al., 2016,* also alluded to a progressive increment in the prevalence rates of urinary tract infections in HIV positive patients in different parts of Nigeria between 2015 and 2016.

In Calabar, urinary tract infections prevalence rate of 25.3% was recorded in HIV positive patients on antiretroviral therapy (Inyang – Etoh *et al*, 2009). De Pinto and his team, investigated whether bacteriuria, specifically, symptomatic urinary tract infections (UTI) occur with increased frequency in men living with HIV (De Pinto, 1994). In a study carried out in Aba, Abia State, overall prevalence of urinary tract infections in patients on antiretroviral therapy was 40.39% (Kanu, 2016). In South South Nigeria, Edo State, an overall prevalence rate of 6.3% was found among adolescents and young adults infected with HIV/AIDS (Michael *et al*., 2006). In related studies in Benin, Edo state, overall prevalence of urinary tract infection was 57.3% (Kemajou *et al*., 2016). In Jos, Plateau state, the overall prevalence of urinary tract infection in same cohort was 23.5% (Bigwan, 2015). In Ethiopia, East Africa, urinary tract infection prevalence rate of 11.3% was recorded for same cohort (Fenta, 2016). In another study carried out in Jimma University, Ethiopia, the overall urinary tract infection prevalence rate of 12% was recorded in HIV positive patients (Debalke, 2014). In Bangalore, India, the prevalence rate of urinary tract infection in HIV positive patients was 4.0% (Banu *et al*., 2013). In a related study, it was reported of a higher prevalence rate of urinary tract infections in ART users than in non ART users in India (Murugesh, 2014). *Schowald et al*. recorded an overall urinary tract infection prevalence rate of 25.0% in HIV positive individuals on ART (Schowald *et al*., 2009). Similarly, urinary tract infection prevalence rate of 41.0% was also recorded in Zagreg,

Croatia (Schowald *et al*., 2009). The findings in Ethiopia recorded a urinary tract prevalence rate of 12.5% for ART users and 10.0% for non ART users (Debalke, 2014). In a related study, Fenta *et al*., recorded a 13.0% prevalence of urinary tract infections in patients on HAART and a 7.0% prevalence rate for non ART users who were not on antiretroviral therapy (Fenta, 2016). Amiri *et al*., in a case – control study carried out in Iran also showed significantly higher prevalence of urinary tract infections among highly active antiretroviral therapy users (ART users) 27.78% compared to the control groups 17.31%, though the control groups were non HIV patients (Amiri *et al*., 2009). In Italy, it was confirmed of a significant reduction in bacterial infections in HIV – infected subjects when HAART became a standard therapy for HIV infection (De Gaetano *et al*., 2003).

Schonwald *et al*. 2009, review described an analysis showing differences in frequencies in UTI prevalence between HIV positive and HIV negative individuals. Apart from the differences in the prevalence, the review also observed differences in etiology; while Enterococci were the most frequent in patients with HIV disease, *Escherichia coli* was most frequently in patients without HIV negative individuals. Other findings also collaborated with a related study in Anambra state implicating gram negative rods as the main cause of urinary tract infections (Ogbukagu, 2016). In Italy, gram negative bacteria represented 90.8% of urinary pathogens in a cohort of HIV positive outpatients (Magliano *et al*., 2012). In other related studies, gram negative bacteria were more prevalent than gram positive bacteria. This finding was comparable with other findings done in Gondar and Jimma, Ethiopia (CLSI, 2014). In 2009, Omoregie *et al.*, researched on the impact of human immunodeficiency virus (HIV) infection and CD_4+ count on the prevalence of urinary tract infections in order to determine the prevalence of UTI

among HIV and non- HIV infected subjects. In the research, *Staphylococcus aureus* was the most implicated etiologic agent responsible for UTI.

Studies on the evaluation of the effects of highly active antiretroviral therapy (HAART), show that ART has a significant impact on the reduction of the incidence of bacterial infections including bacteraemia, bacterial pneumonia, and urinary tract infections that occur in HIV infected persons (De Gaetano *et al*., 2003). According to Debalke *et al*., 2014, *Staphylococcus aureus* is the predominant bacterial uropathogen among ART user patients. Following in order of prevalence are: *Escherichia coli*, *Enterococcus species*, *Pseudomonas aeruginosa*, *klebsiella species*, *Acetobacter*, *Proteus species*, *Candida species*, and *Salmonella species*. *Escherichia coli* was the most significant cause of urinary tract infections in the study in Italy: *Escherichia coli* (67.6%), *Klebsiella pneumonia* (8.8%), *Enterococcus faecalis* (6.3%), *Proteus mirabilis* (5.2%), *Pseudomonas aeruginosa* (2.5%) and Staphylococcus agalactiae (2.3%) (Magliano, 2012). As well as with the study carried out in Jos, Plateau state, *Escherichia coli* (29.7%), *Staphylococcus aureus* (6.5%), *Proteus mirabilis* (2.7%), *Pseudomonas aeruginosa* (2.7%) and Klebsiella species (1.9%) (Bigwan, 2015). Another study in Aba, Abia states also collaborates our findings: *Escherichia coli* (68.18%), *Klebsiella pneumonia* (15.91%), Enterobacter specie (11.36%) and Staphylococcius aureus (4.55%) (Kanu, *et al*., 2016). Findings in other parts of Nigeria, implicating *Staphylococcus aureus* as the use of urinary tract infections most common cause of urinary tract infections in a cohort of HIV positive individuals. In Osun state, *Staphylococcus aureus* (29.7%), *Escherichia coli* (28.7%) and *Pseudomonas aeruginosa* (13.9%) (Adeyemi *et al*., 2012). In Calabar, the predominant bacteria among ART users were *Staphylococcus aureus* (87.2%), followed by Escherichia coli (84.0%) while *Escherichia coli* was most

predominant among Non ART users (Debalke, 2014). Similarly in Oshogbo, South West Nigeria, *Klebsiella spp* was the most implicated etiological agent followed by *Escherichia coli* (Olowe *et al*., 2015). In other parts of the world, *Pseudomonas aeruginosa* (41.9%), *Escherichia coli* (19.35%), *Staphylococcus epidermidis* (9.6%), *Enterococcus faecalis* and *Staphylococcus aureus* (6.45%) (Xavier, 2015). In the distribution of etiologic agents of urinary tract infections between ART users and non ART users, *Escherichia coli* was implicated in high UTI prevalence rates in both the ART users (33.8%) and the non ART users. This is comparable with other related studies carried out in Ibadan, Nigeria (Michael *et al*., 2006); Brazil (De Pinho *et al*., 1994) and Cameroon (Njunda *et al*., 2010). In contrast, *Enterococcus* was more frequently isolated in ART users while *Escherichia coli* were more frequently isolated in non ART users (Schonwald, 1999). Findings in Jos, Plateau state, also observed that *Candida albicans* has the least UTI prevalence rate (Essien, 2015). Anyamene, C., in 2006, characterized a spectrum of bacterial infections associated with a cohort of HIV positive persons in south east Nigeria. According to him, the most frequent bacterial infection common in HIV positives were tuberculosis, followed by bacterial pneumonia, bacteraemia, urinary tract infections, and least on the list being typhoid fever. The urinary tract infections implicate *Streptococcus pyogenes* as the most common etiologic agent responsible for UTI in HIV positives. In high income countries, the most opportunistic infections esophageal candidiasis, cryptococcal meningitis, cytomegalovirus retinitis, toxoplasma encephalitis, cryptosporidium diarrhea, herpes and Kaposi sarcoma (Bertozzi *et al*., 2010). In related studies, the most common infections in HIV positive patients without antiretroviral usage were bacterial pneumonia (25%), pulmonary tuberculosis (10%), oral and esophageal thrush (8%), and extra pulmonary tuberculosis (7%). A similar profile of disease was observed among HIV positive patients on antiretroviral drugs, with bacterial

pneumonia (22%), tuberculosis (9%) and *Varicella zoster* (8%). Prevalence rates of urinary tract infections by gender. In Aba, Abia state, higher urinary tract infection prevalence rate of 52.17% was established among the females; and 17.14% prevalence rate in male patients (Kanu, *et al.*, 2016). Similar findings were reported in the North Central, Jos (Bigwan, 2015); East Africa, Ethiopia (Teshager *et al*., 2008). According to another research in Ethiopia, prevalence of urinary tract infections was significantly higher among the female patients, 14.6% than the male patients, 7.2% (Debalke *et al*., 2014). In related studies, Banu *et al*., 2013 recorded significantly higher prevalence of bacteriuria in female patients (83.3%) than in males (16.7%) in Bangalore, India (Banu *et al*., 2013). However, these findings are in contrast to the study by Inyang – Etoh *et al*., who recorded higher prevalence rate 28.6% of urinary tract infections in males and 23.8% in female patients in Calabar, even though it was not statistically significant (Inyang – Etoh *et al*, 2009). Spence also reported higher urinary tract infection prevalence rate of 15.9% in males (Spence *et al*., 1996). Urinary tract infection prevalence has been estimated to be three times higher in females than in males. Although the disparity in urinary tract infection prevalence rates by gender is reported to be age dependant as reported by Glynn *et al*., who reported that HIV prevalence was six times greater in females than in males (Kanu, *et al.*, 2016). Further research is needed to verify this claim.

Research carried out in Anambra state, Nigeria stating that urinary tract infections occurred highest in age group 26 – 38 years (Ogbukagu, *et al.*, 2016). In Benin, Edo state, it was also observed that the prevalence rate of UTI in HIV seropositive individuals was highest in age group 24 – 30 years and least in age group 44 years and above (Kemajou *et al*, 2016). Findings in Aba, South East Nigeria indicating that age group 60 – above had the highest prevalence of 100% followed by age

group 30 – 44 (44.9%) (Kanu, *et al.*, 2016). In another related study carried out in Jos, Nigeria, age group 46 and above had the highest prevalence rate of urinary tract infections and age group 5 – 15 with the least prevalence rate (Bigwan, 2016).

In a study carried out in Brazil, to estimate the average duration of ART users benefit, it was observed that the mean duration of antiretroviral ART users benefit in HIV positive individuals was 14.1 months. 23% of HIV infected individuals on therapy loose the benefits of ART users after 6 months of commencement while 47% of patients still maintain ART users benefits after 12 months of commencement of therapy (Medeiros *et al*., 2002). In another related research in Spain, it was observed that very young children, adolescents and young adults are at high risk of non adherence to antiretroviral therapy (Palladino *et al*., 2012). In Jos, Plateau State, the highest prevalence of urinary tract infections was observed among participants with CD_4+ count range 200 – 400 cells/µl (Essien, 2015). This can be attributed to massive epileptic antiretroviral availability and ART users' failure. In contrast to our findings, related studies carried out in South Western Nigeria, observed that those with CD_4+ count values less than 200 cells/µl were at significantly higher risk of urinary tract infections (Olowe *et al*., 2015). Sill in contrast to our findings, studies in Calabar, Cross River State noted highest UTI prevalence rate among HIV positive patients with CD_4+ count of less than 200 cells/µl (Inyang – Etoh *et al*., 2009). Several studies have also suggested a correlation between low CD_4+ counts and increased UTI prevalence (Essien, 2015). Higher prevalence rates of urinary tract infections were observed in HIV positive ART users with CD_4+ count greater than 500cells/µl. This collaborates with similar studies in Benin, Edo state. Among both ART users and non ART users, CD_4+ count less than 200 cells/µl was not associated with asymptomatic urinary tract infections (Omoregie, 2009). In contrast, studies in Addis Ababa,

Ethiopia, observed that the highest proportion of bacteria were isolated from patients having CD_4+ count of less than 500 cells/ µl (Fenta, 2016). However, an Indian study reported a higher prevalence of bacteriuria among ART users and ART non ART user participants (Pradip *et al*., 2013).

CHAPTER 3

MATERIALS AND METHODS

3.1 STUDY DESIGN

A comparative, hospital – based, cross – sectional study was employed in this research. The research compared the prevalence rates of urinary tract infections between anti retroviral drug users and non users. The variables under study within the established population (HIV positive individuals) were restricted to the following: Use of antiretroviral usage, patient's CD_4+ counts, previous history of urinary tract infections and length of antiretroviral usage. This research was carried out over a six – month period within Enugu Metropolis of Enugu State, Southeast, Nigeria.

3.2 STUDY SITE

To ensure equal distribution or spread of the sample population for the study, this comparative cross sectional study was carried out at three different healthcare facilities in Enugu State, South East Nigeria. Two tertiary health care institutions and one specialist healthcare institution: Enugu State University Teaching Hospital, Parklane, G.R.A, University of Nigeria Teaching Hospital, Enugu and Annunciation Hospital, Emene, Enugu respectively. All three tertiary health care facilities had functional Anti Retroviral Usage (ART) clinics from where the patients were recruited at the time of the study.

3.3 SAMPLE SIZE

There were a few salient determinants in the range of sample size required for the research. These determinants lent some understanding of the statistics that lead to

this research work's sample size decisions. The final variable in the sample size estimation was the standard deviation. According to Smith, a standard deviation of .5 ensured that the sample size is large enough. In calculating the sample size, the confidence level corresponds to a Z – score. This was a constant value needed for the equation. For this research work, the confidence interval of 95% was chosen. This corresponded to a Z- score of 1.96. Mathematically,

Necessary sample size = $(Z - score)^2 * S.D*(1 - S.D)/ (margin\ of\ error)^2$

Z – Score = 1.96; Confidence level = 95%; S.D = .25; margin of error (confidence interval) = +/- 5% = +/- .05

$((1.96)^2 \times .25(1-.25)) / (.05)^2$

$(3.8416 \times .25(0.75)) / .0025$

.7203 / .0025

285.12. Approximately 285.0.

In conclusion, a grand total of two hundred and eighty five patients were recruited for this research; One hundred and eighty five ART users and one hundred non ART users. Individuals were recruited from Enugu State University Teaching Hospital, Park lane, G.R.A, University of Nigeria Teaching Hospital Enugu and Annunciation Specialist Hospital, Enugu.

3.4 STUDY POPULATION

In this study, a total of 285 individuals with or without symptoms of urinary tract infections (UTI) were sampled. Sample distribution among healthcare facilities: One hundred and forty – five (145) were sampled from Enugu State University Teaching Hospital, Park lane, G.R.A; ninety – four (94) from Annunciation

Hospital, Enugu; while forty – nine (49) were sampled from University of Nigeria Teaching Hospital, Enugu. Out of the two hundred and eighty five HIV – positive individuals sampled, 185 were on Anti retroviral usage (ART users) while 100 were not on anti retroviral usage (non ART users). The study population comprised of 195 females and 90 male patients. The study population was divided into categories according to sex (male and female); and age groups: (18 – 38) years, (39 – 59) years and (60 – 80) years. Overall patient distribution according to age showed that 99 of the subjects were within the 18 – 38 age groups, 105 subjects were within the 39 – 59 age groups, while 81 were within the 60 – 80 age groups. Overall patient distribution according to previous history of urinary tract infections, 152 patients have had at least, one previous episode of urinary tract infection, while 133 patients have had no previous history of urinary tract infection. According to history of ART use (length of time patient has been on ART) those under a year of antiretroviral usage were 12 patients, those between 1 – 3 years on antiretroviral usage were 82 patients. Those between 4 – 6 years on antiretroviral usage were 76 patients; while those on antiretroviral usage for over 6 years were 15 patients. Verbal informed consent was obtained from all patients prior to specimen collection and questionnaire administration. Permission to sample collection and analysis was obtained from the ethical committee of the health facilities.

INCLUSION AND EXCLUSION CRITERIA

Patients eligible for study complied with the following characteristics:

- HIV – positive patients who were 18 years and above.
- HIV – positive males on ART for 6 months
- HIV – positive females on ART for 6 months
- HIV – positive males who are not on ART (naïve)
- HIV – positive females who were not on ART (naïve)
- HIV – positive males or females with or without symptoms of UTI

The criteria for the elimination of potential participants from study population include the following:

- HIV – positive patients under 18 years of age
- HIV – positive patients that have been on ART for less than 6 months
- HIV – negative persons
- Patients with urinary tract abnormalities, diabetes mellitus, and pregnancy were excluded from this study.

3.5 SAMPLING

This research used stratified random sampling method in the selection of both ART users and non – ART users. Patients were organized into sub – groups and categories according to age, sex, CD_4+ values, and previous history of urinary tract infections and length of use of anti retroviral usage.

3.6 ETHICAL CONSIDERATION

Ethical approvals to carry out sample collection and analysis for this study were obtained from the two selected tertiary healthcare facilities and one specialist hospitals' ethical health committees. Informal verbal consent was obtained from each participant prior to the administration of survey (questionnaire) for data collection, analysis and subsequent sample collections. All these were in full assurance that all information collated throughout the study will be kept confidential and treated as such. The results of all patients positive with urinary tract infections were duly disclosed to responsible health professionals in charge of the ART clinics of the health care facility.

