# BACTERIAL PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF ISOLATES CAUSING URINARY TRACT INFECTIONS IN INTENSIVE CARE UNIT PATIENTS AT KENYATTA NATIONAL HOSPITAL

**ISABEL MUTHONI**

**A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF MASTER OF SCIENCE DEGREE IN TROPICAL AND INFECTIOUS DISEASES, UNIVERSITY OF NAIROBI, INSTITUTE OF TROPICAL AND INFECTIOUS DISEASES**.

**Certification**

The undersigned certifies that this dissertation is the work of the candidate carried out during her training in Master of Science under my direct supervision.

The undersigned certifies that I have read and hereby recommend it for consideration by University of Nairobi, the dissertation entitled; **BACTERIAL PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF ISOLATES CAUSING URINARY TRACT INFECTIONS IN CRITICAL CARE UNIT PATIENTS AT KENYATTA NATIONAL HOSPITAL.**

This dissertation is submitted in partial fulfillment of the requirements for the degree of Master of Science -Tropical and Infectious diseases at University of Nairobi-Institute of Tropical and Infectious Diseases (UNITID).

**SUPERVISORS:**

1. Professor Omu Anzala. MBChB ,PhD.

   Director, KAVI, Institute of clinical research,

   Professor, Department of Medical Microbiology

   College of Health Sciences, University of Nairobi.

   Signature _____Date:_____

2. Dr. Peter Mwathi. MBChB, Msc.

   Head, Medical Microbiology Laboratory

   Kenyatta National Hospital

   Signature_____Date:_____

**Declaration and copyright**

I, declare that this dissertation is my original work and that it has not been presented, and will not be presented to any other university for a similar or any other degree award ,and is not previously or currently under copyright.

**Isabell Mwangi (W64/80612/2012)**, isa.m.mwangi@gmail.com

_____ _____

Signature Date

## DEDICATION

This work is dedicated to my family for their love and support.

**ACKNOWLEDGEMENT**

First and foremost I thank the Almighty God for His mercy, grace and the good health he endowed upon me through this journey.

I am most grateful to my supervisors Prof. Omu Anzala and Dr. Peter Mwathi for their dedicated support and for always making available to me their time. I couldn't have made it this far without your unfailing assistance.

I thank the director of Kenyatta National Hospital and the director of Laboratory Medicine for allowing this study to be carried out at KNH microbiology laboratory.

My appreciation goes to all the staff at KNH microbiology laboratory for their assistance and for the friendly environment they provided during the period of my study there.

My special appreciation goes to my parents for giving me the gift of life and for moulding me into the woman I am. To my siblings, my world would not be complete without you.

To Mary, the biostatistician who dedicated her time to transforming the data into valuable information, Thank you.

To my beloved classmates Ukio Kusirye, Milka Mutai ,Moses Masika, Angela Munoko, Naomi Ratemo and Robert kunyera  am forever thankful for your support and friendship.

Last but not least, I am most thankful to the people who in one way or another contributed to the success of this study.

**Table of Contents**

**List of Acronyms**

**UTI** Urinary Tract Infection

**CCU** Critical Care Unit

| | |
|---|---|
| **NCAUTIs** | Nosocomial Catheter-Associated Urinary Tract Infections |
| **CDC** | Center for Disease Control and Prevention |
| **CFU** | Colony Forming Unit |
| **MOH** | Ministry of Health |
| **MIC** | Minimum inhibitory concentration. |
| **TMP/SMX** | Trimethoprim- sulphamethoxazole |
| **WHO** | World Health Organization |
| **MDR** | Multi Drug Resistant |
| **KNH** | Kenyatta National Hospital |
| **ICU** | Intensive Care Unit |
| **ESBLs** | Extended spectrum beta-lactamases |
| **WBCs** | White blood cells |
| **AST** | Antimicrobial susceptibility testing |
| **HDU** | High dependency unit |

**List of figures and tables**

# *Abstract*

Urinary tract infection (UTI) is one of the most common types of nosocomial infections encountered in the inpatient settings including intensive care unit (ICU). Amongst patients

admitted to ICU, studies have revealed the incidence of nosocomial UTIs to range from 9% to 29%.1-3 The risk of patients acquiring a UTI in an ICU was approximately 2.5-fold higher than that of patients in a general hospital ward. Complicated nosocomial UTIs may lead to urosepsis, and increase patient morbidity and mortality.4 Urinary tract infection (UTI) is one of the most common infectious diseases encountered by clinicians and the second ranking after respiratory tract infection which involve about 250 million people in developing countries annually. Despite the extensive use of antimicrobial agents, UTI has become difficult to treat because of manifestation of pathogens with increasing resistance even to more potent antimicrobial agents.

The study was a retrospective study aimed at identifying bacterial profile and antimicrobial susceptibility of organisms causing urinary tract infections in Intensive Care Unit (ICU) patients in KNH medical microbiology laboratory records during the period January 2013 to December 2013. Data were retrieved from the archives. A coded data collection form was used to collect information about the patient's age, sex, bacterial organisms isolated and their antimicrobial susceptibility patterns. The study was approved by the KNH/U.O.N Ethics and Research Commitee. Data was analysed using statistical package for social sciences (SPSS) version 17.0.

In this study ,among both sexes tested the incidence of UTI infections was higher in males than females.The most common bacterial organism included *Escherichia coli, Klebsiella* and *Enterococcos* spp. Organisms showed high resistance to Augmentin and highest sensitivity to Meropenem.

# CHAPTER ONE

## 1.1. Background

Urinary tract infection may be defined as a condition in which bacteria are established and multiplying within the urinary tract (Najar et al., 2009). Urinary tract infection (UTI)is the leading cause of gram negative bacteremia in patients of all ages and are associated with a high risk of morbidity and mortality especially in the young and the elderly (Orenstein et al., 1999).

However, the history of Urinary tract infection ranges far back as it is an important and one of the oldest diseases of man. It has been described since ancient times with its first documentation and description in the Ebers Papyrus dated to c. 1550 BC (Al-Achi et al., 2008). It was described by the Egyptians as "sending forth heat from the bladder" (Graham et al., 1990). Effective treatment did not occur until the advancement and accessibility to antibiotics in the 1930s prior to which time herbs, bloodletting and rest were recommended.

In recent studies microbial species that cause urinary tract infections are classified by their target sites, Such as urine infection (bacteriuria), bladder infection (cystitis), kidney infection (pyelonephritis), which can be asymptomatic or associated with symptoms. There are several common causative agents of urinary tract infections which are gram-negative rods. They include: *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumonia, Proteus spp.* and Enteropathogens. Other important causative agents are Enterococci and Staphylococcus saprophyticus. But *Escherichia coli* is the most common amongst them.

The frequency of pathogens is different, depending on age, gender, catheterization and hospitalization among other factors.

Adult women are most commonly affected between the ages of 16 and 35 years, with 10% getting an infection yearly as their urethra are shorter than men and opens nearer to the anus. This means it is easier for bacteria to enter the urinary tract and cause an infection. About 60% of women get at least one attack of cystitis in their lifetime. It is more common in sexually active women, during pregnancy, after surgery and menopause.

## 1.2. Literature Review

### 1.2.1. Introduction

Hospital-acquired (Nosocomial) UTIs are the most frequent nosocomial infections and can be a source of 10% to 15% of nosocomial bloodstream infections in medical or surgical intensive care units (ICUs). Worldwide, about 150 million people are diagnosed with UTI each year. In 1992 the CDC estimated that more than 900,000 nosocomial UTIs occurred in the United States and as many as 35,000 cases of bacteriumia secondary to nosocomial catheter-associated UTIs (NCAUTIs) occur annually.(CDC morbidity mortality weekly report 1992).

Although patients in ICU are fewer than other units, it has one of the highest occurrence rates of (nosocomial) infections (20-30% of all ICU-admissions) (Hanberger H,et al 1999), leading to an colossal impact on morbidity, hospital costs, and often, survival (Vandijck DM et al 2008). According to the EPIC II 1-day prospective point-prevalence study (Extended Prevalence of Infection in Intensive Care) in 1,265 participating ICUs (75 countries worldwide), 51% of the 13,796 patients were considered infected, although no subdivision was made for hospital-acquired infections (Vincent J, et al., 2009).