3.7 DATA COLLECTION AND VALIDATION OF QUESTIONNAIRE

A standardized and validated questionnaire was used to collect socio demographic data from the patients. The following information was captured in the questionnaire: age, gender, length of antiretroviral drug usage, antiretroviral regimen, previous history of urinary tract infections and CD_4+ status. Data was also collected from patients' folders with permission from the records department of each ART unit. In the course of data collection, an interviewer – based questionnaire was administered to both ART users and ART non - users. Similar close – ended questions were administered to all the patients. Data on socio demographic characteristics and other associated variables were collected using well structured and pretested questionnaires. Data on patient drug history was pooled from the pharmacy departments of the three different ART clinics run in the tertiary healthcare institutions. Some responses to the questions were mutually exclusive while others required selection of more than one option. The questionnaire was designed to measure both qualitative and quantitative data. A

content validation of the questionnaire was carried out. The questionnaire was professionally validated by my thesis supervisor in order to ensure that data collated from the questionnaires were reliable and valid. This was done by ensuring that each item on the questionnaire corresponds to a desired measurement/parameter being investigated. The questionnaire was simple, clear and easy to understand. The questionnaire was divided into two distinct parts; the first twelve – point questions were meant to be answered by the patients while the last three questions were to be filled in by the laboratory personnel. Raw data entry and analysis was done using Microsoft Excel spreadsheet prior to statistical analysis. Statistical analysis was done using the SPSS statistical package. Pearson's Chi – square tests was used for all comparisons in determining any existing correlations/associations or relationships.

3.8 SAMPLE COLLECTION

Mid stream urine and venous blood samples were collected from 185 HIV positive individuals and 100 HIV negative individuals. The samples were collected into a sterile screw capped universal containers, plain and EDTA bottles respectively. The samples were duly labeled, transported to the laboratory and processed within an hour of collection to ensure maximum recovery of organisms.

3.9 MEDIA PREPARATIONS

Routine bacteriological culture of urine specimens and isolation of organisms for colonial characteristics require plating on to culture media. Three different culture media were used in the course of this research work: enrichment media (peptone water broth), enriched media (Blood Agar), differential media (Cystein Lactose Electrolyte Deficient Agar), and Triple Sugar Iron Agar. Culture media were prepared according to manufacturers' instructions.

Blood agar preparation

1. Blood agar base was prepared as instructed by the manufacturer and sterilized by autoclaving at 121°C for 15 minutes.
2. Blood agar base prepared was transferred to a 50°C water bath.
3. The agar base was cooled to 50°C; sterile sheep blood was added aseptically and mixed well gently, avoiding formation of air bubbles.
4. 15 ml of mixture was dispensed into sterile Petri plates aseptically.
5. The plates were stored at 2-8°C.
6. The culture plates were stored at 8-15°C.

Cystein Lactose Electrolyte Deficient Agar preparation

1. 36 g of the medium was suspended in one liter of distilled water.
2. The mixture was heated with frequent agitation and boiled for one minute to completely dissolve the medium.
3. The setup was autoclaved at 121°C for 15 minutes and cooled to 50°C.
4. The medium was mixed well and dispensed into Petri dishes.
5. After solidification, media plates were inverted to avoid excess moisture.
6. The culture plates were stored at 8-15°C.

Triple Sugar Iron Agar preparation

1. 65 g of the medium was suspended in one liter of distilled water.

2. The mixture was mixed thoroughly and heated with occasional agitation and boiled for one minute to dissolve the ingredients.
3. 16 × 150mm tubes were filled 1/3 full and plugged with cotton balls to maintain aerobic conditions.
4. Tubes were autoclaved for 15 minutes at 118°C.
5. Before the media solidification, tubes were inclined to obtain 4-5 cm slant and 2-3 cm butt.
6. The culture plates were stored at 8-15°C.

All agar bases used in this work were manufactured by TM Media Company. Produced and marketed by Titan Biotech Limited, Rajasthan, India.

3.10 URINE CULTURE

A loop full of commercially prepared 0.002 ml of thoroughly mixed, un – centrifuged urine specimen was streaked/inoculated on blood agar and C.L.E.D agar plates; and incubated for 24 hrs at 37˚C. Bacterial organisms were sub cultured into TSIA slants, incubated for 24 hrs at 37˚C under aerobic conditions, and examined for characteristic color changes. Significant bacteuria was established with bacterial growths $\geq 10^5$ cfu/ml. The number of bacteria (CFU) per milliliter or gram of sample was calculated by dividing the number of colonies by the dilution factor. Identification of significant isolates was done based on colonial appearance, gram stain reactions and biochemical tests including catalase tests, coagulase test, indole test, oxidase test, urease tests and sugar fermentation tests.

3.11 BIOCHEMICAL TESTS

Gram Staining

A smear of the colony was made on a clean – grease free slide and allowed to dry. It was then fixed with gentle heat over a bunsen flame. The slide was flooded with 0.5% crystal violet and allowed to stand for thirty seconds. The smear was washed with tap water and flooded with lugol's iodine for one minute. The smear was again washed with tap water and de colorized with 70% ethanol for one minute. The smear was immediately washed with tap water and flooded with 0.5% aqueous solution of neutral red for one minute. Finally, the smear was washed with running water, blotted with filter paper and allowed to dry. The smear was examined microscopically with oil immersion.

Catalase Test (Slide Method)

Procedure:

1. A sterile wooden stick was used to transfer a small amount of colony growth on the surface of a clean, dry glass slide.
2. A drop of 3% hydrogen peroxide (H_2O_2) was place on the glass slide.
3. The evolution of gas bubbles indicated a positive reaction.

Principle:

This test demonstrate the presence of catalase, an enzyme that catalyses the release of oxygen from hydrogen peroxide (H_2O_2). It is used to differentiate those bacteria that produce an enzyme catalase, such as *staphylococci*, from non-catalase producing bacteria such as *streptococci*. The enzyme catalase mediates the breakdown of hydrogen peroxide into oxygen and water. The presence of the enzyme in a bacterial isolate is evident when a small inoculum is introduced into hydrogen

peroxide, and the rapid elaboration of oxygen bubbles occurs. The lack of catalase is evident by a lack of or weak bubble production.

Coagulase Test (Slide Method)

Procedure:

1. A clean, grease free slide was divided into two sections with grease pencil. One was labeled as “test” and the other as “control.
2. A drop of distilled water was place on each area
3. Two colonies of test organism on blood agar plate were emulsified on each drop to make a smooth suspension
4. The test suspension was treated with a drop of citrated plasma and mixed well with a needle while the control was not.
5. The control suspension served to rule out false positivity due to auto agglutination
6. Clumping of cocci within 5-10 seconds was taken as positive.

Principle:

The slide method measures bound coagulase. The bound coagulase is also known as clumping factor. It cross-links α and β chain of fibrinogen in plasma to form fibrin clots that deposit on the cell wall. As a result, individual coccus sticks to each other and clumping is observed.

Indole Test

Procedure:

1. Test organism to be tested was inoculated in typtone broth.
2. Incubated overnight at 37°C.

3. Few drops of Kovac's reagent were added to the incubated broth.
4. Formation of red or pink colored ring at the top of the tube was taken as positive. No color change after addition of reagent was taken as negative.

Principle:

Some bacteria split amino acid tryptophan into indole and pyruvic acid using the enzyme called tryptophanase. Indole can be detected with Kovac's reagent or Ehrlich's reagent. Indole reacts with the aldehyde in the reagent to give a red color which concentrates as a ring at the top.

Methyl Red Test

Procedure:

1. Using sterile inoculating wire loop, the test microorganism was inoculated into the fresh, commercially prepared sterile glucose phosphate peptone water broth for 2 days at 37˚C.
2. A second broth was left un inoculated as control.
3. The inoculated tube was incubated at 35-37C for two to five days.
4. After incubation, 5 drops of Methyl Red reagent was added to the broth
5. The color change was observed.

Principle:

Some bacteria have ability to perform mixed acid fermentation of glucose in MR-VP medium. The products of mixed-acid fermentation are a complex mixture of acids, particularly lactate, acetate, succinate and formate as well as ethanol and equal amounts of H2 and CO2. This causes the medium to acquire an acidic pH. Methyl Red is a pH indicator, which remains red in color at a pH of 4.4 or less

Oxidase Test (Wet Filter Paper Method)

Procedure:

1. A strip of filter paper was soaked with a little freshly made 1% solution of the oxidase reagent (Tetramethyl paraphenylene diamine dihydrochloride).
2. A speck of the test culture was rubbed on it with a wire loop.
3. A positive reaction was indicated by an intense deep-purple hue, appearing within 5-10 seconds, a "delayed positive" reaction by colouration in 10-60 seconds, and a negative reaction by absence of colouration.

Principle:

Cytochrome containing organisms produce an intracellular oxidase enzyme. This oxidase enzyme catalyzes the oxidation of cytochrome C. Organisms which contain cytochrome c as part of their respiratory chain is oxidase-positive and turn the reagent blue/purple. Organisms lacking cytochrome C as part of their respiratory chain do not oxidize the reagent, leaving it colorless within the limits of the test, and are oxidase-negative. Oxidase positive bacteria possess cytochrome oxidase or indophenol oxidase (an iron containing haemoprotein). Both of these catalyse the transport of electrons from donor compounds (NADH) to electron acceptors (usually oxygen). The test reagent, N, N, N', N'-tetramethyl-p-phenylenediamine dihydrochloride acts as an artificial electron acceptor for the enzyme oxidase. The oxidised reagent forms the coloured compound indophenol blue.The cytochrome system is usually only present in aerobic organisms which are capable of utilising oxygen as the final hydrogen receptor. The end product of this metabolism is either water or hydrogen peroxide (broken down by catalase).

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Urease Test

Media preparation:

1. 32g of powder was dissolved in 100 ml of distilled water and filtered (0.45-mm pore size).
2. The agar was suspended in 900 ml of distilled water and boiled to dissolve completely.
3. Autoclaved at 121˚C for 15 minutes.
4. Agar was cooled to 50˚C.
5. 100 ml of urea base was aseptically added to the cooled agar solution and mixed thoroughly.
6. 4 to 5 ml of agar was distributed per sterile tube (13 x 100 mm) and the tubes were slanted during cooling until solidified.

Procedure:

1. The surface of urea agar slant was streaked with a portion of test organism.
2. The cap was loosely placed and the tubes incubated at 35°-37°C in ambient air for 48 hours.
3. The tubes were examined for the development of a pink color.

Principle:

Urea is the product of decarboxylation of amino acids. Hydrolysis of urea produces ammonia and CO_2. The formation of ammonia alkalinizes the medium, and the pH shift is detected by the color change of phenol red from light orange at pH 6.8 to magenta (pink) at pH 8.1. Rapid urease-positive organisms turn the entire medium pink within 24 hours.

Sugar Fermentation Tests (Tripple Sugar Iron Agar)

1. 5-7 ml of the autoclaved TSIA media in a sterile test tube and slant was made by tilting the media till it solidified.
2. Using a flamed inoculating loop, a colony from the test bacterial culture was picked.
3. The organism was inoculated in TSIA slant by stabbing in the butt and then with the same loop streaking on the whole slant surface of the medium
4. The tubes were incubated at 37°C for 18-24 hours.
5. The color change was observed for slant and butt, gas production and H_2S production.

Principle:

Triple sugar iron agar test is used to determine whether gram negative bacilli utilize glucose and lactose or sucrose fermentatively and produce hydrogen sulfide (H_2S). It contains 10 parts of lactose: 10 parts of sucrose: 1 part of glucose and peptone. Phenol red and ferrous sulphate serves as an indicator for acidification of medium and H_2S production respectively.

Glucose is utilized first by a fermentative organism and the entire medium becomes acidic (yellow) in 8 to 12 hours. Butt remains acidic even after 18 to 24 hours incubation peroid because of the presence of organic acids resulting from the fermentation of glucose under anaerobic conditions in the butt of the tube.The slant reverts to alkaline state that is indicated by red color as the fermentation products gets oxidised to carbon dioxide (CO_2) and water (H_2O) and peptone in aerobic condition the slant undergoes oxidation releasing alkaline amines (Phenol red in alkaline pH turns red while in acidid pH turns yellow).

Germ tube test

Candida species were suspended in 0.5 ml of human serum and incubated for 2 hrs at 37˚C. The suspension was examined microscopically. The appearance of **germ tubes indicated the presence of *Candida albicans***.

Rapid test kits for the detection of HIV antibodies

The **Alere** Determine ^{TM} HIV – 1/2; an *invitro*, visually read, qualitative immunoassay HIV test kit was used for the detection of antibodies to HIV in population. Whole blood samples were used in this testing. The test kits were manufactured by **Alere Medical Co., Ltd**. 357 Matsuhidai, Matsudo – shi, Chiba, Japan.

3.12 CD_4+ ANALYSIS USING AUTOMATED *PARTEK CYFLOW* CD4 COUNTING

Procedure:

Patients' blood samples (20µl of whole blood), was mixed with 20µl antibody; and incubated in the dark for 15 minutes at room temperature. 800µl of buffer was added to the solution. Samples were analyzed automatically and reported in standard international units (cells/µl).

Principle:

The basic principle of flow cytometry is the passage of cells in single file in front of a laser so they can be detected, counted and sorted. Cell components are fluorescently labelled and then excited by the laser to emit light at varying wavelengths. The fluorescence can then be measured to determine the amount and type of cells present in a sample.

CHAPTER 4

RESULTS

In this study, two hundred and eighty five (285) patients were enrolled. Of these, one hundred and eighty five (64.9%) were HIV positive patients on anti retroviral therapy, while one hundred (35.1%) were HIV negative patients who were not on antiretroviral therapy. Patient distribution was categorized under the following host factors: gender, age, CD_4+ values, length of antiretroviral therapy usage and previous history of urinary tract infections.

Overall distribution of the 285 patients according to gender showed more female patients, 195 (68.4%) than male patients 90 (31.6%). Distribution of patients according to age showed that age group 39 – 59 years, 105 (36.8%) had the highest distribution of patients. Followed by age group 18 – 38 years, 99 (34.7%). The age group 60 – 80 years, 81 (28.5%) had the least distribution of patients. According to previous history of urinary tract infections, 152 (53.3%) have had at least one prior episode of urinary tract infection while 133 (46.7%) have never had any prior episode of urinary tract infection. Distribution of patients according to length of antiretroviral drug usage showed that out of 185 patients on antiretroviral drug usage, 12 (6.5%) were just under one year of drug usage. Eighty two (44.3%) had been on antiretroviral drug usage for 1 – to 3 years. Those who have been on antiretroviral drug usage up to 4 – 6 years, 76 (41.1%) while 15 (8.1%) had used antiretroviral therapy for over 6 years (Table 1).

Table 1: Categories of patient distributions

Categories of distributions	Number of patients	Percentage (%)
ART USE		
ART Users	185	64.9
Non ART users	100	35.1
Total	**285**	
GENDER		
Male	90	31.6
Female	195	68.4
Total	**285**	
AGE		
18 – 38	99	34.7
39 – 59	105	36.8
60 – 80	81	28.5
Total	**285**	
HISTORY OF UTI		
Yes	152	53.3
No	133	46.7
Total	**285**	
LENGTH OF ART USAGE		
<1yr	12	6.5
1 – 3yrs	82	44.3
4 – 6yrs	76	41.1
>6yrs	15	8.1
Total	**185**	

Distribution of 185 HIV positive patients on antiretroviral therapy showed more female patients, 135 (73.0%) than male patients 50 (27.0%). Distribution of HIV positive patients according to age showed that age group 39 – 59 years, 80 (43.2%) had the highest distribution of patients. Followed by age group 18 – 38 years, 70 (37.8%). The age group 60 – 80 years, 35 (19.0%) had the least distribution of patients. According to previous history of urinary tract infections, 90 (48.6%) have had at least one prior episode of urinary tract infection while 95 (51.4%) have never had any prior episode of urinary tract infection. Distribution of patients according to length of antiretroviral drug usage showed that out of 185 patients on antiretroviral drug usage, 12 (6.5%) were just under one year of drug usage. Eighty two (44.3%) had been on antiretroviral dug usage for 1 – to 3 years. Those who have been on antiretroviral drug usage up to 4 – 6 years, 76 (41.1%) while 15 (8.1%) had used antiretroviral therapy for over 6 year (Table 2).