Urinary tract infection is among the most common infectious diseases, second ranking after respiratory (tract) system infection which infects about 250 million people in developing countries annually (El Astal ., 2005). It is caused by ascending movement of the organisms to the bladder. Organisms after reaching into bladder can be divided and go to the upper parts and infect the ureters and kidney. Growth of bacteria to $10^5$micro-organisms in every milliliter of urine sample is infection-positive.

Uncomplicated UTIs occur in sexually active healthy female patients with structurally and functionally normal urinary tracts. More than 95% of urinary tract infections are caused by a single bacterial species. *Escherichia coli* is the most frequent infecting organism in acute infection. Worldwide, *Escherichia coli* cause 75% – 90% of acute uncomplicated cystitis while *Staphylococcus saprophyticus* accounts for 5% to 15%, mainly in younger women (Gupta K et al., 2001, Fihn SD., 2003).

The distribution of these bacteria is different in different parts of the world and studying the microbial factors that cause this infection in all geographical regions, shows its dispersion. In a study conducted in Iran, the rate of urinary tract infections in ICU, In the study made by sadeghzade and hassani was 25% and in the study made by Talebi and Golestan was 9.2% was (Zadeh V. et al., 2005,Talebi et al.,2009). In another study in Karachi, Rizvi and his colleagues determined the pattern of nosocomial infections in two ICUs, E. coli, P.aeruginosa and K. pneumonia were the most common isolated pathogens. (Rizvi et al., 2007).

Danchaivijitr and colleagues who conducted a study on catheter-associated UTI in Bangkok concluded that catheter associated UTI was common and uropathogens were nosocomial microorganisms with high incidence of resistance to antimicrobials agents (Danchaivijitr et al.,

2005). In addition, a rate of 20% and 33% for UTI were reported from Tunisia and Albania (Kallel *et al*., 2005; Faria *et al*., 2007).

In Ethiopia, previous studies indicated high prevalence of hospital acquired infections. A rate of 15% and 26% for UTI were reported from Addis Ababa (Gedebou *et al*., 1988; Habte-Gabr *et al*., 1988). In Uganda, a study done in 1963 found a prevalence of symptomless bacteriuria among in-patients in Uganda to be 8% in women and 6% in men on medical wards. Out of these, 41% were due to *E.coli*(Tulloch J.A et al., 1963).

Several microbial agents have been found to be responsible for ICU acquired UTIs such as *Escherichia coli, Pseudomonas spp, Proteus mirabilis, Klebsiella spp, Enterobacter spp, Staphylococcus spp, Enterococcus faecalis, Candida spp, and Enterococcus spp*.(Laupland et al., 2005).Along with the problem of nosocomial infection comes with the burden of "multidrug" antimicrobial resistance (MDR). The ongoing emergence of resistance in the community and hospital is considered a major threat for public health. Due to the specific risk profile of its residents, the ICU also is deemed the epicenter of resistance development. Both infection and MDR result in a considerable clinical and economic burden. As such, the presence of MDR boosts the deleterious impact of nosocomial infection (Salgado C.D et al., 2005).

Data from different parts of the world has showed that there is an increase of resistance to conventional drugs in urinary tract pathogens. Most of the past studies carried out usually aim at obtaining the susceptibility patterns of UTI causing pathogens to the antimicrobial agents currently in use. Katarzyna et al. 2010, in their study carried out in Poland tested the resistance of various antibiotics, such as ampicillin, gentamicinco-amoxiclav, piperacillin, tazobactam, ceftazidime, ceftriaxone, trimethoprim, sulphamethoxazole trimethoprim, meropenem, amikacin, cefepime,

aztreonam, doxycycline, netilmicin norfloxacin, ciprofloxacin, nitrofurantoin, fosfomycin and trometamol on UTI causing pathogens (Katarzyna et al. 2010). The results from their study showed that *E.coli* was susceptible to most of the microbial agents. According to Katarzyna et al. 2010, meropenem was the only drug that showed a good activity across most of the UTI causing pathogens. Cefepime, which was a recently introduced fourth generation of cephalosporin, exhibited poor activity compared to piperacillin and ceftazidimine.

Chaudhary et al. also conducted an antibiotic sensitivity test on various antibiotics including Amikacin, Ceftazidime, Cefotaxime , Ceftriaxone , ,Cotrimoxazole, Ciprofloxacin , Nitrofurantoin Nalidixic acid, Meropenem, Imipinenem, Norfloxacin and Gentamicin on various urapathogens. Results from this study showed that sensitivity of ESBLs positive isolates of both *E.coli* and *Klebsiella* pneumonia *were* highest in Meropenem and also in Imipenem. The study also revealed a low resistance of 19.04% to amikacin, and 40% to nitrofurantoin, which is comparable to 24.4% and 34.3% respectively (Chaudhary et al., 2013). There was also, a moderate resistance to cefotaxime 45.71%, ceftriaxone 49.52%, ceftazidime 48.57% and ciprofloxacin 54.28%.

Although UTIs are the most common hospital acquired infections, the epidemiology of these infections and there antimicrobial resistant patterns are not well defined in East Africa and in particular in Kenya. Thus the objective of this study is to determine the bacterial profile and antimicrobial susceptibility of organisms causing urinary tract infections in intensive care unit (ICU) patients in Kenyatta National Hospital.

### 1.2.2. Routes of infection

The main and commonest route of infection is ascending route that involves the passage of bacteria (uropathogen) from urethra to bladder and kidney.

The other route of infection is the haematogenous route where the source of infection is blood.

### 1.2.3. Transmission

Urinary catheters are associated with a number of complications, such as urinary tract infections, which account for 40% of all hospital acquired infections (Burke and Yeo, 2004).

Each year millions of urethral catheters are put in place in these facilities across the United States. Nosocomial catheter-associated urinary tract infections (NCAUTIs) have been one of the major problems in the ICU and have contributed to the mortality and morbidity of the patients.

Urinary catheterization increases the risk for urinary tract infections. The risk of bacteriuria (bacteria in the urine) is between three to six percent per day and prophylactic antibiotics are not effective in decreasing symptomatic infections (Dielubanza et al., 2011).

It is believed that the bacteria are usually transmitted to the urethra from the bowel, with females at greater risk due to their anatomy. After gaining entry to the bladder, *Escherichia Coli* are able to attach to the bladder wall and form a biofilm that resists the body's immune response thus causing an infection (Salvatore et al., 2011).

### 1.2.4. Contributing factors for urinary tract infection

They include 3 main factors i.e.

1. Age: Very young and very old individuals are more at risk for UTI.
2. Sex: UTI is more common in females than males because females have short and wide urethra.
3. Hospitalization
    - Instrumentation: Indwelling catheters and cystoscopic procedures
    - Neurogenic bladder dysfunction: Diabetes mellitus, Spinal injury
    - Obstruction: Congenital anomalies in young ones and prostatic adenoma, stricture and calculi in old ones.
    - Underlying diseases: Diabetes mellitus, sickle cell disease
    - Vesico-ureteral reflex: Associated with recurrent acute
    - pyelonephritis.

### 1.2.5. Clinical Manifestation

Patients with lower urinary tract infection: Infection of urethra and bladder may present with frequency of micturition, pain during micturition, blood-stained or cloudy urine and supra pubic tenderness, usually with no fever.

Patients with upper urinary tract infection: Infection of the kidney parenchyma and pylus may present with the lower UTI symptoms and signs, flank pain, fever and chills, nausea and vomiting, and flank tenderness.

### 1.2.6. Laboratory diagnosis

Specimen collected and submitted to the microbiology laboratory include

- Clean catched midstream urine
- Catheterized urine or
- Suprapubic aspiration

In direct microscopic examination of the specimen is usually done but not in catheterized patients. The presence of more than five WBCs and abundant epithelial cells per HPF supports infection of urinary tract. Dipstick urine testing is NOT usually a reliable way to diagnose UTI and its not usually performed on asymptomatic patients or catheterized patients as it will present as false positives.

In Gram staining the presence of one bacterium in uncentrifuged gram stained urine confirms urinary tract infection .In culture and isolation Blood agar medium, and Mac Conkey agar medium are used to isolate the pathogens causing urinary tract infections.( Monica-Cheesbrough District Laboratory Practice in Tropical Countries Second edition Part 2 )

### 1.2.7. Interpretation of culture results

1. $\geq 10^5$CFU/ml of urine is significant to indicate UTI.

2. $<10^3$CFU/ml of urine indicates contamination of specimen.

3. $10^3$-$10^5$cfu/ml of urine is uncertain.

**NB**: $10^3$-$10^5$cfu/ml of urine in symptomatic patient or suprapubic or catheterized specimen indicates UTI. (Monica-Cheesbrough District Laboratory Practice in Tropical Countries Second edition Part 2 )

### 1.2.8. Treatment of UTI

A urinary tract infection is uncomfortable, but treatment is usually successful. Treatment in complicated UTIs involves the use of antibiotic therapy for about 7-14 days. The choice of empirical antibiotic therapy should be guided by the local resistance patterns where available.

The antibiotics commonly used against UTIs include: Trimethoprim/sulfamethoxazole, Nitrofurantoin, Cephalexin,, cephalosporinS, ceftriaxone, amoxicillin/clavulanic acid and fluoroquinolone. Antibiotic resistance is becoming an increasing concern about the future of treating patients with complicated and recurrent UTIs.

### 1.2.9. Antimicrobial Resistance

Antimicrobial is a general term given to substances including medicines that kill or slow the growth of microbes (Greenwood, *et al* 2002). Antimicrobial resistance occurs when microorganisms thrive in systemic concentrations of an antimicrobial that normally eliminates them (Glenn & Karen, 2005).

### 1.2.10. Categories of antimicrobial resistance

Antimicrobial resistance may be categorized in three ways:

**a) Intrinsic/Natural resistance**

This type of resistance is determined by the presence or absence of the target for the action of the antimicrobial. It is also due to multidrug efflux systems and hence causes drug inactivation.

**b) Genetic mutational resistance**

Mutations, rare spontaneous changes of the bacteria's genetic material, are thought to occur in about one in one million to one in ten million cells. Different genetic mutations yield different types of resistance. The mutations cause target site modification, reduced permeability or uptake, metabolic by-pass and depression of multidrug efflux systems.

**c) Acquired resistance from another bacterium**

Bacteria can acquire antibiotic resistance genes from other bacteria in several ways one of them arising from alteration of the genetic material of microorganisms. There are three main factors affect the frequency of acquired resistance and include the following:

a) The amount of antimicrobial being used.
b) The frequency with which bacteria can undergo spontaneous mutations.
c) The prevalence of plasmids able for transfer of resistance from one bacterium to another.

These changes occur due to mutations as a means of eliminating the effectiveness of the antimicrobials by the microorganism. Chromosomal mutations leading to resistance often produce structural changes in the bacterial cell, whereas transferable resistance tends to code enzymes that metabolize antimicrobials (Todar, 2002).

An organism may lose its sensitivity to an antimicrobial during a course of treatment. Once resistance has appeared, the continuing presence of the antimicrobial exerts a selective pressure in favor of the resistant organism (Greenwood, *et al* 2002).

### 1.2.11. Antimicrobial Susceptibility Testing (AST)

This is indicated for pathogens contributing to an infectious process that warrants antimicrobial therapy if susceptibility to antimicrobials cannot be predicted reliably based on knowledge of their identity. Antimicrobial susceptibility testing (AST) is used routinely by diagnostic microbiology laboratories to direct therapy. The gold standard for susceptibility testing is determination of the minimum inhibitory concentration (MIC), i.e. the lowest concentration of antimicrobial that will inhibit the visible growth of a micro-organism after overnight incubation (Jenkins and Schuetz, 2012).

The range of antibiotic concentrations used for determining MICs is universally accepted to be in doubling dilution steps up or down from 1 mg / l. Methods for determining the MIC include the broth micro dilution method, where wells contain broth with different dilutions of antibiotics added, and agar dilution techniques that use agar into which antimicrobial agents have been incorporated at different concentrations. The E-test is a modified agar diffusion method in which an agar plate is inoculated with a bacterial isolate and a rectangular strip impregnated with antibiotic is overlaid; the drug diffuses out into the agar, producing an exponential gradient of drug concentrations. The MIC corresponding to the zone of inhibition is read off a scale on the strip (Jenkins and Schuetz, 2012).

In practice, estimating precise MICs for various drugs against individual isolates is labour-intensive and time-consuming, so the most common method employed by most diagnostic laboratories is a simpler agar diffusion test (Kirby–Bauer method), in which the organism under investigation is inoculated onto an agar plate and exposed to a diffusion gradient of antibiotic from an impregnated disc of filter paper placed on the agar surface.

The circular area of growth inhibition (zone of inhibition size) reflects the antibiotic activity. This method provides a simple and cheap 'breakpoint technique', using zone of inhibition cut-offs to classify bacterial isolates as either: susceptible, intermediate, or resistant. There is not one universally accepted system for AST, meaning different countries / laboratories use different breakpoints to define susceptibility of different bacteria (CLSI, 2005).

### 1.3 Problem statement

There is increasing drug resistance against the commonly used antimicrobial agents globally especially among the patients in critical units. The ongoing emergence of resistance in the community and hospital is considered a major threat for public health. Due to the specific risk profile of its residents, the CCU also is deemed the epicenter of resistance development. Both infection and MDR result in a considerable clinical and economic burden. The study will try to highlight the bacterial profile and antimicrobial susceptibility of organisms causing urinary tract infections in Critical care unit (CCU) patients in Kenyatta National Hospital.

### 1.4 Justification

Antimicrobial resistance is an increasingly emerging problem worldwide, especially in ICUs. Identifying the resistance pattern of microorganisms in every hospital is the key to success in the appropriate treatment of patients. Urinary tract infection (UTI) is the most common infection experienced by humans after respiratory as the urinary tract is the second most common site for bacterial infections. It is one of the most common infectious diseases encountered by clinicians as it causes both community-acquired and nosocomial infections for patients admitted in hospitals especially ICU patients.

In an era of rapid emergence of antimicrobial resistance, controversies regarding the prolonged use of antibiotics with established activity against uropathogens pose special problems therefore if not treated and eradicated in time, it would lead to serious detrimental impact on human health and economic consequences.

Inadequate data on local resistance patterns on urinary tract infections in CCU patients at the KNH intensive care unit can lead to wrong choices of antimicrobial therapy and increase development of resistance. Therefore the aim of this study is to determine the bacterial profile and antimicrobial susceptibility of organisms causing urinary tract infections in CCU patients in Kenyatta National Hospital.

The results obtained from this study are intended to guide in targeted diagnosis and treatment, provide insight into identifying factors contributing to the spread of antimicrobial resistance to many common antibiotics. The information gathered from this study will also form a basis for further research and whether the drugs used in KNH critical care unit are sensitive to uropathogens.

# CHAPTER TWO

## 2.1 Research questions

1. What are the bacterial profiles of organisms causing urinary tract infections among the CCU patients at Kenyatta National Hospital?

2. What are the antimicrobial susceptibility patterns of specific organisms causing urinary tract infections among CCU patients at Kenyatta National Hospital?

## 2.2 Objectives of the study

### 2.2.1 General objective

To determine the bacterial profile and antimicrobial susceptibility of organisms causing urinary tract infections in CCU patients in Kenyatta National Hospital.

### 2.2.2 Specific objectives

1. To describe the bacterial profile of bacterial organisms causing urinary tract infections in CCU patients in Kenyatta National Hospital.
2. To describe the antimicrobial susceptibility of specific organisms to the commonly used antimicrobial agents used to treat bacterial urinary tract infections among CCU patients in Kenyatta National Hospital .

# CHAPTER THREE

## 3.1 Research Methodology

### 3.1.1 Study site

The study was conducted at the Kenyatta National Hospital (KNH) Medical Microbiology Laboratory. Kenyatta National Hospital (KNH) - a 1,800 bed level 6 Hospital which is the largest hospital in Kenya. It is located 3kms from Kenya's capital city of Nairobi.

KNH has the largest critical care unit with a capacity of 20 beds. It is multidisciplinary and admits patients of all ages. The major reason for admission in ICU arises from severe injuries as a result of mainly road accidents and assaults. The average monthly admission is at 104 patients, with a mortality rate close to 40% of the total admission (ICU and HDU Admission records).