Distribution of 100 HIV negative individuals who were not on antiretroviral therapy showed more female patients, 60 (60.0%) than male patients 40 (40.0%). Distribution of HIV negative patients according to age showed that age group 60 – 80 years, 46 (46.0%) had the highest distribution of patients. Followed by age group 18 – 38 years, 29 (29.0%). The age group 39 – 59 years, 25 (25.0%) had the least distribution of patients. Distribution of patients according to length of antiretroviral drug usage was not applicable since group comprised HIV negative patients who were not on antiretroviral drug usage. According to previous history of urinary tract infections, 62 (62.0%) have had at least one prior episode of urinary tract infection while 38 (38.0%) have never had any prior episode of urinary tract infection (Table 3)

Table 2: Categories of ART patient distributions

Categories of distributions	Number of patients	Percentage (%)
GENDER		
Male	50	27.0
Female	135	73.0
Total	**185**	
AGE		
18 – 38	70	37.8
39 – 59	80	43.2
60 – 80	35	19.0
Total	**185**	
HISTORY OF UTI		
Yes	90	48.6
No	95	51.4
Total	**185**	
LENGTH OF ART USAGE		
<1yr	12	6.5
1 – 3yrs	82	44.3
4 – 6yrs	76	41.1
>6yrs	15	8.1
Total	**185**	

Table 3: Categories of non – ART patient distributions

Categories of distributions	Number of patients	Percentage (%)
GENDER		
Male	40	40.0
Female	60	60.0
Total	**100**	
AGE		
18 – 38	29	29.0
39 – 59	25	25.0
60 – 80	46	46.0
Total	**100**	
HISTORY OF UTI		
Yes	62	62.0
No	38	38.0
Total	**100**	

The overall CD_4+ values of test population was high. Those with CD_4+ values greater than 500 cells/µl, 138 (48.1%) had the highest distribution of patients. Followed by patients with CD_4+ values between 200 and 499 cells/µl, 96 (34.4%). Patients with CD_4+ values less than 200 cells/µl, 51 (17.5%) had the least distribution of patients.

Distribution of patients on antiretroviral drug usage according to CD_4+ values also showed that quite a majority of patients had high CD_4+ values. Patients with CD4+ values greater than 500 cells/µl, 90 (48.6%) had the highest distribution. Followed by patients with CD_4+ values between 200 and 499 cells/µl, 69 (37.3%). Patients with CD_4+ values less than 200 cells/µl, 26 (14.1%) had the least distribution of patients.

Distribution of patients who are not on antiretroviral drug usage according to CD_4+ values showed that patients with CD_4+ values greater than 500 cells/µl, 48 (48.0%) had the highest distribution of patients. Followed by patients with CD_4+ values between 200 and 499 cells/µl, 27 (27.0%). Patients with CD_4+ values less than 200 cells/µl, 25 (25.0%) had the least distribution of patients (Table 4).

Table 4: Patients distribution by CD_4+ values

CD_4+ values	Number of patients	Percentage (%)
OVERALL		
<200cells/µl	51	17.5
200 - 499cells/µl	96	34.4
>500cells/µl	138	48.1
Total	**285**	
ART USERS		
<200cells/µl	26	14.1
200 - 499cells/µl	69	37.3
>500cells/µl	90	48.6
Total	**185**	
NON – ART USERS		
<200cells/µl	25	25.0
200 - 499cells/µl	27	27.0
>500cells/µl	48	48.0
Total	**100**	

Overall distribution of CD_4+ values according to gender showed that males recorded lower distribution of patients than the females, irrespective of antiretroviral drug usage. Male patients with CD_4+ values greater than 500 cells/µl, 35 (37.8%) had the highest distribution of patients; followed by those with CD_4+ values between 200 and 499 cells/µl, 30 (34.4%). Male patients with CD_4+ values less than 200 cells/µl, 25 (27.8%) had the least distribution. Overall, female patients with CD_4+ values greater than 500 cells/µl, 103 (52.8%) had the highest distribution of patients; followed by those with CD_4+ values between 200 and 499 cells/µl, 66 (34.4%). Female patients with CD_4+ values less than 200 cells/µl, 26 (12.8%) had the least distribution.

Distribution of CD_4+ values according to gender, in patients on antiretroviral therapy, showed that 52% of male respondents had CD_4+ values greater than 500 cells/µl; followed by those with CD_4+ values less than 200 cells/µl, 13 (26.0%). Male patients with CD_4+ values between 200 and 499 cells/µl, 11 (22.0%) had the least distribution. Female patients with CD_4+ values greater than 500 cells/µl, 78 (57.8%) had the highest distribution of patients; followed by those with CD_4+ values between 200 and 499 cells/µl, 48 (35.6%). Female patients with CD_4+ values less than 200 cells/µl, 9 (5.2%) had the least distribution (Table).

Distribution of CD_4+ values according to gender, in patients who are not on antiretroviral therapy, showed that male patients with CD_4+ values between 200 and 499 cells/µl, 19 (47.5%) had the highest distribution of patients; followed by those with CD_4+ values less than 200 cells/µl, 12 (30.0%). Male patients with CD_4+ values greater than 500 cells/µl, 9 (22.5%) had the least distribution. In this category, female patients with CD_4+ values between 200 and 499 cells/µl, 28 (46.7%) had the highest distribution of patients; followed by those with CD_4+

values greater than 500 cells/µl, 25 (41.7%). Female patients with CD_4+ values less than 200 cells/µl, 17 (28.3%) had the least distribution (Table 5).

Table 5: CD_4+ distribution by gender

CD_4+ values	male	female	Total (%)
OVERALL			
<200cells/µl	25 (27.8)	26 (12.8)	51(17.5)
200 - 499cells/µl	30 (34.4)	66 (34.4)	96(34.4)
>500cells/µl	35 (37.8)	103 (52.8)	138(48.1)
Total	**90**	**195**	**285**
ART USERS			
<200cells/µl	13(26.0)	9(5.2)	22(11.9)
200 - 499cells/µl	11(22.0)	48(35.6)	59(31.9)
>500cells/µl	26(52.0)	78(57.8)	104(56.2)
Total	**50**	**135**	**185**
NON – ART USERS			
<200cells/µl	12 (30.0)	17(28.3)	29(29.0)
200 - 499cells/µl	19 (47.5)	28 (46.7)	47 (47.0)
>500cells/µl	9(22.5)	25 (41.7)	34(34.0)
Total	**40**	**60**	100

Overall distribution of CD_4+ values according to age group 18 – 38 years showed that the highest distribution of patients were those with CD_4+ values greater than 500 cells/µl, 58 (20.4%); followed by those with CD_4+ values between 200 and 499 cells/µl, 24 (8.4%). Patients with CD_4+ values less than 200 cells/µl, 18 (6.0%) had the least distribution of this age category. Distribution of CD_4+ values in age group 39 – 59 years; highest distribution of patients were those with CD_4+ values greater than 500 cells/µl, 42 (14.7%); followed closely by those with CD_4+ values between 200 and 499 cells/µl, 40 (14.4%). Patients with CD_4+ values less than 200 cells/µl, 23 (8.1%) had the least distribution in this age category. Distribution of CD_4+ values in age group 60 – 80 years; the highest distribution of patients were those with CD_4+ values greater than 500 cells/µl, 23 (12.4%); followed by those with CD_4+ values between 200 and 499 cells/µl, 22 (11.9%). Patients with CD_4+ values less than 200 cells/µl, 10 (3.5%) had the least distribution in this age category.

Distribution of CD_4+ values, in patients on antiretroviral therapy, according to age group 18 – 38 years showed that the highest distribution of patients were those with CD_4+ values greater than 500 cells/µl, 36 (19.5%); followed by those with CD_4+ values between 200 and 499 cells/µl, 14 (7.6%). Patients with CD_4+ values less than 200 cells/µl, 9 (4.9%) had the least distribution of this age category. Distribution of CD_4+ values in age group 39 – 59 years; highest distribution of patients were those with CD_4+ values between 200 and 499 cells/µl, 33 (17.8%); followed closely by those with CD_4+ values greater than 500 cells/µl, 31 (16.8%). Patients with CD_4+ values less than 200 cells/µl, 10 (5.4%) had the least distribution in this age category. Distribution of CD_4+ values in age group 60 – 80 years; the highest distribution of patients were those with CD_4+ values greater than 500 cells/µl, 23 (12.4%); followed by those with CD_4+ values between 200 and

499 cells/µl, 22 (11.9%). Patients with CD_4+ values less than 200 cells/µl, 7 (3.8%) had the least distribution in this age category.

Overall distribution of CD_4+ values, in patients who were not on antiretroviral drug usage, according to age group 18 – 38 years showed that the highest distribution of patients were those with CD_4+ values greater than 500 cells/µl, 22 (22.0%); followed by those with CD_4+ values between 200 and 499 cells/µl, 9 (9.0%) and patients with CD_4+ values less than 200 cells/µl, 9 (9.0%). Distribution of CD_4+ values in age group 39 – 59 years showed that the highest distribution of patients were those with CD_4+ values less than 200 cells/µl 13 (13.0%); followed closely by those with CD_4+ values greater than 500 cells/µl, 11 (11.0%). Patients with CD_4+ values between 200 and 499 cells/µl, 8 (8.0%) had the least distribution in this age category. Distribution of CD_4+ values in age group 60 – 80 years showed that the highest distribution of patients were those with CD_4+ values greater than 500 cells/µl, 15 (15.0%); followed by those with CD_4+ values between 200 and 499 cells/µl, 10 (10.0%). Patients with CD_4+ values less than 200 cells/µl, 3 (3.0%) had the least distribution in this age category (Table 6).

Table 6: CD_4+ distribution by age

Patient age	CD_4+ values	Number of patients	Percentage (%)
OVERALL			
18 – 38	<200	18	6.0
	200 - 499	24	8.4
	>500	58	20.4
39 – 59	<200	23	8.1
	200 - 499	40	14.4
	>500	42	14.7
60 – 80	<200	10	3.5
	200 – 499	22	11.9
	>500	23	12.4
ART USERS			
18 – 38	<200	9	4.9
	200 - 499	14	7.6
	>500	36	19.5
39 – 59	<200	10	5.4
	200 - 499	33	17.8
	>500	31	16.8
60 – 80	<200	7	3.8
	200 – 499	22	11.9
	>500	23	12.4
NON – ART USERS			
18 – 38	<200	9	9.0
	200 - 499	9	9.0
	>500	22	22.0
39 – 59	<200	13	13.0
	200 - 499	8	8.0
	>500	11	11.0
60 – 80	<200	3	3.0
	200 – 499	10	10.0
	>500	15	15.0

Overall distribution of CD_4+ values according to length of antiretroviral drug usage showed that the highest distribution of patients who were under one year of drug usage was among patients with CD_4+ values between 200 and 499 cells/µl, 11 (5.9%); followed by those with CD_4+ values greater than 500 cells/µl, 5 (2.7%). Patients with CD_4+ values less than 200 cells/µl, 3 (1.6%) had the least distribution in this category. The highest distribution of patients who were between 1 – 3 years of drug usage was among patients with CD_4+ values greater than 500 cells/µl, 31 (16.8%); followed by those with CD_4+ values between 200 and 499 cells/µl, 26 (14.1%). Patients with CD_4+ values less than 200 cells/µl, 16 (8.6%) had the least distribution in this category. The highest distribution of patients who were between 4 – 6 years of drug usage was among patients with CD_4+ values greater than 500 cells/µl, 40 (21.6%); followed by those with CD_4+ values between 200 and 499 cells/µl, 24 (13.0%). Patients with CD_4+ values less than 200 cells/µl, 4 (2.2%) had the least distribution in this category. The highest distribution of patients who were over six years of drug usage was among patients with CD_4+ values greater than 500 cells/µl, 14 (7.6%); followed by those with CD_4+ values between 200 and 499 cells/µl, 8 (4.3%). Patients with CD_4+ values less than 200 cells/µl, 3 (1.6%) had the least distribution in this category (Table 7).

Table 7: CD_4+distribution by length of ART use

CD_4+ values	Number of patients (%)			
	<1yr	1 – 3yrs	4 – 6yrs	>6yrs
<200	3(1.6%)	16(8.6%)	4(2.2%)	3(1.6%)
200 – 499	11(5.9%)	26(14.1%)	24(13.6%)	8(4.3%)
>500	5(2.7%)	31(16.8%)	40(21.6%)	14(7.6%)

Overall distribution of CD_4+ values according to previous history of urinary tract infections showed that that the highest distribution of patients who had at least one previous history of urinary tract infections was among patients with CD_4+ values greater than 500 cells/µl, 67 (23.5%); followed by those with CD_4+ values between 200 and 499 cells/µl, 50 (17.5%). Patients with CD_4+ values less than 200 cells/µl, 35 (12.3%) had the least distribution in this category. The highest distribution of patients who had never had any previous history of urinary tract infections was among those with CD_4+ values greater than 500 cells/µl, 71(24.9%); followed by those with CD_4+ values between 200 and 499 cells/µl, 46 (16.1%). Patients with CD_4+ values less than 200 cells/µl, 16 (5.6%) had the least distribution in this category.

Distribution of CD_4+ values, in patients on antiretroviral therapy, according to previous history of urinary tract infections showed that the highest distribution of patients was among patients with CD_4+ values greater than 500 cells/µl, 45 (24.3%); followed by those with CD_4+ values between 200 and 499 cells/µl, 38 (20.5%). Patients with CD_4+ values less than 200 cells/µl, 5 (2.7%) had the least distribution in this category. The highest distribution of patients who had never had any previous history of urinary tract infections was among those with CD_4+ values greater than 500 cells/µl, 65(35.1%); followed by those with CD_4+ values between 200 and 499 cells/µl, 26 (14.1%). Patients with CD_4+ values less than 200 cells/µl, 4 (2.2%) had the least distribution in this category.

Distribution of CD_4+ values in patients who were not on antiretroviral drug usage, according to previous history of urinary tract infections showed that the highest distribution was among patients with CD_4+ values less than 200 cells/µl, 30 (30.0%); followed by those with CD_4+ values greater than 500 cells/µl, 20 (20.0%). Patients with CD_4+ values between 200 and 499 cells/µl, 12 (12.0%) had the least distribution in this category. The highest distribution of patients who had never had any previous history of urinary tract infections was among those with CD_4+ values between 200 and 499 cells/µl, 20 (20.0%); followed by those with CD_4+ values less than 200 cells/µl, 12 (12.0%) (P = 0.655). Patients with CD_4+ values greater than 500 cells/µl, 6 (6.0%) had the least distribution in this category (Table 8).

Table 8: CD_4+distribution by history of UTI

CD_4+ values	YES	NO
OVERALL		
<200	35(12.3%)	16(5.6%)
200 – 499	50(17.5%)	46(16.1%)
>500	67(23.5%)	71(24.9%)
ART USE		
<200	5(2.7%)	4(2.2%)
200 – 499	38(20.5%)	26(14.1%)
>500	45(24.3%)	65(35.1%)
NON ART USE		
<200	30(30.0%)	12(12.0%)
200 – 499	2(12.0%)	20(20.0%)
>500	20(20.0%)	6(6.0%)

Table 9 shows the overall prevalence of urinary tract infections. Generally, there was no significant difference in the prevalence of urinary tract infections between HIV patients on antiretroviral therapy and HIV negative patients who are not on antiretroviral therapy. Of the two hundred and eighty five patients enrolled, a little over half of the patients, 143 (50.2%) had urinary tract infections; while 142 (49.8%) had no urinary tract infections. Out of the one hundred and eighty five patients who were on antiretroviral drug usage, 133 (71.9%) had urinary tract infections while 52 (28.1%) had no urinary tract infections. Of the one hundred patients who were not on antiretroviral drug usage, 10 (10.0%) had urinary tract infections while 90 (90%) had no urinary tract infections. The prevalence of urinary tract infections was significantly higher in patients on antiretroviral drug usage than patients who are not on antiretroviral therapy. However, there was no statistically significant association with urinary tract infections and antiretroviral drug usage ($P = 0.780$). Null hypothesis (H_O) assumes that there is significant association between urinary tract infections and antiretroviral drug usage. The P value suggests the alternative.

Likewise there were no statistically significant associations between urinary tract infections and associated host factors like gender ($P = 0.199$), age ($P = 0.157$), CD_4+ values ($P = 0.655$), length of antiretroviral drug usage ($P = 0.124$) and previous history of urinary tract infections ($P = 0.968$).