### 3.1.2 Study design

The study was a retrospective study involving the review of Critical Care Unit patients' medical microbiology laboratory records between the period January 2013 to December 2013.

### 3.1.3. Study population

Data of urine samples from the Critical Care Unit ward of KNH received at the KNH medical microbiology laboratory in which isolation and identification and antimicrobial susceptibility testing was done using standard microbiological methods were studied.

### 3.1.4 Inclusion criteria

Laboratory records of Critical Care Unit patients urine samples. The presence of a single bacteria growing at colony counts $10^3$ indicates UTI. Cultures in which isolation and identification of bacterial organisms along with their antimicrobial susceptibility tests was done during the period January 2013 to December 2013 were included in the study.

### 3.1.5 Exclusion criteria

1.Laboratory records of patients not admitted to the Critical care unit at KNH.

2. Laboratory data of CCU urine samples with no bacterial growth.

3. Laboratory records of bacterial isolates from CCU urine samples that were not tested for antimicrobial susceptibility.

### 3.1.6 Sample size determination

The prevalence of urinary tract infections in CCU patients in Kenya is unknown. Therefore 50% prevalence was assumed.

The sample size is estimated according to Fisher's formula (Fisher 1991)

Fishers formula is $N = Z^2PQ/d^2$,

Where: N = Minimum sample size

Z = Constant, standard normal deviation (1.96 for 95% confidence interval)

P = Population proportion with characteristic of interest

Q = 1-P

d = Acceptable margin of error

Z = 1.96

P = 0.5

Q = 0.5

d = 0.05

$$N = \frac{(1.96)^2 \times 0.5\ (1- 0.5)}{(0.05)^2}$$

=384 was the minimal sample size.

### 3.1.7 Data sampling technique

The sampling frame included laboratory records of critical care urine samples having bacterial isolates which were tested for antimicrobial susceptibility during the period January 2013 to December 2013 at KNH medical microbiology laboratory that met the inclusion criteria. Systematic random sampling was used to select the records. A sampling fraction *k* was obtained by dividing the 'total number of urine records with bacterial isolates', which is approximately 1,040 during the year 2013 by 384. The first records were selected randomly and the rest by subsequently adding the value of *k*, which is 2, until the sample size is achieved.

### 3.1.8 Data collection

A coded form was used as the study instrument to abstract the information. Information regarding patients age, sex, bacterial organisms isolated and their antimicrobial susceptibility was extracted. For confidentiality patients' names were left out.

### 3.1.9 Data management and analysis

Data was collected and entered into an Ms Excel spreadsheet in a password protected computer. Filled forms were stored in lockable drawers ,backup copies were stored in an external hard drive and a compact disc and were solely in custody of the principal investigator.

Data collected was entered into an Ms Excel spreadsheet and a statistical package for social sciences (SPSS) version 17.0 was used to analyze the data. Descriptive statistics was used to summarize the collected data. Chi square test and fishers exact test were used to determine association between categorical variables while t-test will be used to determine association between continuous variables.

P- Value < 0.05 was considered to be statistically significant.

# CHAPTER FOUR

## 4.1. Ethical consideration

Local approval was sought from the Kenyatta National Hospital/University of Nairobi-Ethics Review Committee (KNH/UoN-ERC). Permission to extract data from the hospital registries and laboratory records was obtained from Kenyatta National Hospital Head of Laboratory Medicine.

This study was a minimal risk study since there is no patient involvement but a review of the laboratory records. For confidentiality the patients laboratory file were used in the confines of the KNH microbiology and only the investigator had access to the laboratory records for the purposes of the study. The patients name and Hospital number were not included in the data collection form.

Raw data in form of filled forms, data stored in password protected computer, backup copies in hard drives and compact disc were destroyed at the end of the study.

## 4.2 Study limitation

One of the major study limitation was incomplete data.

# CHAPTER FIVE

## RESULTS

### 5.1.DEMOGRAPHICS

In the year 2013, there were 1040 records of bacterial organisms isolated from urine samples of CCU patients in KNH medical microbiology laboratory and, of these, 385 were sampled randomly.

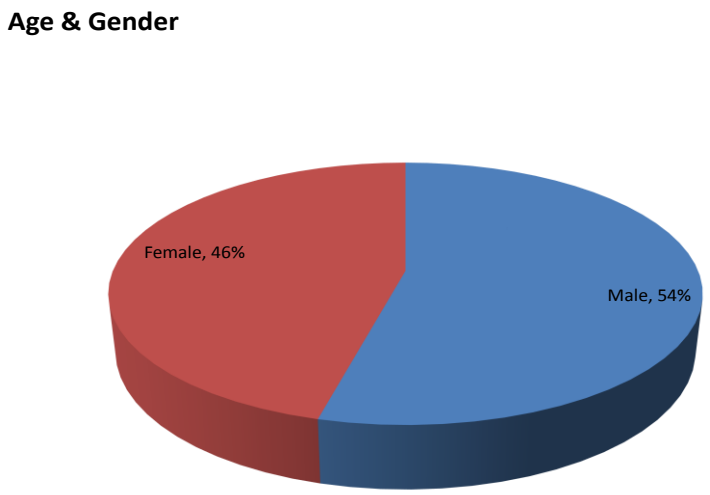


**Figure 1: Gender of the study population**

Females were 46% (177) while males were 54% (208)

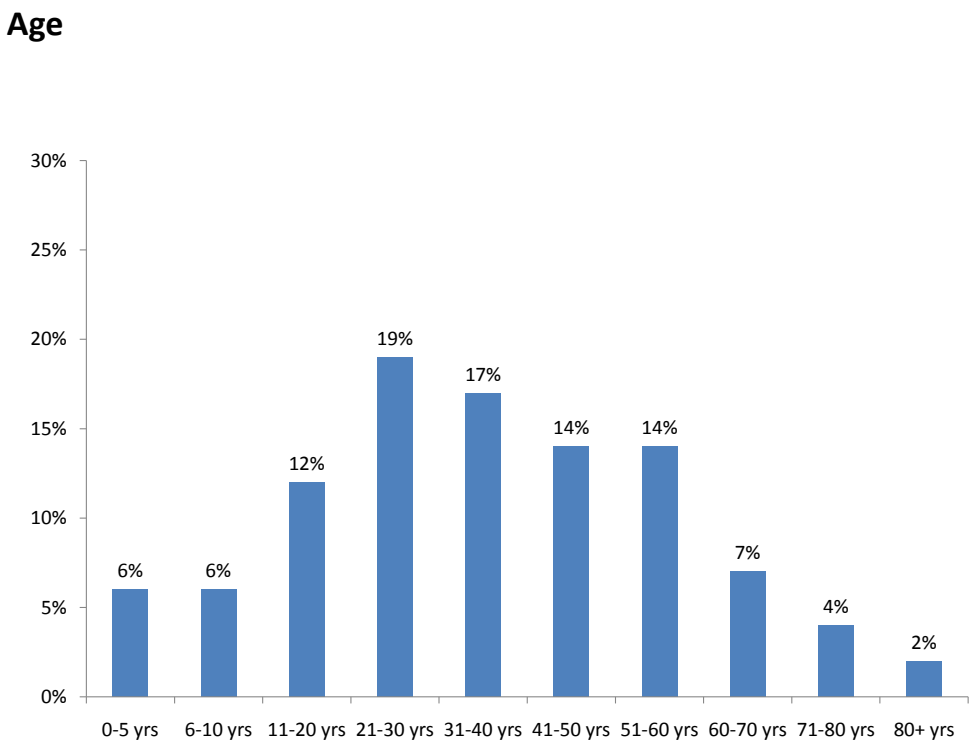


**Figure 2: Age distribution of the study population.**

The patients' ages ranged from 1 year to 80 years..Those aged between 21 to 30 years were the majority (19%) while those aged 31-40years were 17.0%. patients above 80 accounted for the least which was 2%.

## DISTRIBUTION OF ORGANISMS ISOLATED

| Distribution of isolated organism | | |
|---|---|---|
| | 385 | |
| Staphylococcus | 11 | 2.9% |
| Escherichia coli | 88 | 23% |
| Klebsiella | 76 | 19.7% |
| Proteus | 9 | 2.3% |
| Enterobacter | 23 | 6.0% |
| Citrobacter | 29 | 7.5% |
| Acinectobacter | 38 | 9.9% |
| Pseudomonas | 39 | 10.1% |
| Enterococcos | 72 | 18.7% |

**Table 1.distribution of isolated organisms**

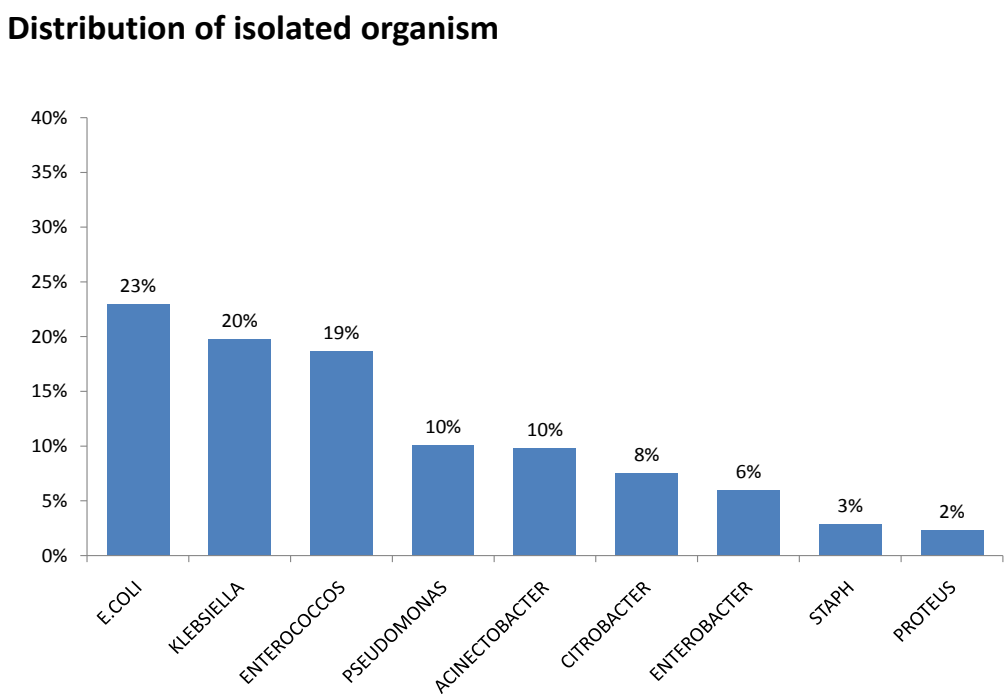


Figure 3:Distribution of isolated organisms.

**ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF URINE BACTERIAL ISOLATES**

Twenty four antibiotics were tested against the isolated organisms. Overall the highest sensitivity was demonstrated by Meropenem (33.0%) and teicoplanin (15.6.%) while Augmentin (48.8.%), Ampicillin (61.9%), Amplicillin (39.2%) ,Gentamycin (37.1%) and Cefotaxime (33.8%)showed the highest resistance as shown in table 2.

| | **Resistance** | | | **Sensitive** | |
|---|---|---|---|---|---|
| | **count** | **%** | | **count** | **%** |
| Amoxylclav | 188 | 48.8% | Amoxylclav | 30 | 7.8% |
| Doxycycline | 61 | 15.8% | Doxycycline | 25 | 6.5% |
| Cefuroxime | 87 | 22.6% | Cefuroxime | 6 | 1.6% |
| Ampicillin | 151 | 39.2% | Ampicillin | 20 | 5.2% |
| Levofloxacin | 119 | 30.9% | Levofloxacin | 35 | 9.1% |
| Gentamycin | 143 | 37.1% | Gentamycin | 35 | 9.1% |
| Piperacillin | 52 | 13.5% | Piperacillin | 34 | 8.8% |
| Imipenem | 50 | 13.0% | Imipenem | 47 | 12.2% |
| Cefeime | 85 | 22.1% | Cefeime | 19 | 4.9% |
| Amikacin | 47 | 12.2% | Amikacin | 61 | 15.8% |
| Cefriaxone | 144 | 37.4% | Cefriaxone | 11 | 2.9% |
| Cefotaxime | 130 | 33.8% | Cefotaxime | 11 | 2.9% |
| Cotrimoxazole | 31 | 8.1% | Cotrimoxazole | 10 | 2.6% |
| Nalidixicacid | 88 | 22.9% | Nalidixicacid | 13 | 3.4% |
| Nitrofurantion | 73 | 19.0% | Nitrofurantion | 50 | 13.0% |
| Ceftazidime | 84 | 21.8% | Ceftazidime | 18 | 4.7% |
| Meropenem | 78 | 20.3% | Meropenem | 127 | 33.0% |
| Teicoplanin | 8 | 2.1% | Teicoplanin | 60 | 15.6% |
| Vancomycin | 8 | 2.1% | Vancomycin | 50 | 13.0% |
| Ciprofloxacin | 63 | 16.4% | Ciprofloxacin | 21 | 5.5% |
| Tazobactam | 3 | 0.8% | Tazobactam | 2 | 0.5% |
| Streptomycin | 5 | 1.3% | Streptomycin | 3 | 0.8% |
| Erthomycin | 8 | 2.1% | Erthomycin | 2 | 0.5% |
| Leniozid | 0 | 0.0% | Leniozid | 11 | 2.9% |

**Table 2: General sensitivity and resistance patterns of Antibiotics.**

**Resistance and Sensitivity of selected organisms**

Among the top three isolated organisms *E.coli* (23%), *Klebsiella* (20%), and *enterococcus* (19%)followed by *Pseudomonas* spp (10%), *Acinetobacter* spp (10%), *Citrobacter* spp (8%) *Enterobacter* spp( 6%) *Staphylococcous* spp (3%) and *Proteus* spp (2%)

*E.coli* spp had a high resistance to Augmentin (65%),Cefriaxone (44%)and Ampicillin (43%) and showed a high sensitivity to meropenem (56%),amikacin (27%) and nitrofuratoin (26%) Table 3

| | **Resistance** | | | **Sensitive** | |
|---|---|---|---|---|---|
| | **count** | **%** | | **count** | **%** |
| Amoxylclav | 57 | 64.8% | Amoxylclav | 13 | 14.8% |
| Doxycycline | 13 | 14.8% | Doxycycline | 6 | 6.8% |
| Cefuroxime | 24 | 27.3% | Cefuroxime | 3 | 3.4% |
| Ampicillin | 38 | 43.2% | Ampicillin | 3 | 3.4% |
| Levofloxacin | 28 | 31.8% | Levofloxacin | 6 | 6.8% |
| Gentamycin | 26 | 29.5% | Gentamycin | 10 | 11.4% |
| Piperacillin | 6 | 6.8% | Piperacillin | 14 | 15.9% |
| Imipenem | 6 | 6.8% | Imipenem | 22 | 25.0% |
| Cefeime | 19 | 21.6% | Cefeime | 11 | 12.5% |
| Amikacin | 6 | 6.8% | Amikacin | 24 | 27.3% |
| Cefriaxone | 39 | 44.3% | Cefriaxone | 5 | 5.7% |
| Cefotaxime | 37 | 42.0% | Cefotaxime | 6 | 6.8% |
| Cotrimoxazole | 10 | 11.4% | Cotrimoxazole | 2 | 2.3% |
| Nalidixicacid | 20 | 22.7% | Nalidixicacid | 5 | 5.7% |
| Nitrofurantion | 8 | 9.1% | Nitrofurantion | 23 | 26.1% |
| Ceftazidime | 15 | 17.0% | Ceftazidime | 9 | 10.2% |
| Meropenem | 7 | 8.0% | Meropenem | 49 | 55.7% |
| Teicoplanin | 0 | 0.0% | Teicoplanin | 1 | 1.1% |
| Vancomycin | 0 | 0.0% | Vancomycin | 1 | 1.1% |
| Ciprofloxacin | 13 | 14.8% | Ciprofloxacin | 5 | 5.7% |