Table 9: Prevalence of urinary tract infections

Urinary tract infections	Number of patients	Percentage (%) P value
OVERALL		
Positive	143	50.2
Negative	142	49.8
Total	**285**	
ART USERS		
Positive	133	71.9
Negative	52	28.1
Total	**185**	
NON – ART USERS		
Positive	10	10.0
Negative	90	90.0
Total	**100**	

Table 10 shows the prevalence of urinary tract infections according to gender. Of the ninety male patients enrolled, 23 (8.0%) had urinary tract infections while 67 (23.5%) had no urinary tract infections. Of the one hundred and ninety five female enrolled, 120 (42.1%) had urinary tract infections while 75 (26.3%) had no urinary tract infections. Out of a total of fifty male patients who were on antiretroviral drug usage, 20 (10.8%) had urinary tract infections while 30 (16.2%) had no urinary tract infections. Of a total of one hundred and thirty five female patients on antiretroviral drug usage, 113 (61.1%) while 22 (11.8%) had no urinary tract infections. Of a total of forty male patients who were not on antiretroviral drug usage, 3 (3.0%) had urinary tract infections while 37 (37.0%) had no urinary tract infections. Out of a total of sixty female patients who were not on antiretroviral drug usage, 7 (7.0%) had urinary tract infections while 53 (53.0%) had no urinary tract infections.

Overall prevalence of urinary tract infections was significantly higher in female patients than the male patients (P = 0.199). Female patients on antiretroviral drug usage recorded five times more prevalence of urinary tract infections than the males. Female patients who were not on antiretroviral drug usage recorded twice more prevalence of urinary tract infections than their male counterparts. The male patients were less likely to have urinary tract infections irrespective of antiretroviral drug usage. Similarly, the female patients were more likely to have urinary tract infections irrespective of antiretroviral drug usage. Irrespective of gender, female patients on antiretroviral drug usage had higher prevalence of urinary tract infections more than those who were not on antiretroviral therapy. However, there was no statistically significant association with urinary tract infections and patients' gender (P = 0.199). Null hypothesis (H_O) assumes that

there is significant association between urinary tract infections and patients' gender. The P value suggests the alternative (Table 12).

Table 10: Prevalence of urinary tract infections by gender

Gender	Positive UTI (%)	Negative UTI (%)	Total
OVERALL			
Male	23 (16.1)	67 (47.2)	90
Female	120 (83.9)	75 (52.8)	195
ART USERS			
Male	20 (15.0)	30(17.0)	50
Female	113 (85.0)	22 (57.7)	135
NON – ART USERS			
Male	3(30.0)	37 (41.1)	40
Female	7 (70.0)	53 (58.9)	60

Table 11 shows the prevalence of urinary tract infections according to patients' age. High prevalence of urinary tract infections were generally observed in patients who fell within the two age group extremities. Overall, of a total of 285 patients, age group 18 – 38 years, 54 (18.9%) had the highest prevalence of urinary tract infections; followed by patients within age group 60 – 80 years, 51 (17.9%). The age group 39 – 59 years, 38 (13.3%) had the least prevalence of urinary tract infections. Prevalence of urinary tract infections according to age in patients who are on antiretroviral drug usage showed that of a total of 185 patients, those within 18 – 38 years, 52 (28.1%) had the highest prevalence of urinary tract infections; followed by patients within age group 60 – 80 years, 48 (25.9%). Patients within the age group 39 – 59 years, 33 (17.8%) had the least prevalence of urinary tract infections in this category. Prevalence of urinary tract infections according to age in patients who were not on antiretroviral drug usage showed that patients within 39 – 59 years, 5 (5.0%) had the highest prevalence of urinary tract infections; followed by patients within age group 60 – 80 years, 3 (3.0%). Patients within age group 18 – 38 years, 2 (2.0%) had the least prevalence of urinary tract infections in this category.

Irrespective of age category, patients on antiretroviral drug usage had higher prevalence of urinary tract infections more than those who were not on antiretroviral therapy. However, there was no statistically significant association with urinary tract infections and patients' age ($P = 0.157$). Null hypothesis (H_O) assumes that there is significant association between urinary tract infections and patients' gender. The P value suggests the alternative (Table 12).

Table 11: Prevalence of urinary tract infections by age

Age	Positive UTI (%)	Negative UTI (%)	Total (%)
OVERALL			
18 – 38	54 (18.9)	45 (15.8)	99 (34.7)
39 – 59	38 (13.3)	67 (23.5)	105 (36.8)
60 – 80	51 (17.9)	30 (10.5)	81 (28.4)
ART USERS			
18 – 38	52 (39.1)	12 (23.1)	64 (34.6)
39 – 59	33 (24.8)	31 (59.6)	64 (34.6)
60 – 80	48 (36.1)	9 (17.3)	57 (30.8)
NON ART USERS			
18 – 38	2 (20.0)	33(36.7)	35(35.0)
39 – 59	5 (50.0)	36(40.0)	41(41.0)
60 – 80	3 (30.0)	21(23.3)	24(24.0)

Table 12: Significance of age and gender in the prevalence of UTI

	No. of patients with UTI				
	Obs. Result	**Exp. Result**	**Lev. Sig**	**P - value**	**(χ2)**
ART					
18-38	52.0	50.2	<0.05	0.157	0.200
39-59	33.0	35.3			
60-80	48.0	47.4			
NON ART					
18-38	2.0	3.8			
39-59	5.0	2.7			
60-80	3.0	3.7			
ART					
Male	20.0	21.4	<0.05	0.199	0.259
Female	113.0	111.6			
NON ART					
Male	3.0	1.72			
Female	7.0	8.39			

Key:

Obs. result: Observed Result, Exp. Result: Expected Result, Lev.sig: Level of significance, (χ2): chi – square value.

Table 13 shows the prevalence of urinary tract infections according to length of antiretroviral drug usage. Highest prevalence of urinary tract infections were observed in patients who had been on antiretroviral drug usage within one to three years, 58 (31.4%); followed by patients who had been on antiretroviral drug usage within four to six years, 52 (28.6%) and patients who had been on antiretroviral drug usage over six years, 12 (6.5%). Patients who were under antiretroviral drug usage for less than one year, 11 (5.9%) had the least prevalence of urinary tract infections in this category.

Figure 1 shows a steady and incremental observation in the prevalence of urinary tract infections after the commencement of antiretroviral drug usage. There seemed to be a sharp increase in prevalence of urinary tract infections, the progression gradually peaks between 1 – 3 years after commencement of antiretroviral drug usage, after which it gradually declines. However, there was no statistically significant association with urinary tract infections and length of antiretroviral drug usage ($P = 0.124$). Null hypothesis (H_O) assumes that there is significant association between urinary tract infections and length of antiretroviral drug usage. The P value suggests the alternative (Table 15).

Table 13: Prevalence of UTI by length of ART use

History	Positive UTI (%)	Negative UTI (%)	Percentage (%)
<1yr	11 (8.3)	1 (1.9)	12 (6.5)
1 – 3yrs	58 (43.6)	24 (46.2)	82 (44.3)
4 – 6yrs	52 (36.1)	24(46.2)	76 (41.1)
>6yrs	12 (12.0)	3 (5.8)	15 (8.1)

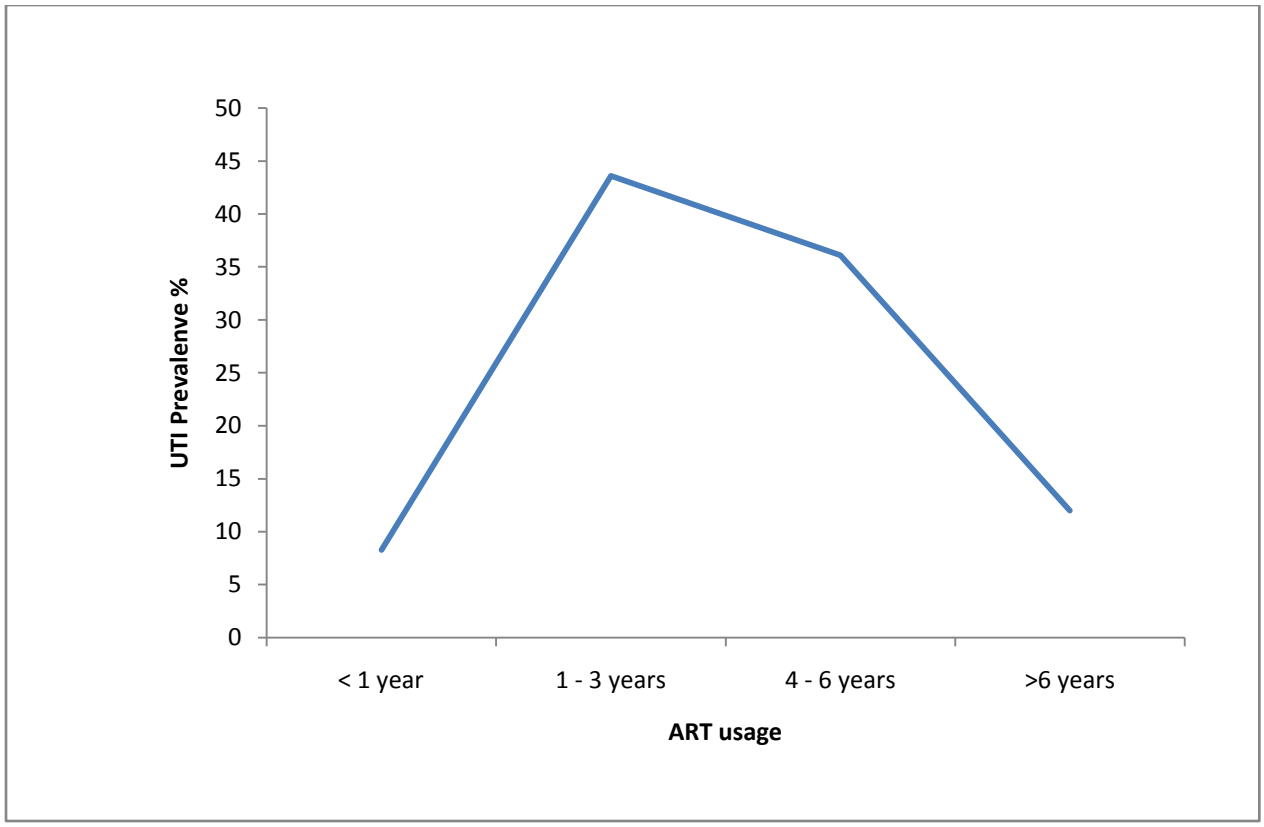

Figure 1: UTI prevalence by length of ART usage

Table 14 shows the prevalence of urinary tract infections according to patients' previous history of urinary tract infections. In patients on antiretroviral drug usage, higher prevalence of urinary tract infections was observed in those who have had at least one previous episode of urinary tract infections. Out of 185 antiretroviral drug users, 122 (65.9%) had urinary tract infections; while urinary tract infection prevalence rate of 63 (34.1%) was observed in those who have never had any previous history of urinary tract infections. In patients who were not on antiretroviral drug usage, higher prevalence of urinary tract infections was observed in those who have never had any previous episode of urinary tract infections, 70 (70.0%); while urinary tract infection prevalence rate of 30 (30.0%) was observed in those who have had at least one previous episode of urinary tract infections.

Irrespective of antiretroviral drug usage, patients who have had at least one episode of urinary tract infection had higher prevalence of urinary tract infections more than those who were not on antiretroviral therapy. However, there was no statistically significant association with urinary tract infections and patients' previous history of urinary tract infections ($P = 0.968$). Null hypothesis (H_O) assumes that there is significant association between urinary tract infections and patients' previous history of urinary tract infections. The P value suggests the alternative (Table 15).

Table 14: Prevalence of UTI according to history of urinary tract infections.

CD_4+ values	Positive UTI	Percentage (%)
OVERALL		
YES	133	46.7
NO	152	53.3
ART USE		
YES	122	65.9
NO	63	34.1
NON ART USE		
YES	30	30.0
NO	70	70.0

Table 15: Significance of length of ART usage & previous history of UTI in the prevalence of UTI

	No. of patients with UTI				
	Obs. Result	**Exp. Result**	**Lev.Sig.**	**P - value**	**(χ2)**
<1yr	11	8.63	<0.05	0.124	0.34
1 – 3 yrs	58	58.95			
4 – 6 yrs	52	54.64			
>6 yrs	12	10.78			
UTI HISTORY					
ART					
YES	90	98.7	<0.05	0.968	0.31
NO	95	86.3			
Non ART					
YES	62	53.3			
NO	38	46.7			

Key:

Obs. result: Observed Result, Exp. Result: Expected Result, Lev.Sig: Level of significance, (χ2): chi – square value.

Table 16 shows the prevalence of urinary tract infections according to patients' CD_4+ values. Overall, out of the 51 patients with CD_4+ values less than 200 cells/µl, 20 (7.0%) had urinary tract infections; of the 96 patients with CD_4+ values within 200 – 499 cells/µl, 53 (18.6%) had urinary tract infections and out of the 138 patients with CD_4+ values greater than 500 cells/µl, 70 (24.6%) had urinary tract infections.

Prevalence of urinary tract infections according to CD_4+ values, in patients who are on antiretroviral drug usage, showed that the highest prevalence of urinary tract infections was among patients with CD_4+ values greater than 500 cells/µl, 76 (41.1%); followed by patients with CD_4+ values between 200 – 499 cells/ µl, 43 (32.3%). Patients with CD_4+ values less than 200 cells/µl, 14 (7.6%) had the least prevalence of urinary tract infections.

Prevalence of urinary tract infections according to CD_4+ values, in patients who are not on antiretroviral drug usage, showed that the highest prevalence of urinary tract infections was among patients with CD_4+ values less than 200 cells/µl, 6 (6.0%); followed by patients with CD_4+ vales greater than 500 cells/µl, 4 (4.0%). Patients with CD_4+ values between 200 – 499 cells/ µl, 0 (0%) had the least prevalence of urinary tract infections.

Patients on antiretroviral drug usage had higher prevalence of urinary tract infections more than those who were not on antiretroviral therapy, irrespective of CD_4+ values. However, there was no statistically significant association with urinary tract infections and patients' CD_4+ values (P = 0.655). Null hypothesis (H_O) assumes that there is significant association between urinary tract infections and patients' CD_4+ values. The P value suggests the alternative (Table 17).

Table 16: Prevalence of urinary tract infections by CD_4+ values

CD_4 +	Positive UTI (%)	Negative UTI (%)	Total (%)
OVERALL			
<200cells/µl	20 (13.9)	31 (21.8)	51
200 - 499cells/µl	53 (37.1)	43 (30.3)	96
>500cells/µl	70 (49.0)	68 (47.9)	138
ART USERS			
<200cells/µl	14 (10.5)	12 (23.1)	26
200 - 499cells/µl	43 (32.3)	26 (50.0)	69
>500cells/µl	76 (57.1)	14 (26.9)	90
NON ART USERS			
<200cells/µl	6 (60.0)	19 (21.1)	25
200 - 499cells/µl	0 (0)	27 (30.0)	27
>500cells/µl	4 (40.0)	44 (48.9)	48

Table 17: Significance of CD_4+ in the prevalence of UTI

	No. of patients with UTI				
	Obs. Result	**Exp. Result**	**Lev. Sig**	**P - value**	**(χ2)**
ART					
< 200cells/µl	14.0	18.6	<0.05	0.655	4.54
200 – 499cells/µl	43.0	40.0			
>500 cells/µl	76.0	74.4			
NON ART					
< 200cells/µl	6.0	1.4			
200 – 499cells/µl	0	3.0			
>500 cells/µl	4.0	5.6			

Key:

Obs. result: Observed Result, Exp. Result: Expected Result, Lev.sig: Level of significance, (χ2): chi – square values.

Nine different etiologic agents were isolated from urine culture of patients on antiretroviral drug usage whereas only four types of bacteria were isolated from patients who were not on antiretroviral drug usage: *Escherichia coli, Staphylococcus aureus, Klebsiella pneumonia*, *Enterococcus faecalis, Proteus mirabilis, Pseudomonas aeruginosa, Streptococcus pyogenes*, *Candida albicans* and *Staphylococcus epidermidis*

In the overall distribution of isolated etiologic agents, the most implicated isolate responsible for urinary tract infections in HIV positive individuals was *Escherichia coli* 49 (34.3%); followed by *Staphylococcus epidermidis* 33 (23.1%), *Staphylococcus aureus* 26 (18.2%), *Klebsiella pneumonia* 12 (8.4%), *Enterococcus faecalis* 7 (4.9%), *Proteus mirabilis* 7 (4.9%), *Pseudomonas aeruginosa* 5 (3.5%), *Streptococcus pyogenes* 3 (2.1%) and *Candida albicans* 1 (0.7%). Table 18

Table 18: Isolated etiologic agents

Isolate	Number of patients	Percentage (%)
Escherichia coli	49	34.3
K. pneumoniae	12	8.4
P. aeruginosa	5	3.5
S. aureus	26	18.2
E. faecalis	7	4.9
S. pyogenes	3	2.1
S. epidermidis	33	23.1
P. mirabilis	7	4.9
C. albicans	1	0.7
Total	**143**	**100**

Table 19 shows the prevalence of etiologic agents according to antiretroviral drug usage. Patients on antiretroviral drug usage showed the following etiologic agent prevalence: *Escherichia coli* 45 (33.8%); *Staphylococcus epidermidis* 31 (23.3%), *Staphylococcus aureus* 26 (19.5%), *Klebsiella pneumonia* 10 (7.5%), *Enterococcus faecalis* 7 (5.3%), *Proteus mirabilis* 7 (5.2%), *Pseudomonas aeruginosa* 3 (2.3%), *Streptococcus pyogenes* 3 (2.3%) and *Candida albicans* 1 (0.8%).

Patients who were not on antiretroviral drug usage showed the following etiologic agent prevalence: *Escherichia coli* 4 (4.0%); *Klebsiella pneumonia* 2 (2.0%), *Pseudomonas aeroginosa* 2 (2.0%), *Staphylococcus epidermidis* 2 (2.0%),

Table 19: Prevalence of isolated etiologic agents

Isolate	Number of patients	Percentage (%)
ART USERS		
Escherichia coli	45	33.8
S.epidermidis	31	23.3
S. aureus	26	19.5
K. pneumoniae	10	7.5
E. faecalis	7	5.3
P. mirabilis	7	5.2
P. aeruginosa	3	2.3
S. pyogenes	3	2.3
C. albicans	1	0.8
NON – ART USERS		
Escherichia coli	4	4.0
K. pneumoniae	2	2.0
P. aeruginosa	2	2.0
S.epidermidis	2	2.0
Total	**143**	**100**

According to Table 20, gram negative bacteria were the predominant isolates 73 (51.0%) compared to gram positive bacteria which comprise 70 (49.0%) table. In the study, four gram negative organisms, *Escherichia coli, Klebsiella pneumonia, Proteus mirabilis, Pseudomonas aeruginosa* and five gram positive organisms, *Staphylococcus epidermidis*, *Staphylococcus aureus, Enterococcus faecalis*, *Streptococcus pyogenes* and *Candida albicans* were isolated. The most predominant gram negative isolate was *Escherichia coli* while the most predominant gram positive organism was *Staphylococcus epidermidis*. There was almost a 50/50 chance of isolating either a gram positive or a gram positive organism.

Table 20: Etiologic agents by Grams reaction

Etiology	Number of patients	Percentage
Gram neg		
Escherichia coli	49	34.3
K. pneumoniae	12	8.4
P. aeruginosa	5	3.5
P. mirabilis	7	4.9
	73	**51.0**
Gram pos		
S. aureus	26	18.2
E. faecalis	7	4.9
S. pyogenes	3	2.1
S. epidermidis	33	23.1
C. albicans	1	0.7
	70	**49.0**

Table 21 shows the prevalence of etiologic agents according to gender. Higher distributions of eight etiologic agents were observed in the female patients more than the male patients; out of a total of forty nine *Escherichia coli* isolates, 43 (30.1%) were obtained from female patients; while 6 (4.1%) were isolated from the male patients. Of the thirty three *Staphylococcus epidermidis* isolates, 23 (16.1%) were obtained from the female patients; while 10 (6.9%) were isolated from the male patients. Out of twenty six *Staphylococcus aureus* isolates, 24 (16.8%) were obtained from the female patients; while 2 (1.4%) were isolated from the male patients. Higher distribution of one etiologic agent was observed in the male patients more than the female patients: out of seven *Proteus mirabilis isolates*, 5 (3.5%) were isolated from the male patients; while 2 (1.4%) were isolated from the female patients.

The rest of the etiologic agents were only isolated from the female patients; *Klebsiella pneumonia* 12 (8.4%), *Enterococcus faecalis* 7 (4.9%), *Pseudomonas aeruginosa* 5 (3.5%), *Streptococcus pyogenes* 3 (2.1%) and *Candida albicans 1* (0.7%).

Table 21: Prevalence of etiologic agents according to gender

Gender	Isolate	Number of patients	Percentage (%)
OVERALL			
Male	*Escherichia coli*	6	26.1
	S. epidermidis	10	43.5
	S. aureus	2	8.7
	P. mirabilis	5	21.7
Total		**23**	
Female	*Escherichia* coli	43	35.8
	S. epidermidis	23	19.2
	S. aureus	24	20.0
	K. pneumonia	12	10.0
	E. faecalis	7	5.8
	P. aeruginosa	5	4.2
	S. pyogenes	3	2.5
	P. mirabilis	2	1.7
	C. albicans	1	0.3
Total		**120**	

Table 22 shows the prevalence of etiologic agents according to age. Highest spectrum of organisms was observed among patients within the 18 – 38 years age group. Highest distributions of *Escherichia coli* were observed in the patients within the 18 – 38 years age groups, 26 (18.2%); followed by patients within the 39 – 59 age groups, 14 (9.8%). Patients within age group 60 – 80 years had the least distribution, 9 (6.3%). Highest distributions of *Staphylococcus epidermidis* were observed in patients within 60 – 80 years, 14 (9.8%); followed by patients within 18 – 38 years age group, 11 (7.7%). Patients within age group 39 – 59 years had the least distribution, 8 (5.6%). Highest distribution of *Staphylococcus aureus* were observed in patients within 60 – 80 years, 11 (7.7%); followed by patients within age group 31 – 45 years, 9 (6.3%). Patients within age group 18 – 38 years had the least distribution, 5 (3.5%). Higher distributions of *Klebsiella pneumonia* were observed in patients within the 39 – 59 and 60 – 80 age groups, 4 (2.4%). Patients within age group 18 – 38 years had the least distribution, 3 (2.1%). Highest distributions of *Proteus mirabilis* were observed in patients within 60 – 80 years, 4 (2.8%); followed by patients within 18 – 38 years age group, 2 (1.4%) and those within the age group 39 – 59 years, 1 (0.7%). Higher distribution of *Pseudomonas aeruginosa* was observed in patients within age group 18 – 38 years, 3 (2.1%); while those in age group 39 – 59 years, 2 (1.4%), had the lesser distribution. Equal distribution of *Streptococcus pyogenes* was observed in patients within age group 18 – 38 years and 39 – 59 years, 2 (1.4%). Distribution of *Enterococcus faecalis*, 7 (4.9%) was only observed in patients within the 46 – 75 years age group, while *Candida albicans*, 1 (0.7%) was only observed in patients within the 18 – 38 years age group.

Table 22: Prevalence of etiologic agents according to age

Age	Isolate	Number of patients	Percentage
18 – 38	*Escherichia coli*	26	48.1
	S. epidermidis	11	20.4
	S. aureus	5	9.3
	K. pneumonia	3	5.6
	P. aeruginosa	3	5.6
	S. pyogenes	2	3.7
	P. mirabilis	2	3.7
	C. albicans	1	1.9
39 – 59	*Escherichia coli*	14	35.9
	S. aureus	9	23.1
	S. epidermidis	8	12.8
	K. pneumonia	4	10.3
	S. pyogenes	2	5.1
	P. aeruginosa	2	5.1
	P. mirabilis	1	2.6
60 – 80	*S. epidermidis*	14	28.0
	S. aureus	11	22.0
	Escherichia coli	9	16.0
	E. faecalis	7	14.0
	K. pneumonia	4	8.0
	P. mirabilis	4	8.0

Table 23 shows the prevalence of etiologic agents according to length of antiretroviral therapy usage, all the isolated spectrum of organisms was obtained from patients on ART. The highest spectrum of organisms was observed in patients who had been on antiretroviral usage between four to six years.

The highest prevalence of *Escherichia coli* was observed in patients who had been on antiretroviral dug usage between one to three years, 29 (21.8%); followed by patients who had been on antiretroviral drug usage between four to six years, 11 (8.3%); then by patients who had been on antiretroviral therapy for less than one year, 5 (3.8%). Patients who had been on antiretroviral drug usage for over six years, 4 (3.5%) had the least prevalence of *Escherichia coli.*

The highest prevalence of *Staphylococcus epidermidis* was observed in patients who had been on antiretroviral dug usage between four to six years, 17 (12.8%); followed by patients who had been on antiretroviral drug usage between one to three years 10 (7.5). Patients who had been on antiretroviral drug usage for less than one year and over six years, 3 (2.3%) had the least prevalence of *Staphylococcus epidermidis.*

The highest prevalence of *Staphylococcus aureus* was observed in patients who had been on antiretroviral dug usage between one to three years, 13 (9.8%); followed by patients who had been on antiretroviral drug usage between four to six years, 9 (6.7%); then by patients who had been on antiretroviral therapy for over six years, 3 (2.3%). Patients who had been on antiretroviral drug usage for less than one year, 1 (0.7%) had the least prevalence of *Staphylococcus aureus.*

The highest prevalence of *Klebsiella pneumoniae* was observed in patients who had been on antiretroviral dug usage between one to three years, 8 (6.3%); followed by patients who had been on antiretroviral drug usage between four to six

years, 3 (2.3%); then by patients who had been on antiretroviral therapy for less than one year, 1 (0.7%). Patients who had been on antiretroviral drug usage for over six years, 0 (0%) had the least prevalence of *Klebsiella pneumonia.*

The highest prevalence of *Pseudomonas aeruginosa* was observed in patients who had been on antiretroviral dug usage between one to three years, 3 (2.3%); followed by patients who had been on antiretroviral drug usage between four to six years, 2 (1.5%). Patients who had been on antiretroviral drug usage for less than one year and over six years, 0 (0%) had the least prevalence of *Pseudomonas aeruginosa.*

The highest prevalence of *Enterococcus faecalis* was observed in patients who had been on antiretroviral dug usage between four to six years, 5 (3.8%); followed by patients who had been on antiretroviral drug usage between one to three years, 2 (1.5%). Patients who had been on antiretroviral drug usage for less than one year and over six years, 0 (0%) had the least prevalence of *Pseudomonas aeruginosa.*

The highest prevalence of *Streptococcus pyogenes* was observed in patients who had been on antiretroviral dug usage between four to six years, 2 (1.5%); followed by patients who had been on antiretroviral drug usage between one to three years, 1 (0.7%). Patients who had been on antiretroviral drug usage for less than one year and over six years, 0 (0%) had the least prevalence of *Streptococcus pyogenes.*

The highest prevalence of *Proteus mirabilis* was observed in patients who had been on antiretroviral dug usage between four to six years, 3 (2.3%); followed by patients who had been on antiretroviral drug usage between one to three years and those over six years of antiretroviral drug usage, 2 (1.5%). Patients who had been on antiretroviral drug usage for less than one year 0 (0%) had the least prevalence of *Proteus mirabilis.*

The highest prevalence of *Candida albicans* was observed in patients who had been on antiretroviral dug usage between four to six years, 1 (0%). Patients who had been on antiretroviral drug usage between less than one year, one to three years and over six years, 0 (0%) had the least prevalence of *Candida albicans.*

Table 23: Prevalence of etiologic agents according to length of antiretroviral therapy usage

Age	Isolate	Number of patients	Percentage
<1 yr	*Escherichia coli*	*5*	3.8
	Staphylococcus epidermidis	3	2.3
	Staphylococcus aureus	1	0.7
	Klebsiella pneumoniae	1	0.7
1 – 3 yrs	*Escherichia coli*	29	21.8
	Staphylococcus epidermidis	10	7.5
	Staphylococcus aureus	13	9.8
	Klebsiella pneumonia	8	6.3
	Pseudomonas aeruginosa	3	2.3
	Enterococcus faecalis	2	1.5
	Streptococcus pyogenes	1	0.7
	Proteus mirabilis	2	1.5
4 – 6 yrs	*Escherichia coli*	11	8.3
	Staphylococcus epidermidis	17	12.8
	Staphylococcus aureus	9	6.7
	Klebsiella pneumoniae	3	2.3
	Pseudomonas aeruginosa	2	1.5
	Enterococcus faecalis	5	3.8
	Streptococcus pyogenes	2	1.5
	Proteus mirabilis	3	2.3
	Candida albicans.	1	0.7
> 6yrs	*Escherichia coli*	4	3.5
	Staphylococcus epidermidis	3	2.3
	Staphylococcus aureus	3	2.3
	Proteus mirabilis	2	1.5

Table 24 shows the prevalence of etiologic agents according to previous history of urinary tract infections. More spectrums of organisms were observed in patients who had previous episodes of urinary tract infections more than those who never had any episode of urinary tract infections. The higher prevalence of *Escherichia coli* was observed in patients who have had at least one previous episode of urinary tract infection, 27 (19.8%); while patients who have never had any episode of urinary tract infections had *Escherichia coli* prevalence of 22 (16.5%). The higher prevalence of *Staphylococcus epidermidis* was observed in patients who have never had any previous episode of urinary tract infection, 26 (19.5%); while patients who have had at least one episode of urinary tract infections had *Staphylococcus epidermidis* prevalence of 7 (4.6%). The higher prevalence of *Staphylococcus aureus* was observed in patients who have had at least one previous episode of urinary tract infection, 18 (11.8%); while patients who have never had any episode of urinary tract infections had prevalence of 8 (6.0%). The higher prevalence of *Klebsiella pneumoniae* was observed in patients who have never had any episode of urinary tract infections, 6 (4.5%); while patients who have had at least one previous episode of urinary tract infection had *Klebsiella pneumoniae* prevalence of 6 (3.9%).

The higher prevalence of *Streptococcus pyogenes* was observed in patients who have had at least one previous episode of urinary tract infections, 2 (1.3%); while patients who have never had any episode of urinary tract infections had prevalence of 1 (0.8%). The higher prevalence of *Proteus mirabilis* was observed in patients who have never had any episode of urinary tract infections, 6 (4.5%); while patients who have had at least one previous episode of urinary tract infection had prevalence of 1 (0.7%). *Pseudomonas aeruginosa*, 5 (3.3%) and *Candida albicans*

1 (0.7%) were observed in patients who have had at least one episode of urinary tract infections.

Table 24: Prevalence of etiologic agents according to previous history of urinary tract infections.

History	Isolate	Number of patients	Percentage (%)
OVERALL			
YES	*Escherichia coli*	27	40.3
	S. epidermidis	7	10.4
	S. aureus	18	26.9
	K. pneumonia	6	9.0
	P. aeruginosa	5	7.5
	S. pyogenes	2	3.0
	P. mirabilis	1	1.5
	C. albicans	1	1.5
NO	*Escherichia coli*	22	28.9
	S. epidermidis	26	34.2
	S. aureus	8	10.5
	E. faecalis	7	9.2
	K. pneumonia	6	7.9
	S. pyogenes	1	1.3
	P. mirabilis	6	7.9

Table 25 shows the prevalence of etiologic agents according to patients' CD_4+ values. Overall, the highest prevalence of *Escherichia coli* was observed in patients with CD_4+ values within 200 – 499 cells/µl, 21 (7.4%); followed by patients with CD_4+ values greater than 500 cells/µl, 19 (6.7%). Patients with CD_4+ values of less than 200 cells/µl, 9 (3.2%); had the least prevalence of *Escherichia coli.* It was observed that the highest prevalence of *Staphylococcus epidermidis* was observed in patients with CD_4+ values greater than 500 cells/µl, 15 (5.3%); followed by patients with CD_4+ values within 200 – 499 cells/µl, 12 (4.2%). Patients with CD_4+ values of less than 200 cells/µl, 8 (2.8%); had the least prevalence of *Staphylococcus epidermidis*. The highest prevalence of *Staphylococcus aureus* was observed in patients with CD_4+ values within 200 – 499 cells/µl, 16 (5.6%); followed by patients with CD_4+ values greater than 500 cells/µl, 10 (3.5%). Patients with CD_4+ values less than 200 cells/µl, 3 (1.1%) had the least prevalence of *Staphylococcus aureus.* The highest prevalence of *Streptococcus pyogenes* was observed in patients with CD_4+ values within 200 – 499 cells/µl and those with CD_4+ values greater than 500 cells/µl, 2 (0.7%). Patients with CD_4+ values of less than 200 cells/µl, 0 (0%); had the least prevalence of *Streptococcus pyogenes.*

The highest prevalence of *Klebsiella pneumonia* was observed in patients with CD_4+ values greater than 500 cells/µl, 10 (3.5%); followed by patients with CD_4+ values less than 200 cells/µl, 3 (1.1%). Patients with CD_4+ values within 200 – 499 cells/µl, 1 (0.4%) had the least distribution of *Klebsiella pnuemoniae*. The highest prevalence of *Pseudomonas aeruginosa* was observed in patients with CD_4+ value of less than 200 cells/µl, 3 (1.1%); followed by patients with CD_4+ count greater than 500 cells/µl, 2 (0.7%). Patients with CD_4+ values within 200 – 499 cells/µl, 0 (0%) had the least prevalence of *Pseudomonas aeruginosa.* The highest prevalence of *Proteus mirabilis* was observed in patients CD_4+ values greater than 500

cells/µl, 5 (1.8%); followed by patients with CD_4+ values within 200 – 499 cells/µl, 1 (0.4%). Patients with CD_4+ values of less than 200 cells/µl, 0 (0%) had the least prevalence of *Proteus mirabilis*. The highest prevalence of *Enterococcus faecalis* was observed in patients with CD_4+ values of greater than 500 cells/µl, 8 (2.8%); followed by patients with CD_4+ values within 200 – 499 cells/µl, 2 (0.7%). Patients with CD_4+ values of less than 200 cells/µl, 0 (0%) had the least prevalence of *Enterococcus faecalis*. The highest prevalence of *Candida albicans* was observed in patients with CD_4+ values of greater than 500 cells/µl, 1 (0.4%). Patients with CD_4+ values within 200 – 499 cells/µl and those with CD_4+ values of less than 200 cells/µl, 0 (0%) had the least prevalence of *Candida albicans*.