**Table 3.Antimicrobial patterns among Escherichia coli spp**

*Klebsiella* spp. had high resistance to Augmentin (61.8%), Gentamicin (47.4%) and cefotaxime (39.5%) and showed high sensitivity to meropenem (47.4%) Amikacin (34.2%) and piperacillin (18.4%) .

| | Resistance | | | Sensitive | |
|---|---|---|---|---|---|
| | **Count** | **%** | | **Count** | **%** |
| Amoxylclav | 47 | 61.8% | Amoxylclav | 9 | 11.8% |
| Doxycycline | 10 | 13.2% | Doxycycline | 4 | 5.3% |
| Cefuroxime | 27 | 35.5% | Cefuroxime | 0 | 0.0% |
| Ampicillin | 29 | 38.2% | Ampicillin | 0 | 0.0% |
| Levofloxacin | 14 | 18.4% | Levofloxacin | 8 | 10.5% |
| Gentamycin | 36 | 47.4% | Gentamycin | 9 | 11.8% |
| Piperacillin | 13 | 17.1% | Piperacillin | 14 | 18.4% |
| Imipenem | 9 | 11.8% | Imipenem | 11 | 14.5% |
| Cefeime | 21 | 27.6% | Cefeime | 2 | 2.6% |
| Amikacin | 15 | 19.7% | Amikacin | 26 | 34.2% |
| Cefriaxone | 28 | 36.8% | Cefriaxone | 1 | 1.3% |
| Cefotaxime | 30 | 39.5% | Cefotaxime | 1 | 1.3% |
| Cotrimoxazole | 7 | 9.2% | Cotrimoxazole | 4 | 5.3% |
| Nalidixicacid | 23 | 30.3% | Nalidixicacid | 3 | 3.9% |
| Nitrofurantion | 25 | 32.9% | Nitrofurantion | 8 | 10.5% |
| Ceftazidime | 30 | 39.5% | Ceftazidime | 4 | 5.3% |
| Meropenem | 16 | 21.1% | Meropenem | 36 | 47.4% |
| Teicoplanin | 0 | 0.0% | Teicoplanin | 0 | 0.0% |
| Vancomycin | 0 | 0.0% | Vancomycin | 0 | 0.0% |
| Ciprofloxacin | 12 | 15.8% | Ciprofloxacin | 9 | 11.8% |
| Tazobactam | 2 | 2.6% | Tazobactam | 1 | 1.3% |

**Table 4:Antimicrobial sensitivity pattern of Klesiella spp.**

*Enterococcos* spp had a high resistance to ampicillin (58.3%) levofloxacin (45.8%) and gentamicin (37.5%) and showed high sensitivity to teicoplanin (72.2%) vancomycin (63.9%) and nitrofuratonin (20.8%)

| | Resistance | | | Sensitive | |
|---|---|---|---|---|---|
| | **count** | **%** | | **count** | **%** |
| Amoxylclav | 4 | 5.6% | Amoxylclav | 1 | 1.4% |
| Doxycycline | 22 | 30.6% | Doxycycline | 9 | 12.5% |
| Cefuroxime | 0 | 0.0% | Cefuroxime | 0 | 0.0% |
| Ampicillin | 42 | 58.3% | Ampicillin | 15 | 20.8% |
| Levofloxacin | 33 | 45.8% | Levofloxacin | 2 | 2.8% |
| Gentamycin | 27 | 37.5% | Gentamycin | 1 | 1.4% |
| Piperacillin | 0 | 0.0% | Piperacillin | 0 | 0.0% |
| Imipenem | 1 | 1.4% | Imipenem | 3 | 4.2% |
| Cefeime | 0 | 0.0% | Cefeime | 0 | 0.0% |
| Amikacin | 0 | 0.0% | Amikacin | 0 | 0.0% |
| Cefriaxone | 0 | 0.0% | Cefriaxone | 0 | 0.0% |
| Cefotaxime | 0 | 0.0% | Cefotaxime | 0 | 0.0% |
| Cotrimoxazole | 1 | 1.4% | Cotrimoxazole | 2 | 2.8% |
| Nalidixicacid | 5 | 6.9% | Nalidixicacid | 2 | 2.8% |
| Nitrofurantion | 9 | 12.5% | Nitrofurantion | 15 | 20.8% |
| Ceftazidime | 0 | 0.0% | Ceftazidime | 0 | 0.0% |
| Meropenem | 2 | 2.8% | Meropenem | 3 | 4.2% |
| Teicoplanin | 6 | 8.3% | Teicoplanin | 52 | 72.2% |
| Vancomycin | 8 | 11.1% | Vancomycin | 46 | 63.9% |
| Ciprofloxacin | 9 | 12.5% | Ciprofloxacin | 1 | 1.4% |
| Tazobactam | 0 | 0.0% | Tazobactam | 0 | 0.0% |
| Streptomycin | 5 | 6.9% | Streptomycin | 3 | 4.2% |
| Erthomycin | 8 | 11.1% | Erthomycin | 2 | 2.8% |
| Leniozid | 0 | 0.0% | Leniozid | 10 | 13.9% |

**Table 5: Antimicrobial sensitivity pattern among Enterococcos spps**

*Pseudomonas* spp had a high resistance to cefriaxone 56.4% and cefotaxime 48.7% and showed h sensitivity to meropenem 30.8% levofloxacin 17.9% and gentamacin 12.8%

| | Resistance | | | Sensitive | |
|---|---|---|---|---|---|
| | count | % | | count | % |
| Amoxylclav | 0 | 0.0% | Amoxylclav | 0 | 0.0% |
| Doxycycline | 0 | 0.0% | Doxycycline | 0 | 0.0% |
| Cefuroxime | 2 | 5.1% | Cefuroxime | 0 | 0.0% |
| Ampicillin | 0 | 0.0% | Ampicillin | 0 | 0.0% |
| Levofloxacin | 15 | 38.5% | Levofloxacin | 7 | 17.9% |
| Gentamycin | 15 | 38.5% | Gentamycin | 5 | 12.8% |
| Piperacillin | 9 | 23.1% | Piperacillin | 4 | 10.3% |
| Imipenem | 13 | 33.3% | Imipenem | 1 | 2.6% |
| Cefeime | 9 | 23.1% | Cefeime | 4 | 10.3% |
| Amikacin | 15 | 38.5% | Amikacin | 2 | 5.1% |
| Cefriaxone | 22 | 56.4% | Cefriaxone | 2 | 5.1% |
| Cefotaxime | 19 | 48.7% | Cefotaxime | 2 | 5.1% |
| Cotrimoxazole | 0 | 0.0% | Cotrimoxazole | 0 | 0.0% |
| Nalidixicacid | 2 | 5.1% | Nalidixicacid | 0 | 0.0% |
| Nitrofurantion | 0 | 0.0% | Nitrofurantion | 0 | 0.0% |
| Ceftazidime | 5 | 12.8% | Ceftazidime | 4 | 10.3% |
| Meropenem | 19 | 48.7% | Meropenem | 12 | 30.8% |
| Teicoplanin | 0 | 0.0% | Teicoplanin | 0 | 0.0% |
| Vancomycin | 0 | 0.0% | Vancomycin | 0 | 0.0% |
| Ciprofloxacin | 8 | 20.5% | Ciprofloxacin | 1 | 2.6% |
| Tazobactam | 1 | 2.6% | Tazobactam | 0 | 0.0% |

**Table 6: Antimicrobial sensitivity pattern among Pseudomonas spp**

## CHAPTER 6: DISCUSSION, CONCLUSION AND RECOMMENDATIONS
## 6.1. DISCUSSION

### Discussions

The results from this study are an indication that antimicrobial resistance is a major problem in the healthcare setting and more so in patients in critical care. This research concurs with others in the past that show that UTI is the most common hospital acquired infection in the ICU. In Iran, a study by Sadeghzade and Hassani and Talebi and Golestan showed that rate of UTI infection in the ICU was 25% and 9.2 % respectively. Similarly, a study by Danchaivijitr and colleagues in Bangkok on catheter associated UTI ascertained that UTI resulting from catheter use was common and it was mainly caused by nosocomial microorganisms that had a high resistance to microbial agents. The high prevelanece of UTI in the critical care setting can be attributed to the widespread use of catheters, which increases the risk of getting this infection.