Table 25: Overall prevalence of etiologic agents according to CD_4+ values

Organism	***<200cells/µl***	***200 - 499cells/µl***	***>500cells/µl***
E, coli	9 (3.2%)	21(7.4%)	19(6.7%)
S. epidermidis	8(2.8%)	12(4.2%)	15(5.3%)
S. aureus	3(1.1%)	16(5.6%)	10(3.5%)
S. pyogenes	0(0%)	2(0.7%)	2(0.7%)
K. pneumoniae	3(1.1%)	1(0.4%)	10(3.5%)
P. aeroginosa	3(1.1%)	0(0%)	2(0.7%)
P. mirabilis	0(0%)	1(0.4%)	5(1.8%)
E. faecalis	0(0%)	2(0.7%)	8(2.8%)
C. albicans	0(0%)	0(0%)	1(0.4%)

Table 26 shows the prevalence of etiologic agents according to CD_4+ values in patients who are on antiretroviral drug usage. The highest prevalence of *Escherichia coli* was observed in patients with CD_4+ values within 200 – 499 cells/µl, 21 (11.4%); followed by patients with CD_4+ values greater than 500 cells/µl, 17 (9.2%). Patients with CD_4+ values of less than 200 cells/µl, 8 (4.5%); had the least prevalence of *Escherichia coli.* It was observed that the highest prevalence of *Staphylococcus epidermidis* was observed in patients with CD_4+ values greater than 500 cells/µl, 15 (8.1%%); followed by patients with CD_4+ values within 200 – 499 cells/µl, 12 (6.5%). Patients with CD_4+ values of less than 200 cells/µl, 5 (2.7%); had the least prevalence of *Staphylococcus epidermidis*. The highest prevalence of *Staphylococcus aureus* was observed in patients with CD_4+ values within 200 – 499 cells/µl, 16 (8.6%); followed by patients with CD_4+ values greater than 500 cells/µl, 10 (5.4%). Patients with CD_4+ values less than 200 cells/µl, 3 (1.6%) had the least prevalence of *Staphylococcus aureus* The highest prevalence of *Streptococcus pyogenes* was observed in patients with CD_4+ values within 200 – 499 cells/µl and those with CD_4+ values greater than 500 cells/µl, 2 (1.1%). Patients with CD_4+ values of less than 200 cells/µl, 0 (0%); had the least prevalence of *Streptococcus pyogenes*. The highest prevalence of *Klebsiella pneumonia* was observed in patients with CD_4+ values greater than 500 cells/µl, 9 (4.8%); followed by patients with CD_4+ values less than 200 cells/µl, 2 (1.1%). Patients with CD_4+ values within 200 – 499 cells/µl, 0 (0%) had the least distribution of *Klebsiella pnuemoniae*. The highest prevalence of *Pseudomonas aeruginosa* was observed in patients with CD_4+ value greater than 500 cells/µl, 2 (1.1%); followed by patients with CD_4+ value of less than 200 cells/µl, 1 (0.5%). Patients with CD_4+ values within 200 – 499 cells/µl, 0 (0%) had the least prevalence of *Pseudomonas aeruginosa*. The highest prevalence of *Proteus mirabilis* was observed in patients CD_4+ values greater than 500 cells/µl, 5 (2.7%);

followed by patients with CD_4+ values within 200 – 499 cells/µl, 1 (0.5%). Patients with CD_4+ values of less than 200 cells/µl, 0 (0%) had the least prevalence of *Proteus mirabilis*. The highest prevalence of *Enterococcus faecalis* was observed in patients with CD_4+ values of greater than 500 cells/µl, 8 (4.3%); followed by patients with CD_4+ values within 200 – 499 cells/µl, 2 (1.1%). Patients with CD_4+ values of less than 200 cells/µl, 0 (0%) had the least prevalence of *Enterococcus faecalis.* The highest prevalence of *Candida albicans* was observed in patients with CD_4+ values of greater than 500 cells/µl, 1 (0.5%). Patients with CD_4+ values within 200 – 499 cells/µl and those with CD_4+ values of less than 200 cells/µl, 0 (0%) had the least prevalence of *Candida albicans.*

Table 26: Overall prevalence of etiologic agents according to CD_4+ values in ART users

Organism	***<200cells/µl***	***200 - 499cells/µl***	***>500cells/µl***
E, coli	8 (4.5%)	21(11.4%)	17(9.2%)
S. epidermidis	5(2.7%)	12(6.5%)	15(8.1%)
S. aureus	3(1.6%)	16(8.6%)	10(5.4%)
S. pyogenes	0(0%)	2(1.1%)	2(1.1%)
K. pneumoniae	2(1.1%)	1(0.5%)	9(4.8%)
P. aeroginosa	1(0.5%)	0(0%)	2(1.1%)
P. mirabilis	0(0%)	1(0.5%)	5(2.7%)
E. faecalis	0(0%)	2(1.1%)	8(4.3%)
C. albicans	0(0%)	0(0%)	1(0.5%)

Table 27 shows the prevalence of etiologic agents according to CD_4+ values in patients who are not on antiretroviral drug usage. The highest prevalence of *Escherichia coli* was observed in patients with CD_4+ values greater than 500 cells/µl, 2 (2.0%); followed by patients with CD_4+ values of less than 200 cells/µl, 1 (1.0%). Patients with CD_4+ values within 200 – 499 cells/µl, 0 (0%); had the least prevalence of *Escherichia coli.* It was observed that the highest prevalence of *Staphylococcus epidermidis* was observed in patients with CD_4+ values of less than 200 cells/µl, 3 (3.0%). Patients with CD_4+ values within 200 – 499 cells/µl and those with CD_4+ values greater than 500 cells/µl, 0 (0%); had the least prevalence of *Staphylococcus epidermidis*. There was zero prevalence of *Staphylococcus aureus* across all three CD_4+ categories, 0 (0%). There was zero prevalence of *Streptococcus pyogenes* across all three CD_4+ categories, 0 (0%). The highest prevalence of *Klebsiella pneumonia* was observed in patients with CD_4+ values less than 200 cells/µl and those with CD_4+ values greater than 500 cells/µl, 1 (1.0%). Patients with CD_4+ values within 200 – 499 cells/µl, 0 (0%) had the least distribution of *Klebsiella pnuemoniae*. The highest prevalence of *Pseudomonas aeruginosa* was observed in patients with CD_4+ values of less than 200 cells/µl, 2 (2.0%). Patients with CD_4+ values greater than 500 cells/µl and those with CD_4+ values within 200 – 499 cells/µl, 0 (0%) had the least prevalence of *Pseudomonas aeruginosa*. There was zero prevalence of *Proteus mirabilis* across all three CD_4+ categories, 0 (0%). There was zero prevalence of *Enterococcus faecalis* across all three CD_4+ categories, 0 (0%). There was zero prevalence of *Candida albicans* across all three CD_4+ categories, 0 (0%).

Table 27: Overall prevalence of etiologic agents according to CD_4+ values in non ART users

Organism	***<200cells/µl***	***200 - 499cells/µl***	***>500cells/µl***
E, coli	1 (1.0%)	0(0%)	2(2.0%)
S. epidermidis	3(3.0%)	0(0%)	0(0%)
S. aureus	0(0%)	0(0%)	0(0%)
S. pyogenes	0(0%)	0(0%)	0(0%)
K. pneumoniae	1(1.0%)	0(0%)	1(1.0%)
P. aeroginosa	2(2.0%)	0(0%)	0(0%)
P. mirabilis	0(0%)	0(0%)	0(0%)
E. faecalis	0(0%)	0(0%)	0(0%)
C. albicans	0(0%)	0(0%)	0(0%)

CHAPTER 5

DISCUSSIONS

5.1 DISCUSSIONS

From the study, the prevalence rate of urinary tract infections among the population under study was high. Although the overall prevalence of urinary tract infections among HIV – infected patients on anti retroviral therapy was higher than those among patients who are not on ART usage. Related studies showed varying urinary tract infection prevalence rates at different parts of the country and the rest of the world. Inyamba et al, 2016, recorded the closest prevalence rate of 56.7% of urinary tract infections in HIV/AIDS patients under ART (Inyamba et al., 2016). *Inyang – Etoh et al., 2009,* recorded prevalence rate of 25.3% of urinary tract infections in HIV positive patients on antiretroviral therapy in Calabar (Inyang – Etoh *et al,* 2009). In Aba, Abia State, overall prevalence of urinary tract infections in patients on antiretroviral therapy was 40.39% (Kanu, *et al.,* 2016). In South South Nigeria, Edo State, an overall prevalence rate of 6.3% was found among adolescents and young adults infected with HIV/AIDS (Michael *et al*., 2006). In related studies in Benin, Edo state, overall prevalence of urinary tract infection was 57.3% (Kemajou *et al.,* 2016). In Jos, Plateau state, the overall prevalence of urinary tract infection in same cohort was 23.5% (Bigwan, 2015). In Ethiopia, East Africa, urinary tract infection prevalence rate of 11.3% was recorded (Fenta, 2016). In Jimma University, Ethiopia, the overall urinary tract infection prevalence rate of 12% was recorded in HIV positive patients (Debalke, 2014). In Bangalore, India, the prevalence rate of urinary tract infection in HIV positive patients was 4.0% (Banu *et al*., 2013). *Schowald et al*. recorded an overall urinary tract infection prevalence rate of 25.0% in HIV positive individuals on ART (Schowald

et al., 2009). Similarly, urinary tract infection prevalence rate of 41.0% was also recorded in Zagreg, Croatia (Schowald *et al.*, 2009). This study carried out in Enugu, South East Nigeria, had the highest urinary tract infection prevalence rate in HIV positive patients.

The divergence in the prevalence rates of urinary tract infections could be due to the difference in the immune levels/ HIV status of the patients who had participated in the studies which might have contributed to the increase or decrease in the prevalence rates of urinary tract infections in different geographic locations. The variation in prevalence rate of urinary tract infections in HIV infected persons from one geographical area to another could also be attributed to differences in UTI perception, mode of screening, compounding risk factors such as age, host behavioral factors and parity (Ogbukagu, *et al.*, 2016). In addition, due to differences in study methods, designs population, prevalence rates can differ from place to place. Also, the difference in the disease stage among patients can also contribute to the differences in prevalence rates. The difference in prevalence rates goes to also suggest that geographical location could be a pre disposing cofounding factor in the prevalence of urinary tract infections in HIV positive patients. *Iyamba et al, 2016,* alluded to the fact that this could be primarily due to interruption of ART use due to lack of availability and ART user failure. ART users on antiretroviral therapy had a higher urinary tract infection prevalence rate 56.6% (n = 133/143) than non ART users who are not on antiretroviral therapy 20.0% (n = 10/143). This agrees with an observation by Murugesh, 2014, which reported a higher prevalence rate of urinary tract infections in ART users than in non – ART users. This also collaborates with findings in other parts of Nigeria. In Calabar, urinary tract infection prevalence rate of ART users 25.3% was higher than the prevalence rate of the non ART users 13.0% (Inyang – Etoh *et al*, 2009). The

findings in Ethiopia recorded a urinary tract prevalence rate of 12.5% for ART users and 10.0% for non ART users (Debalke, *et al*., 2014). In a related study, Fenta et al., 2016 recorded a 13.0% prevalence of urinary tract infections in patients on HAART and a 7.0% prevalence rate for non ART users who were not on antiretroviral therapy. Amiri et al., in a case – control study carried out in Iran also showed significantly higher prevalence of urinary tract infections among highly active antiretroviral therapy users (ART users) 27.78% compared to the control groups 17.31%, though the control groups were non HIV patients (Amiri *et al.,* 2009). Conversely, the findings from this report are in contrast to reports from Italy that confirmed that a significant reduction in bacterial infections occurred in HIV – infected subjects when HAART became a standard therapy for HIV infection (De Gaetano *et al.,* 2003). Although this might be due to other urinary tract infection – related factors like genital hygiene practices, sexual activities, etc. In ART users, anti retroviral therapy has been confirmed to reduce the risk of acquiring opportunistic infections including urinary tract infections by 57% to 91% and this was greatest in the first year of ART users (WHO, 2016). The possibility of antiretroviral (ART) usage failure among ART users may result in increased prevalence of urinary tract infections even in ART users on ART. However, in this study, data on such factors were not collected. Additional research is needed to better understand this condition. The differences in prevalence rates between ART users and non ART users can also be attributed to lowered CD_4+ counts and disease staging among ART users who may have been infected for a while.

The healthy urinary tract, like other body systems, is normally able to resist bacterial infections; numerous studies have indicated that the frequency of urinary tract infections is greater in women than in men. According to prevalence of

urinary tract infections by gender, the overall prevalence of UTI was significantly higher in the females 83.9% (n = 120/285), than in the male patients 16.1% (n = 23/285). This collaborates with findings in other parts of South East Nigeria. In Aba, Abia state, higher urinary tract infection prevalence rate of 52.17% was established among the females; and 17.14% prevalence rate in male patients (Kanu, 2016). Similar findings were reported in the North Central, Jos (Bigwan, 2015); East Africa, Ethiopia (Teshager *et al*., 2008). Debalke et al., 2014, working in Ethiopia, observed that prevalence of urinary tract infections was significantly higher among the female patients,14.6%, than the males, 7.2%. In related studies, Banu et al., 2013 recorded significantly higher prevalence of bacteriuria in female patients (83.3%) than in males (16.7%) in Bangalore, India (Banu *et al.,* 2013). This follows the trend of normal healthy individuals where females are at higher risk of being infected with urinary tract infections due to their short, straight urethra. The close proximity of the female urethra to the anus as well as increased sexual activities, autoinfection, incontinence, poor hygiene and bad toilet habits, have all been reported as factors that influence higher prevalence rate of urinary tract infections in females. The large intestines and the perinea area serve as reservoir for pathogenic bacteria. Different studies have indicated that women who are prone to urinary tract infections possess epithelial cells with significantly more receptors for uropathogenic bacteria than healthy controls (Debalke *et al.,* 2014). This observation is supported by the reports of Ogbukagu *et al.,* 2016. However, these findings are in contrast to the study by Inyang – Etoh *et al.,* who recorded higher prevalence rate 28.6% of urinary tract infections in males and 23.8% in female patients in Calabar, even though it was not statistically significant (Inyang – Etoh *et al*, 2009). Spence also reported higher urinary tract infection prevalence rate of 15.9% in males (Spence *et al.,* 1996). Urinary tract infection prevalence has been estimated to be three times higher in females than in males. Although the

disparity in urinary tract infection prevalence rates by gender is reported to be age dependant and that HIV prevalence was six times greater in females than in males (Kanu, 2016). Further research is needed to verify this claim. According to this study, females on antiretroviral therapy were observed to have a higher urinary tract infection prevalence rate 43.1% compared to their non ART users counterparts 14.3%. Likewise, males on antiretroviral therapy were also observed to have a higher urinary tract infection prevalence rate 16.1% compared to their non ART users counterparts 4.1% who are not on anti retroviral therapy. This may be attributed to the possibility of antiretroviral ART users failure among ART users may result in increased prevalence of urinary tract infections even in both male and female patients on ART. Interestingly, our findings indicated that had females had higher urinary tract infection prevalence rate although it was also observed that females had more impressive CD_4+ levels more than the males. Maskew *et al*, (2013) alluded that women showed consistently better immune response to treatment than did men. Another related study acceded to the fact that females have a relatively higher CD_4+ values than men. This goes to show that ART usage treatment outcomes expressed by CD_4+ count values may vary by gender. Incidentally, this high level of CD_4+ counts in the female population did not directly translate to a reduction in the prevalence rate of urinary tract infections.

In this study, there was high prevalence of urinary tract infections among patients on antiretroviral drug usage who fell within the two age extremities. The youngest and the oldest age groups were more predisposed to urinary tract infections. They had increased prevalence of urinary tract infections compared to those within the middle age category. More patients within 18 – 30 and 46 – 75 years had higher urinary tract infection prevalence than those within the same age groups without

UTI. The findings collaborate with a study carried out in United States of America. This study alluded that the prevalence of urinary tract infections is highest in young man aged 18 – 24. It further states that the prevalence of urinary tract infections decreases during middle age but rises in older adults; in both men and women over the age of 65, the prevalence of urinary tract infections increase substantially (Rowe *et al*., 2013), this fact can be attributed to overutilization of antibiotics by the older population. The overall relationship between urinary tract infections and age indicates that the highest urinary tract infection prevalence rate occurred in the youngest age group. Age group 18 – 30 had the highest prevalence of urinary tract infections 37.7%; age group 31 – 45 had UTI prevalence of 26.6% while age group 46 – 75 had UTI prevalence of 35.7%.The findings in this work agree with similar research carried out in Anambra state, Nigeria stating that urinary tract infections occurred highest in age group 26 – 38 years (Ogbukagu, *et al.*, 2016). In Benin, Edo state, it was also observed that the prevalence rate of UTI in HIV seropositive individuals was highest in age group 24 – 30 years and least in age group 44 years and above (Kemajou *et al*, 2016). The prevalence of asymptomatic bacteriuria in younger age groups was almost twice as high as what was found in the older age group (Olowe, *et al.*, 2015). This may be as a result of increased sexual activity which predisposes that age group to urinary tract infections. A significant association was also found between age and the presence of bacteriuria with younger individuals at higher risk (Olowe *et al.*, 2015). However, this is in contrast to findings in Aba, South East Nigeria indicating that age group 60 – above had the highest prevalence of 100% followed by age group 30 – 44 (44.9%) (Kanu, *et al.*, 2016). In another related study carried out in Jos, Nigeria, age group 46 and above had the highest prevalence rate of urinary tract infections and age group 5 – 15 with the least prevalence rate (Bigwan, 2016). In ART users on antiretroviral therapy, urinary tract infections were more prevalent in

the youngest age category, and least in the middle age category. ART users under the age group 18 – 30 had highest urinary tract infection prevalence rate of 22.1% while those under age group 31 – 45 recorded the least urinary tract infection prevalence 14.1%. Conversely, non ART patients under the group 31 – 45 recorded the highest urinary tract infection prevalence rate 10.2%. Our findings indicate that urinary tract infections were distributed across the different age groups. The occurrence of the infection across all age groups may be attributed to their exposure to HIV/AIDS being the major predisposing risk factor to urinary tract infections. Other risk factors like diabetes, increased sexual activity and anal contamination during defecation, can also be implicated.

Majority of patients in this study had high CD_4+ values. This goes to show that majority of HIV positive patients receiving antiretroviral therapy are responding to the treatment which is evident by elevated CD_4+ cell values. The latest WHO guidelines call for anyone with HIV to begin treatment as soon as possible after diagnosis regardless of the level of immune suppression (CD_4+ count). Patients who are on anti retroviral treatment but fail to experience increased CD_4+ cell counts (immune recovery) almost always start therapy late into the infection. The study population therefore showed high immune recovery index (CD_4+ count). This shows that the level of awareness of HIV infection is impressive as individuals find out their status and commence treatment as soon as possible. Younger age groups had high CD_4+ values. According to studies carried out by Lewis *et al*, 2012, it was observed that the immature immune system can recover well from HIV infection via the naïve pool. This potential, he stated, is progressively damaged with age and/or duration of infection. Hence, the younger the patient, the higher the CD_4+ level and, the increase in length of ART usage, decrease in CD_4+ counts. Older age groups had lower CD_4+ values. Our findings

collaborate with a novel exploration of relationship between age and CD_4/CD_8. It was observed that low CD_4+/CD_8 values were strongly associated with older age in HIV infected adults on stable antiretroviral therapy (Lewis *et al*, 2012). Females had higher CD_4+ values than the males. Several studies have shown higher CD_4+ counts and reduced viral loads in female HIV positive patients who are on antiretroviral therapy. Although the reason (s) for this seem unclear (Moroni *et al*, 2015). It is speculated that higher estrogen concentrations or other gender - specific factors can reduce HIV replication in women. However, disease staging and time of infection were not considered in this study as they could be co – founding factors in causing increased CD_4+ counts in the female patients. Patients on ART had impressive CD_4+ values more than those who are not on antiretroviral drugs. Patients with high CD_4+ count values greater than 500cells/µl had the highest urinary tract infection prevalence rate; while patients with CD_4+ count values less than 200cells/µl had the least urinary tract infection prevalence 13.9%. This is moderately in line with related studies in Jos, Plateau State. The highest prevalence of urinary tract infections was observed among participants with CD_4+ count range 200 – 400 cells/µl (Essien, 2015). This can be attributed to massive epileptic antiretroviral availability and ART users' failure. In contrast to our findings, related studies carried out in South Western Nigeria, observed that those with CD_4+ count values less than 200 cells/µl were at significantly higher risk of urinary tract infections (Olowe *et al.,* 2015). Sill in contrast to our findings, studies in Calabar, Cross River State noted highest UTI prevalence rate among HIV positive patients with CD_4+ count of less than 200 cells/µl (Inyang – Etoh *et al.,* 2009). Several studies have also suggested a correlation between low CD_4+ counts and increased UTI prevalence (Essien, 2015).This is in keeping with the high risk of opportunistic infections that result from immune suppression.

In this study, ART users recorded higher prevalence rates of urinary tract infections despite being on anti retroviral therapy. Contrary to the fact that HIV+ Patients with low CD_4+ counts are at risk of urological complications which can lead to urinary stasis and ultimately, infection; higher prevalence rates of urinary tract infections were observed in HIV positive ART users with CD_4+ count greater than 500cells/µl. This collaborates with similar studies in Benin, Edo state. Among both ART users and non ART users, CD_4+ count less than 200 cells/µl was not associated with asymptomatic urinary tract infections (Omoregie, 2009). In contrast, studies in Addis Ababa, Ethiopia, observed that the highest proportion of bacteria were isolated from patients having CD_4+ count of less than 500 cells/ µl (Fenta, 2016). However, an Indian study reported a higher prevalence of bacteriuria among ART users than ART non ART users participants (Pradip *et al.*, 2013). These differences could be due to lowered CD_4+ count among included patients and contradicts our findings of a higher prevalence of urinary tract infections in patients with CD_4+ counts higher than 500 cells/ µl. In comparison to non ART users, patients on antiretroviral therapy recorded higher prevalence rates of urinary tract infections across all CD_4+ categories. This may be as a result antiretroviral ART usage failure and unavailability, lack of compliance and adherence to antiretroviral drugs, sampling error as the numbers in ART user's category was more than those in the non ART user's category.

In the study, there was almost a 50% chance of isolating either a gram positive or a gram positive organism, however, majority of isolated bacteria were gram negative organisms with overall prevalence rate of 51.0% (n =73/143); while gram positive organisms were 49.0% (n = 70/143). This finding also collaborate with a related study in Anambra State implicating gram negative rods as the main cause of urinary tract infections (Ogbukagu, *et al.*, 2016). In Italy, gram negative bacteria

represented 90.8% of urinary pathogens in a cohort of HIV outpatients (Magliano *et al.*, 2012). The greater prevalence of members of enterobacteriaceae group, especially the coliforms proved that a high percentage of urinary tract infections in our cohort may be due to fecal contamination and poor hygiene. In other related studies, gram negative bacteria were more prevalent than gram positive bacteria. This finding was comparable with other findings done in Gondar and Jimma, Ethiopia (CLSI, 2014). This might be due to the presence of unique structures in gram negative bacteria used attachment to uroepithelial cells and prevent them from urinary lavage allowing for multiplication and tissue invasion resulting in invasive infections and pyelonephritis (Ifeanyichukwu *et al*., 2013). In this study, *Escherichia coli* 34.3% (n = 49/143), *Staphylococcus epidermidis* 23.1% (n = 33/143) and *Staphylococcus aureus* 18.2% (n = 26/143) were most frequently isolated whereas, *Klebsiella pneumoniae* 8.4% (n = 12/143), *Streptococcus faecalis (Enterococcus)* 4.9% (n = 7/143), *Proteus mirabilis* 4.9% (n = 7/143), *Pseudomonas aeruginosa* 3.5% (n = 5/143), *Streptococcus pyogenes* 2.1% (n = 3/143) and *Candida albicans* 0.7% (n = 1/143), were the least frequent isolates from cultures of all study participants. This finding is comparative to similar studies in other parts of South East Nigeria. In Anambra state, urinary tract pathogens implicated include *Escherichia coli* (24.2%), *Klebsiella spp.* (18.2%), *Staphylococcus aureus* (18.2%), *Proteus mirabilis* (9.1%), *Pseudomonas aeruginosa* (9.1%), *Enterococcus faecalis* (9.1%) (Ogbukagu, *et al.*, 2016), indicating the possibility of a cofounding factor responsible for the pathogenesis of the most implicated organisms in the cohort. In other related studies, same findings were observed in Ethiopia; Gondar (CLSI, 2014) and Jimma (Biradar *et al.*, 2013). Studies have demonstrated that the large intestines and the perinea area serve as reservoir for pathogenic bacteria like *Escherichia coli* (Debalke, 2014). Other collaborating related studies indicate gram negative bacteria of *Escherichia coli*

and *Klebsiella pneumoniae* as the most common uropathogenic bacteria causing urinary tract infections (Behzadi *et al*., 2010). In addition, our findings also showed similarity with another study in South Africa (Jordi *et al.*, 2010). *Escherichia coli* was the most significant cause of urinary tract infections in this study, this is in consonance with the study in Italy: *Escherichia coli* (67.6%), *Klebsiella pneumonia* (8.8%), *Enterococcus faecalis* (6.3%), *Proteus mirabilis* (5.2%), *Pseudomonas aeruginosa* (2.5%) and Staphylococcus agalactiae (2.3%) (Magliano, 2012). As well as with the study carried out in Jos, Plateau state, *Escherichia coli* (29.7%), *Staphylococcus aureus* (6.5%), *Proteus mirabilis* (2.7%), *Pseudomonas aeruginosa* (2.7%) and Klebsiella species (1.9%) (Bigwan, 2015). Another study in Aba, Abia states also collaborates our findings: *Escherichia coli* (68.18%), *Klebsiella pneumonia* (15.91%), Enterobacter specie (11.36%) and Staphylococcius aureus (4.55%) (Kanu, *et al*., 2016). *Escherichia coli* is a common finding as the cause of urinary tract infections and is associated with organisms ascending from the periurethral areas contaminated with faecal flora due to the close proximity of the anus and the warm moist environment of the genitalia. Staphylococcus specie which also has high propensity for causing infections especially in young sexually active adults is also a predominant normal flora of the skin. The above findings are in direct contrast with the findings in other parts of Nigeria, implicating *Staphylococcus aureus* as the use of urinary tract infections most common cause of urinary tract infections in a cohort of HIV positive individuals. In Osun state, *Staphylococcus aureus* (29.7%), *Escherichia coli* (28.7%) and *Pseudomonas aeruginosa* (13.9%) (Adeyemi *et al.*, 2012). In Calabar, the predominant bacteria among ART users were *Staphylococcus aureus* (87.2%), followed by *Escherichia coli* (84.0%) while *Escherichia coli* was most predominant among Non ART users (Debalke, 2014). Similarly in Oshogbo, South West Nigeria, *Klebsiella spp* was the most implicated etiological agent followed by

Escherichia coli (Olowe *et al*., 2015). In other parts of the world, *Pseudomonas aeruginosa* (41.9%), *Escherichia coli* (19.35%), *Staphylococcus epidermidis* (9.6%), *Enterococcus faecalis* and *Staphylococcus aureus* (6.45%) (Xavier, 2015). In the distribution of etiologic agents of urinary tract infections between ART users and non ART users, *Escherichia coli* was the most prominent isolate in both the ART users (33.8%) and the non ART users (40.0%) patients. This is comparable with other related studies carried out in Ibadan, Nigeria (Michael *et al*., 2006); Brazil (De Pinho *et al*., 1994) and Cameroon (Njunda *et al*., 2010). In contrast, *Enterococcus* was more frequently isolated in ART users while *Escherichia coli* were more frequently isolated in non ART users (Schonwald, 1999). According to this study, the types of bacterial etiologies associated with urinary tract infections were higher in ART users who are on antiretroviral therapy than in non ART users who are not on antiretroviral therapy. The analysis showed that patients with HIV on ART usage had UTI more frequently than those who were not on ART usage. Besides the difference in the frequency, a difference in etiology was also observed at different geographical locations. In this study, *Candida albicans* had the least prevalence 0.8% as the cause of urinary tract infections in HIV positive individuals who are on ART. This is in tandem with findings in Jos, plateau state, where it was also observed that *Candida albicans* has the least UTI prevalence rate (Essien, 2015). This is as a result of routine OI (opportunistic infection) drugs given to ART users along with the anti retroviral therapy.

In the overall relationship between urinary tract infections and history of ART use, patients between 1 – 3 years of ART use had the highest UTI prevalence of 43.6%, while those under a year of antiretroviral therapy had least urinary tract infection

prevalence rate of 8.3%. According to this study, there seemed to be a steady incremental progression in the prevalence of urinary tract infection after commencement of antiretroviral therapy. This progression gradually peaks between 1 – 3 years after commencement of therapy. After which the prevalence of urinary tract infections gradually declines. In a study carried out in Brazil, to estimate the average duration of antiretroviral ART users benefit, it was observed that the mean duration of antiretroviral ART users benefit in HIV positive individuals was 14.1 months. 23% of HIV infected individuals on therapy loose the benefits of ART users after 6 months of commencement while 47% of patients still maintain ART user's benefits after 12 months of commencement of therapy (Medeiros *et al.,* 2002). Therefore, the progression of prevalence of urinary tract infections, and the eventual regression could be as a result of drug intolerance, lack of patient compliance and adherence to drug use as well as viral rebound regardless of ART users. In another related research in Spain, it was observed that very young children, adolescents and young adults are at high risk of non adherence to antiretroviral therapy (Palladino *et al.*, 2012). Adjustments in life style also play a part in decreasing the risk of acquiring urinary tract infections. The time required to make these adjustments in order to get results may fall between the first two to three years post infection hence the increase in prevalence rates of urinary tract infections in this research. Patients who are on antiretroviral drug usage with no previous history of urinary tract infections had higher urinary tract infection prevalence than patients who have had no prior episode of urinary tract infections. patients who have experienced at least one episode of urinary tract infections were not prone or predisposed to recurring infection (UTI),

5.2 STRENGTHS OF STUDY

Data on all variables for this study was collected at a single point in time over a period of six months and these made it fairly possible to measure and analyze prevalence for every required variable under investigation. Consequently, this study, by assessing the prevalence of urinary tract infections in a cohort of HIV positive patients; is of great public health importance as per planning and the allocation of health resources, reduction of HIV – related morbidity and mortality and improvement of patients' quality of life. Patient willingness and cooperation during sample collection and administration of questionnaires aided in the issuance of laboratory analysis and sensitivity reports to patients with urinary tract infections in order to commence antimicrobial therapy.

5.3 LIMITATIONS OF STUDY

Analyses of data collated from questionnaire were limited to accuracy of patient information, and therefore susceptible to bias.

5.4 CONCLUSIONS

Although studies on the evaluation of the effect of anti retroviral therapy show that it has a significant impact on reduction of the prevalence of bacterial infections including bacteremia, bacterial pneumonia, and urinary tract infections, that occur in HIV patients (Debalke, 2014), the prevalence of urinary tract infections among HIV – infected patients on anti retroviral therapy, in this current study, was high. This could be predicated on poor anti retroviral treatment adherence and treatment failure as well as unavailability of anti retroviral drugs. This cross sectional study provides very little support to the hypotheses that antiretroviral therapy has some form of impact on the prevalence rates of urinary tract infections by improving CD_4+ counts, and by improving the body's immunity, which reduces prevalence rate of opportunistic infections (UTIs) in a cohort of HIV positive individual in

Enugu metropolis. Furthermore, this study also lends little credence to the hypothesis that high CD_4+ counts translate to reduction in the prevalence rates of opportunistic infections in the same cohort, urinary tract infections inclusively.

There were no significant associations between the other host factors and urinary tract infections. Sociodemographic variables analyzed in this work, like age, sex showed remarkable impact on the prevalence rates of urinary tract infections although there were not statistically significant. Findings on the impact of other variables like previous history of urinary tract infections and length of use of antiretroviral therapy showed that they also have little impact on the prevalence of urinary tract infections on HIV positive patients.