For this study, UTI was more common in males at 54 percent that in females at 46 percent. Although other past studies have showed that women are more susceptible to UTI, it is also important to note that it is one of the serious health issue affecting millions of men annually. In fact, they are the second most common form of infection among men. In addition, these infections are also more common among black and African men compared to other races. The causes of UTI in men in clued sexual transmission by *Mycoplasma* and *Chlamydia,* bladder outlet obstruction resulting from benign prostatic hyperplasia, especially in older men. Uncircumcised men are also at a higher risk due to accumulation of bacteria in the folds of the foreskin, enlarged prostate gland and diabetes increases the risk of UTI in men.

This study also concurs with past research that shows that showed that the most common isolated pathogens were *Escherichia coli,* which is in tandem with results from Gupta K et al., 2001, Fihn

SD., 2003) that showed that this organism causes 75 to 90 percent of acute infection worldwide. It is also in line with another study carried out by Karachi, Rizvi and his colleagues to determine the patterns of nosocomical infections in two ICUs whereby it was ascertained that *Escherichia coli, P.aeruginosa* and *K. pneumonia* were the most isolated pathogens. *Escherichia coli* is commonly found in bowel and is transmitted to the urethra. After it enters the bladder, it attaches on the bladder wall forming a resistant biofilm which compromises the body immune response thereby resulting in a chronic recurrent infection.

In the drugs used to treat the different microorganisms' causing UTI in the ICU, Amoxylclav showed the highest resistance at 48.8 % followed by Doxycycline at 15.8 percent. On the other hand, Leniozid showed no resistance to all the microorganisms followed by Erthomycin at 2.1 percent. In terms of sensitivity, Meropenem was the highest at 33 percent, while the lowest was Tazobactam and Erthomycin at 0.5 percent. When it comes to individual microorganisms', antimicrobial resistance for Klebsiella was high in Amoxylclav at 61. 8 percent and showed no resistance for Telcoplanin, Vancomycin, Streptomycin, Erythromycin and Leniozid. Meropenem showed the highest sensitivity at 47.4 percent and none for Leniozid, Streptomycin and Erythromycin.

The results are similar to those carried out by Chaudhary et al. (2013), on sensitivity of various antibiotics including Amikacin, Ceftazidime, Cefotaxime , Ceftriaxone , ,Cotrimoxazole, Ciprofloxacin , Nitrofurantoin Nalidixic acid, Meropenem, Imipinenem, Norfloxacin and Gentamicin on various urapathogens. Results from this study showed that sensitivity of ESBLs positive isolates of both *E.coli* and *Klebsiella* pneumonia *were* highest in Meropenem and also in Imipenem. The study also revealed a low resistance of 19.04% to amikacin, and 40% to nitrofurantoin, which is comparable to 24.4% and 34.3% respectively (Chaudhary et al., 2013).

There was also, a moderate resistance to cefotaxime 45.71%, ceftriaxone 49.52%, ceftazidime 48.57% and ciprofloxacin 54.28%.

Similar results were obtained by Katarzyna et al. 2010, in their study carried out in Poland tested the resistance of various antibiotics, such as ampicillin, gentamicinco-amoxiclav, piperacillin, tazobactam, ceftazidime, ceftriaxone, trimethoprim, sulphamethoxazole trimethoprim, meropenem, amikacin, cefepime, aztreonam, doxycycline, netilmicin norfloxacin, ciprofloxacin, nitrofurantoin, fosfomycin and trometamol on UTI causing pathogens (Katarzyna et al. 2010). The results from their study showed that *E.coli* was susceptible to most of the microbial agents. According to Katarzyna et al. 2010, meropenem was the only drug that showed a good activity across most of the UTI causing pathogens. Cefepime, which was a recently introduced fourth generation of cephalosporin, exhibited poor activity compared to piperacillin and ceftazidimine.

Results from this study showed that Amoxylclav showed the highest resistance in most of the organisms while Meropenem showed the highest sensitivity. These results on sensitivity are similar to those other studies by Katarzyna et al. 2010 and Chaudhary et al. (2013) that showed that Meropenem was the most effective in treating uropathogens.

**CONCLUSIONS**

Escherichia coli was the most common bacterial pathogen followed by klebsiella spp and enterococcos spp. Carbapenems, especially Meropenem, was found to be the most effective compared to other drugs in treating the isolated pathogens. However, these drugs are not commonly used in healthcare settings with limited resources/low income countries because they are expensive. Amoxylclav showed the highest resistance in most of the uropathogens because it is commonly used to treat other conditions in the critical care setting, such as head injuries due to its capability

of covering a wide spectrum of bacteria. Most patients are put on Amoxylclav after admission in the CCU, so they can develop resistance to it when it is used in treating UTI.

## RECOMMENDATIONS

1. A combination of ongoing surveillance for bacterial resistance, monitoring of antibiotic utilization patterns and effective infection control practice should be put in place.
2. Antimicrobial stewardship programs and antibiograms should be developed by healthcare institutions to reduce inappropriate antimicrobial use, improve patient outcomes and reduce adverse consequences of antimicrobial use.
3. Considering that Carbapenems are very effective in treating *Enterobacteriaceae* infections, the government and other relevant stakeholders should consider subsidizing the cost of these drugs, so that they can be used across most healthcare settings.

## CHAPTER SEVEN :

### 7.1 REFERENCES


1. Al-Achi, Antoine (2008). **An introduction to botanical medicines: history, science, uses, and dangers.** Westport, Conn.: Praeger Publishers. p. 126

2. Burke J.P and Yeo T.W (2004). **Nosocomial urinary tract infection in Mayhall C.G ed hospital epidemiology and infection control** 3rd edition pp 279-270

3. Centers for Disease Control (CDC).(1992). **Public health focus: surveillance,prevention, and control of nosocomial infections**. MMWR Morb Mortal Wkly Rep ; 41:783—7.

4. Chaudhary et al. (2013). **Extended Expectrum Betalactamases in Uropathogen**. Asian journal of pharmaceutical and clinical research, 6 (3): 207-210.

5. Clinical and laboratory standards institute, 2005. **Performance standards for antimicrobial susceptibility testing; fifteenth informational supplement**. CLSI Publication M100-S15, M2-A8 and M7-A6. Pennsylvania.

6. Danchaivijitr S, Dhiraputra C, Cherdrungsi R, Jintanothaitavorn D, Srihapol N. (2005). **Catheter–associated urinary tract infection**. J Med Assoc Thai pp. 88

7. Dielubanza E., Schaeffer A**. Urinary tract infections in women**.( 2011). Med Clin North Am 95: 27–41

8. El Astal Z. (2005).**Increasing ciprofloxacin resistance among prevalent urinary tract bacterial isolates in Gaza Strip, Palestine**.

9. Faria S, Sodano L, Gjata A, Dauri M, Sabato AF, Bilaj A, Mertiraj O, Llazo E, Kodra Y, Schinaia N .(2007).**Prevalence Study Group. The first prevalence survey of nosocomial infections in the University Hospital Centre 'Mother Teresa' of Tirana, Albania**. *J Hosp Infect*. **65:**244-250.

10. Fihn S.D.(2003) **Acute Uncomplicated Urinary Tract Infection in Women.** The new england journal *of* medicine N Engl J Med:349(3):259-66 .

11. Gedebou M, Habte-Gabr E, Kronvall G, Yoseph S (1988**). Hospital-acquired infections among obstetric and gynecological patients at Tikur Anbessa Hospital, Addis Ababa**. *J Hosp Infect.* **11**:50-59.

12. Graham (1990). **Topley and Wilson's Principles of bacteriology, virology and immunity : in 4 volumes** (8. ed. ed.). London: Arnold. p. 198.

13. Greenwood, D., Richard, C.B., Slack&Peutherer, J.F. (2002): **Antimicrobial Sensitivity**: Medical Microbiology. Elsevier science.

14. Gupta K, Sahm DF, Mayfield D, Stamm WE. (2001).**Antimicrobial Resistance Among Uropathogens that Cause Community-Acquired Urinary Tract Infections in Women: A Nationwide Analysis** *Clin Infect Dis: 33 (1): 89-94*

15. Habte-Gabr E, Gedebou M, Kronvall G (1988). **Hospital-acquired infections among surgical patients in Tikur Anbessa Hospital, Addis Ababa, Ethiopia**.*Am J Infect Control*. **16**:7-13.