Part of the significance of this study lies in the determination of the common pathogens responsible for urinary tract infections in a cohort of HIV positive patients in Enugu Metropolis. It was observed that *Escherichia coli* were predominant etiologic agents responsible for UTI, implicating geographical location as a possible factor causing the difference in etiologic agents that cause UTI in different locations. In conclusion, ART can be said to impact on prevalence of opportunistic infections when there is complete adherence and compliance to treatment, no treatment failure and availability of ART as and when due. In summary, CD_4+ counts, socio demographic factors like age, gender, previous history of urinary tract infections and length of anti retroviral therapy had no significant impact in the prevalence of UTI in patients. Although ART boosted CD_4+, it didn't really translate to reduced prevalence of UTI. High CD_4+ counts and the prevalence of opportunistic infections (UTI) may not be directly related but a confounding factor related to both might be responsible for the relationship, if any. There is a strong possibility of drug failure, non – compliance and non – adherence to antiretroviral therapy in patients on ART drug usage. In conclusion,

- Antiretroviral drug usage had no direct impact in increasing or decreasing the prevalence of urinary tract infections in HIV positive patients.
- Long term antiretroviral therapy allows for increased prevalence of urinary tract infections.
- CD_4+ values had no direct impact in increasing or decreasing the prevalence of UTI in patients.
- High CD_4+ values did not result in low prevalence of urinary tract infections.
- There was no significant relationship between sociodemographic factors and prevalence of urinary tract infections.
- Patients with previous history of urinary tract infections had higher prevalence of UTI compared to those without a prior history of UTI.
- Gram negative, enteric organisms were most implicated as the etiologic agents responsible for UTI in patients.
- Different etiologic agents are implicated as the causative agents of UTI in different geographical locations.

5.5 CONTRIBUTION OF KNOWLEDGE

This study showed that there is increased risk and prevalence of urinary tract infections in HIV positive individuals on ART which is contrary to the norm that ART reduces prevalence of opportunistic infections by improving the CD_4+ counts. This study also revealed increased prevalence of urinary tract infections especially in patients on long term anti retroviral therapy. The study therefore shows a gap in treatment and management of HIV patients in terms of proper management of opportunistic infections which are attendant in HIV infection. Noteworthy is the fact that high CD_4+ counts do not directly result in reduce prevalence of urinary tract infections. It also revealed a possibility of reduction in

the efficacy of antiretroviral drugs when they are administered in a patient after a long haul. A better understanding of ART usage dynamics will help extend our attention & understanding of possible treatment gaps, drug failures, behavioral/attitudinal factors that can sabotage therapy and host immunity.

5.6 RECOMMENDATIONS

The study recommends a strategy that focuses on improving the rate of compliance and of therapy success is recommended in order to drastically reduce urinary tract infection prevalence in HIV patients especially among those already on antiretroviral therapy. In addition, more concerted efforts are needed; in order to review the current effectiveness of antiretroviral therapy and improve the benefits acquired with therapy; improve adherence and better management of adverse drug effects. This will ensure saving of resources and improving patients quality of life. However, more studies on these issues are necessary in order to compare the situation in other geographical locations. Intermittent review and evaluation of efficacy of antiretroviral therapy in patients is paramount. The evaluation of the results of AIDS treatment will provide an important tool to improve the quality of assistance and care to these patients and to optimize governmental efforts to control the epidemic. The findings of this study revealed that the important infecting organisms were found to be commensals of perianal and vaginal regions. There should therefore be widespread awareness and sensitization towards improved personal hygiene.

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APPENDIX 1

Table 28: Morphology and biochemical characteristics of the bacterial isolates

Bacteria Isolates	Morph.	Lac fer.	Haem	G/Stain	Ind.	Meth. Red	Oxid.	Catal.	Coag.	Urea.	Motil.
Pseudomonas aeruginosa	rod	-ve	NA	-ve	-ve	-ve	+ve	-ve	NA	+ve	+ve
Staphylococcus aureus	cocci	-ve	-ve	+ve	-ve	+ve	-ve	+ve	+ve	+ve	-ve
Staph. epidermidis	cocci	-ve	-ve	+ve	-ve	-ve	-ve	+ve	-ve	-ve	-ve
Enterococcus faecalis	cocci	-ve	α	+ve	-ve	-ve	-ve	+ve	-ve	-ve	-ve
Streptococcus pyogenes	cocci	-ve	β	+ve	-ve	-ve	-ve	+ve	-ve	-ve	-ve
Escherichia coli	rod	+ve	NA	-ve	+ve	+ve	-ve	-ve	NA	–ve	+ve
Klebsiella pneumonia	rod	+ve	NA	-ve	-ve	-ve	-ve	-ve	NA	+ve	-ve
Proteus mirabilis	rod	-ve	NA	-ve	-ve	-ve	-ve	-ve	NA	+ve	+ve

Key: Morph. = Morphology, Lac fer. =Lactose Fermenter, Haem = Haemolysis, G/Stain = Gram Stain, Ind. = Indole test, Meth. Red = Methyl Red test, Oxid. = Oxidase test, Catal. = Catalase test, Coag. = Coagulase test, Urea. = Urease test, Motil. = Motility test; +ve =Positive, -ve =Negative, NA = Not Applicable, α = Alpha Haemolysis, β = Beta Haemolysis.

APPENDIX II

QUESTIONNAIRE

ART FACILITY----------

DATE ----------

ISSUED BY----------

Thank you for participating in this survey. Kindly choose your options and fill in the blank spaces as correctly as you can. Tick (√) the appropriate item(s) in brackets

1. Name of respondent ----------
2. Age (18 – 30)yrs (31 – 45)yrs (46 and above)yrs
3. Sex (Male) (Female)
4. Are you currently on anti retroviral drugs? (yes) (no)
5. How long have you been on anti retroviral drugs? ----------
6. What regimen of anti retroviral drugs are you currently taking? ----------
7. How often do you carry out CD4 test? ----------
8. How often do you carry out creatinine and ALT tests? ----------
9. Have you ever carried out a urine culture test? ----------
10. Are you currently experiencing any of these symptoms?
    (Frequent urination) (Lower abdominal pain) (Painful urination) (Lower back pain) (Urine incontinence) (Vaginal itching) (Vaginal discharge) (None of the above).
11. Are you currently taking OI drugs? (Yes) (No)
12. Are you currently taking antibiotics? (Yes) (No)

For laboratory personnel only.

Kindly indicate the values and corresponding units of the blow listed parameters.

1. Patient's recent CD4 count value ----------
2. Patient's recent serum creatinine value ----------
3. Patient's recent Alanine aminoTransferase value ----------

APPENDIX III

high CD4 values of patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	500	8	12.5	12.5	12.5
	600	21	32.8	32.8	45.3
	700	16	25.0	25.0	70.3
	800	10	15.6	15.6	85.9
	900	6	9.4	9.4	95.3
	1000	3	4.7	4.7	100.0
	Total	64	100.0	100.0	

organisms causing UTI in high CD4 values

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Candida	1	1.6	1.6	1.6
	e.coli	16	25.0	25.0	26.6
	Kleb	7	10.9	10.9	37.5
	Pseudo	2	3.1	3.1	40.6
	s.aureus	10	15.6	15.6	56.2
	s.faecal	7	10.9	10.9	67.2
	s.pyogen	2	3.1	3.1	70.3
	Proteus	1	1.6	1.6	79.7
	staph sp	13	20.3	20.3	100.0
	Total	64	100.0	100.0	

APPENDIX IV

low CD4 values of patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	80	1	1.4	1.4	1.4
	90	2	2.9	2.9	4.3
	100	12	17.4	17.4	21.7
	200	7	10.1	10.1	31.9
	300	31	44.9	44.9	76.8
	400	16	23.2	23.2	100.0
	Total	69	100.0	100.0	

organisms causing UTI in low CD4 values

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	28	40.6	40.6	40.6
	Kleb	3	4.3	4.3	44.9
	Pseudo	1	1.4	1.4	46.4
	s.aureus	16	23.2	23.2	69.6
	s.pyogen	2	2.9	2.9	72.5
	Proteus	3	4.3	4.3	76.8
	staph sp	16	23.2	23.2	100.0
	Total	69	100.0	100.0	

APPENDIX v

high creatinine values of patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0.8	42	29.0	29.0	29.0
	0.9	30	20.7	20.7	49.7
	1	18	12.4	12.4	62.1
	1.1	21	14.5	14.5	76.6
	1.2	13	9.0	9.0	85.5
	1.3	9	6.2	6.2	91.7
	1.4	2	1.4	1.4	93.1
	1.5	2	1.4	1.4	94.5
	1.6	3	2.1	2.1	96.6
	6.8	1	.7	.7	97.2
	7.4	1	.7	.7	97.9
	7.8	1	.7	.7	98.6
	10	2	1.4	1.4	100.0
	Total	145	100.0	100.0	

APPENDIX VI

organisms causing UTI in high creatinine levels

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	17	11.7	11.7	11.7
	Kleb	9	6.2	6.2	17.9
	Nbg	58	40.0	40.0	57.9
	Nsbg	15	10.3	10.3	68.3
	s.aureus	13	9.0	9.0	77.2
	s.faecal	4	2.8	2.8	80.0
	s.pyogen	3	2.1	2.1	82.1
	Proteus	3	2.1	2.1	84.1
	Pseudo	3	2.1	2.1	86.2
	staph sp	20	13.8	13.8	100.0
	Total	145	100.0	100.0	

APPENDIX VII

low creatinine values of patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0.4	4	4.5	4.5	4.5
	0.5	5	5.7	5.7	10.2
	0.6	38	43.2	43.2	53.4
	0.7	41	46.6	46.6	100.0
	Total	88	100.0	100.0	

organisms causing UTI in low creatinine values

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Candida	1	1.1	1.1	1.1
	e.coli	26	29.5	29.5	30.7
	Kleb	1	1.1	1.1	31.8
	Nbg	19	21.6	21.6	53.4
	Nsbg	9	10.2	10.2	63.6
	Pseudo	3	3.4	3.4	67.0
	s.aureus	13	14.8	14.8	81.8
	s.faecal	4	4.5	4.5	86.4
	s.pyogen	1	1.1	1.1	87.5
	Salm	1	1.1	1.1	88.6
	Proteus	2	2.3	2.3	90.9
	staph sp	8	9.1	9.1	100.0
	Total	88	100.0	100.0	

APPENDIX VIII

high alanine amino transaminase values of patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	9	7	7.3	7.3	7.3
	10	18	18.8	18.8	26.0
	11	18	18.8	18.8	44.8
	12	3	3.1	3.1	47.9
	13	11	11.5	11.5	59.4
	14	7	7.3	7.3	66.7
	15	10	10.4	10.4	77.1
	16	2	2.1	2.1	79.2
	18	13	13.5	13.5	92.7
	20	2	2.1	2.1	94.8
	40	3	3.1	3.1	97.9
	60	1	1.0	1.0	99.0
	70	1	1.0	1.0	100.0
	Total	96	100.0	100.0	

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APPENDIX IX

organisms causing UTI in high alanine amino transaminase

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	20	20.8	20.8	20.8
	Kleb	5	5.2	5.2	26.0
	Nbg	36	37.5	37.5	63.5
	Nsbg	8	8.3	8.3	71.9
	Pseudo	1	1.0	1.0	72.9
	s.aureus	8	8.3	8.3	81.2
	s.faecal	4	4.2	4.2	85.4
	s.pyogen	1	1.0	1.0	86.5
	proteus	4	4.2	4.2	90.6
	staph sp	5	5.2	5.2	100.0
	Total	96	100.0	100.0	

APPENDIX X

low alanine amino transaminase values of patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	3	18	13.1	13.1	13.1
	4	10	7.3	7.3	20.4
	5	28	20.4	20.4	40.9
	6	19	13.9	13.9	54.7
	7	38	27.7	27.7	82.5
	8	24	17.5	17.5	100.0
	Total	137	100.0	100.0	

APPENDIX XI

high cd4 lymphocyte values of naïves

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	500	5	29.4	29.4	29.4
	600	5	29.4	29.4	58.8
	700	3	17.6	17.6	76.5
	1000	3	17.6	17.6	94.1
	1200	1	5.9	5.9	100.0
	Total	17	100.0	100.0	

Organisms causing UTI in naïve high cd4 lymphocyte

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	2	11.8	11.8	11.8
	kleb	2	11.8	11.8	23.5
	nbg	11	64.7	64.7	88.2
	nsbg	2	11.8	11.8	100.0
	Total	17	100.0	100.0	

APPENDIX XII

low cd4 lymphocyte values of naïves

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	25	1	3.1	3.1	3.1
	30	1	3.1	3.1	6.2
	35	1	3.1	3.1	9.4
	40	1	3.1	3.1	12.5
	50	2	6.2	6.2	18.8
	60	3	9.4	9.4	28.1
	70	1	3.1	3.1	31.2
	80	1	3.1	3.1	34.4
	100	4	12.5	12.5	46.9
	150	1	3.1	3.1	50.0
	200	11	34.4	34.4	84.4
	300	4	12.5	12.5	96.9
	400	1	3.1	3.1	100.0
	Total	32	100.0	100.0	

organisms causing UTI in naïve low cd4 lymphocyte

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	1	3.1	3.1	3.1
	nbg	22	68.8	68.8	71.9
	nsbg	5	15.6	15.6	87.5
	pseudo	2	6.2	6.2	93.8
	staph sp	2	6.2	6.2	100.0
	Total	32	100.0	100.0	

APPENDIX XIII

high creatinine values of naives

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0.7	5	14.7	14.7	14.7
	0.8	14	41.2	41.2	55.9
	0.9	5	14.7	14.7	70.6
	1	10	29.4	29.4	100.0
	Total	34	100.0	100.0	

organisms causing UTI in high creatinine values

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	3	8.8	8.8	8.8
	kleb	1	2.9	2.9	11.8
	nbg	22	64.7	64.7	76.5
	nsbg	5	14.7	14.7	91.2
	pseudo	1	2.9	2.9	94.1
	staph sp	2	5.9	5.9	100.0
	Total	34	100.0	100.0	

APPENDIX XIV

low creatinine values of naives

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0.4	1	6.2	6.2	6.2
	0.5	12	75.0	75.0	81.2
	0.7	3	18.8	18.8	100.0
	Total	16	100.0	100.0	

organisms causing UTI in low electrolyte levels

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	2	12.5	12.5	12.5
	Nbg	12	75.0	75.0	87.5
	Nsbg	2	12.5	12.5	100.0
	Total	16	100.0	100.0	

APPENDIX XV

High alanine amino transferase values

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	9	5	17.2	17.2	17.2
	10	5	17.2	17.2	34.5
	20	13	44.8	44.8	79.3
	30	3	10.3	10.3	89.7
	40	3	10.3	10.3	100.0
	Total	29	100.0	100.0	

Table 16a: low alanine amino transferase values

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	5	4	20.0	20.0	20.0
	6	5	25.0	25.0	45.0
	7	2	10.0	10.0	55.0
	8	9	45.0	45.0	100.0
	Total	20	100.0	100.0	

APPENDIX XVI

organism causing UTI in high alanine amino transferase levels

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	1	3.4	3.4	3.4
	kleb	2	6.9	6.9	10.3
	nbg	19	65.5	65.5	75.9
	nsbg	5	17.2	17.2	93.1
	pseudo	2	6.9	6.9	100.0
	Total	29	100.0	100.0	

organisms causing UTI in low alanine amino transaminase

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	e.coli	2	10.0	10.0	10.0
	Nbg	14	70.0	70.0	80.0
	Nsbg	2	10.0	10.0	90.0
	staph sp	2	10.0	10.0	100.0
	Total	20	100.0	100.0	

APPENDIX XVII

Prevalent bacteria causing UTI in HIV positive individuals ART

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	s.aureus	26	11.1	11.1	11.1
	staph sp	29	12.3	12.4	23.5
	s.pyogenes	4	1.7	1.7	25.2
	e.coli	43	18.3	18.4	43.6
	kleb	10	4.3	4.3	47.9
	pseudo	3	1.3	1.3	49.1
	pseudomonas	1	.4	.4	49.6
	proteus	2	.9	.9	53.0
	s.faecalis	8	3.4	3.4	56.4
	candida sp	1	.4	.4	56.8
	nbg	74	31.5	31.6	88.5
	nsbg	27	11.5	11.5	100.0
	Total	234	99.6	100.0	
Missing	System	1	.4		
Total		235	100.0		

APPENDIX XVIII

urinary tract pathogen

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	STAPH SP	2	4.1	4.1	4.1
	E.COLI	3	6.1	6.1	10.2
	KLEB	2	4.1	4.1	14.3
	PSEUDO	2	4.1	4.1	18.4
	NBG	33	67.3	67.3	85.7
	NSBG	7	14.3	14.3	100.0
	Total	49	100.0	100.0	

UTI history of all patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Symptomatic	121	51.5	51.5	51.5
	Asymptomatic	114	48.5	48.5	100.0
	Total	235	100.0	100.0	