16. Håkan Hanberger,; José-Angel Garcia-Rodriguez; Miguel Gobernado, et.al (1999). **Antibiotic Susceptibility Among Aerobic Gram-negative Bacilli in Intensive Care Units in 5 European Countries.** JAMA.;281(1):67-71.

17. Jean-Louis Vincent; Jordi Rello ; John Marshall, MD; Eliezer Silva et. al (2009).**International Study of the Prevalence and Outcomes of Infection in Intensive Care Units** .JAMA.;302(21):2323-2329

18. Jenkins, S. G. And Audrey, N.Schuetz, A. G., (2012). **Current Concepts in Laboratory Testing to Guide Antimicrobial therapy.** *Mayo Clin Proc*, 87(3), p.290-308.

19. Kallel H, Bahoul M, Ksibi H, Dammak H, Chelly H, Hamida CB, Chaari A, Rekik N, Bouaziz M (2005). **Prevalence of hospital-acquired infection in a Tunisian hospital**. *J Hosp Infect*. **59**:343-347.

20. Katarzyna et al. (2010). **Antibiotic sensitivity of bacteria associated with community-acquired urinary tract infection in Britain**. Journal of Antimicrobial Chemotherapy, 44(3):359-365.

21. Laupland KB, Bagshaw SM, Gregson DB, Kirkpatrick AW, Ross T,Church DL. (2005).**Intensive care unit-acquired urinary tract infections in a regional critical care system**.Crit Care 9:R60—5.

22. **Monica -Cheesbrough District Laboratory Practice in Tropical Countries Second edition** Part 2 pp 107-115

23. Najar MS, Saldanha CL, Banday KA. (2009). **Approach to urinary tract infections.** Indian J Nephrol 19(4): 129-39.

24. Orenstein R, Wong ES.(1999).**Urinary tract infections in adults**. Am Fam Physician. 59:1225-1234.

25. Rizvi MF, Hassan Y, Memon AR, Abdullah M,Saleem S.(2007).**Pattern of nosocomial infection in two intensive care units of a tertiary care hospital in Karachi**. JColl Physicians Surg Pak ;17(3):136-9.

26. Salgado, Cassandra D. MD, MS; O'Grady, Naomi MD; Farr, Barry M. MD, MSc (2005).**Prevention and control of antimicrobial-resistant infections in intensive care patients**. Critical Care Medicine: October 2005 - Volume 33 - Issue 10 - pp 2373-2382

27. Salvatore, S, Cattoni, E, Siesto, G, Serati, M, Sorice, P, Torella, M (June 2011). **"Urinary tract infections in women."**. European journal of obstetrics, gynecology, and reproductive biology 156 (2): 131–6

28. Talebi M , Golestanpour A (2009).**Symptomatic nosocomial urinary tract infection in ICU patients: identification of antimicrobial resistance pattern**. Iranian Journal of Clinical Infectious Disease;4(1):25-29 **.**

29. Todar, K.(2002): **Bacteria resistance to antibiotics.** University of Wisconsin-Madison (http:/www.textbookofbacteriology.net)

30. Tulloch JA, Wilson AMM, King MH.(1963). **Symptomless bacteriuria among African inpatients in Uganda.** East Afr Med J. 40:433–439

31. Vandijck DM, Depaemelaere M, Labeau SO, Depuydt PO, Annemans L, Buyle FM, Oeyen S, Colpaert KE, Peleman RP, Blot SI, Decruyenaere JM.(2008).**Daily cost of antimicrobial therapy in patients with Intensive Care Unit-acquired, laboratory confirmed bloodstream infection.** Int J Antimicrob Agents.;31(2):161-165.

32. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y, Reinhart K; EPIC II Group of Investigators.(2009). **International study of the prevalence and outcomes of infection in intensive care units.** 302(21):2323-2329.

33. Zadeh S.V. Hassani N. (2005).**The frequency rate of nosocomial urinary tract infection in intensive care unit patients in Shafiieh hospital in Zanjan 2004**. Zanjan univ med sci 50(13);28-3

34. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in combined medical-surgical intensive care units in the United States. Infect Control Hosp Epidemiol 2000;21:510-5.

35. Alvarez-Moreno C, Rosenthal VD, Olarte N, Gomez WU, Sussman O, Agudelo JG, et al. Device-associated infection rate and mortality in intensive care units of 9 Colombian hospitals: Findings of the International Nosocomial Infection Control Consortium. Infect Control Hosp Epidemiol 2006;27:349-56.

36. Rosenthal VD, Maki DG, Salomao R, Moreno CA, Menta Y, Higuera F, et al. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. Ann Intern Med 2006;145:582-91.

37. Rosser CJ, Bare RL, Meredith JW. Urinary tract infections in the critically ill patient with a urinary catheter. Am J Surg 1999;177:287-90.

# 8.CHAPTER EIGHT.

## 8.1 APPENDIX A: DATA COLLECTION FORM

**TOPIC**: Bacterial Profile and Antimicrobial Susceptibility Patterns of Isolates Causing Urinary Tract Infections in Intensive Care Unit Patients at Kenyatta National Hospital.

**QUESTIONNAIRE NUMBER: .....**

**SOCIO DEMOGRAPHIC CHARACTERISTICS**

Age of patient: .....years

Sex: Male……. Female……..

**Organisms isolated**

Staphylococcus spp …….. Enterococcus spp.....

E. coli ……. Other organisms specify.....

Klebsiela spp……..

Proteus spp……..

Enterobacter spp……

Citrobacter spp…….

Pseudomonas spp…….

**ANTIBIOTIC SUSCEPTIBILITY PATTERNS**

| **Antibiotics** | **Sensitive (S)** | **Resistant (R)** |
|---|---|---|
| Amoxy/Clav(Augmentin) | | |
| Doxycycline | | |
| Cefuroxime | | |
| Ampicillin | | |
| Levofloxacin | | |
| Chloramphenical | | |
| Gentamycin | | |
| Piperacillin | | |
| Imipenem | | |
| Cefepime | | |
| Amikacin | | |
| Ceftriaxone | | |
| Cefotaxime | | |
| Cotrimoxazole | | |
| Nalidixic acid | | |
| Nitrofurantion | | |
| Ceftazidime | | |
| Meropenem | | |
| Teicoplanin | | |
| Vancomycin | | |
| Ciprofloxacin | | |
| Streptomycin | | |

| | | |
|---|---|---|
| Erythromycin | | |
| Linezolid | | |

8.2 APPENDIX B:KNH/UoN-Ethics and Research Committee Approval letter.

**UNIVERSITY OF NAIROBI**
**COLLEGE OF HEALTH SCIENCES**
**P O BOX 19676 Code 00202**
**Telegrams: varsity**
**(254-020) 2726300 Ext 44355**

**KNH/UON-ERC**
**Email: uonknh_erc@uonbi.ac.ke**
**Website: www.uonbi.ac.ke**

**KENYATTA NATIONAL HOSPITAL**
**P O BOX 20723 Code 00202**
**Tel: 726300-9**
**Fax: 725272**
**Telegrams: MEDSUP, Nairobi**

Ref: KNH-ERC/A/329 **Link:www.uonbi.ac.ke/activities/KNHUoN**

29th September 2014

Isabel Muthoni
W64/80612/2012
UNITID
College of Health Sciences
University of Nairobi

Dear Isabel

**RESEARCH PROPOSAL: BACTERIAL PROFILE AND ANITIMICROBIAL SUSCEPTIBILITY PATTERNS OF BACTERIAL ISOLATES CAUSING URINARY TRACT INFECTIONS IN INTENSIVE CARE UNIT PATIENTS AT K.N.H. (P460/07/2014)**

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 29th September 2014 to 28th September 2015.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **www.uonbi.ac.ke/activities/KNHUoN.**

Protect to Discover

Yours sincerely

**PROF.M.L. CHINDIA**
**SECRETARY, KNH/UON-ERC**

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director CS, KNH
The Chair, KNH/UoN-ERC
The Assistant Director, Health Information, KNH
The Director, UNITID,UoN
Supervisors: Prof. Omu Anzala, Dr. P. Mwanthi