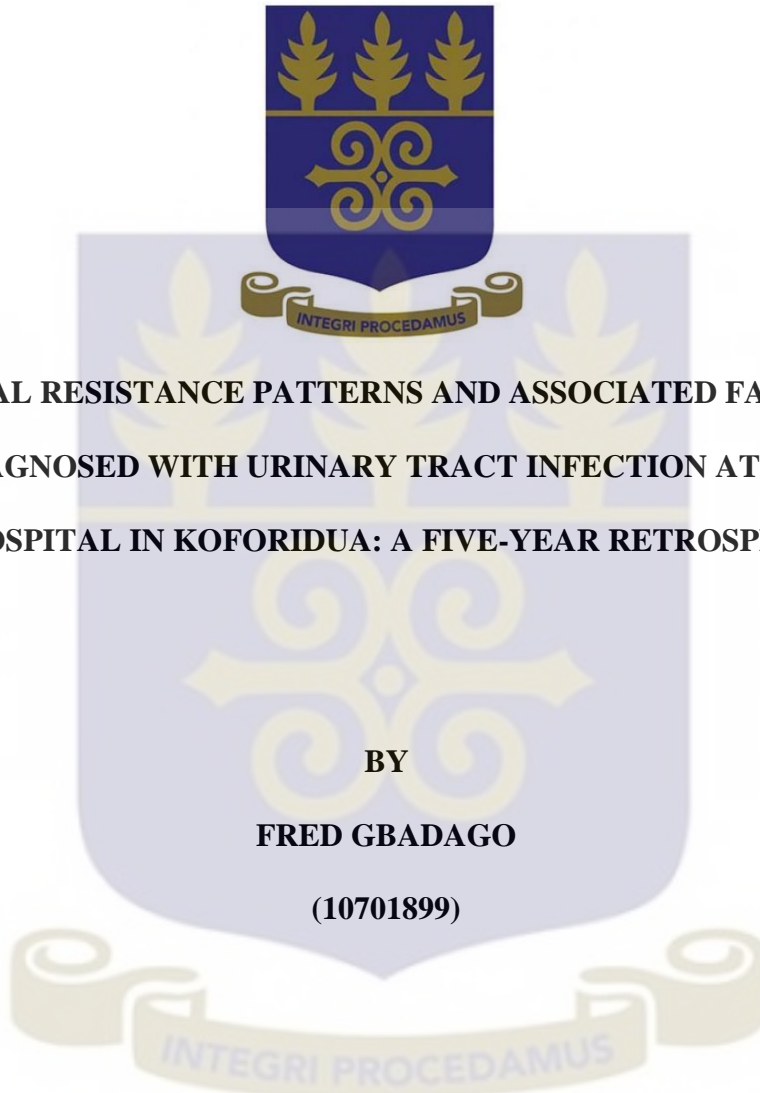


**SCHOOL OF PUBLIC HEALTH,
COLLEGE OF HEALTH SCIENCES
UNIVERSITY OF GHANA, LEGON**



**ANTIMICROBIAL RESISTANCE PATTERNS AND ASSOCIATED FACTORS AMONG
PATIENTS DIAGNOSED WITH URINARY TRACT INFECTION AT THE EASTERN
REGIONAL HOSPITAL IN KOFORIDUA: A FIVE-YEAR RETROSPECTIVE STUDY**

**BY
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MASTER OF PUBLIC HEALTH DEGREE**

JULY, 2019

DECLARATION

I, Fred Gbadago, hereby declare that except for references to work by other persons that have been duly cited, this dissertation is the product of my own research.

Signed: Date.....

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Signed..... Date.....

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(Supervisor)

DEDICATION

This work is dedicated to my parents Mr & Mrs Gbadago and siblings for their immense support and motivation towards this academic achievement.

ACKNOWLEDGEMENT

I am grateful to the God Almighty for His continuous protection and guidance in my life and towards the completion of yet another academic programme.

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ABSTRACT

Background: Urinary tract infections (UTI) are among the most common bacterial infections affecting people worldwide. The misuse of antibiotics used to treat UTIs has led to the development of resistance among the major uropathogens in Ghana. The local antimicrobial resistance pattern among uropathogens to help empirical decision making is not known at the Eastern Regional Hospital, Koforidua.

Objective: This study examined the resistance pattern of uropathogenic bacteria over a five year period and associated factors among patients diagnosed with UTI at the Eastern Regional Hospital, Koforidua.

Methods: A retrospective cross-sectional study design was used to review records of urine culture and sensitivity data to determine resistance patterns and associated factors among patients diagnosed with UTI at the Regional Hospital in Koforidua from 2014 to 2018.

Results: The prevalence of UTI was 20.3% among study subjects. Out of fourteen isolates assessed, *Escherichia coli* (42.98%), *Klebsiella spp* (29.97%) and *Citrobacter spp* (12.51%) were the most dominant uropathogens accounting for UTI. Resistance to antibiotics was very high among uropathogens isolated with Ampicillin (90.8%), Co-trimoxazole (89.7%) and Tetracycline (88.6%) being the most resistant antibiotics and Amikacin (8.7%), Nitrofurantoin (35.9%) and Ciprofloxacin (37.5%) being the least resistant. Increasing age (AOR=2.53 CI=1.83, 3.47) and In-patient (AOR=1.26, CI=1.05, 1.53) are associated with ciprofloxacin resistance.

Conclusion: This study showed that uropathogens responsible for UTI showed generally high resistance to the commonly prescribed antibiotics with few exceptions. These results could help inform empirical treatment decisions for Urinary Tract Infections locally and also contribute to AMR surveillance in general.

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LIST OF ABBREVIATIONS

AMR	-	Antimicrobial Resistance
AOR	-	Adjusted Odds Ratio
AMC	-	Amoxicillin/Clavulanic Acid
APUA	-	Alliance for the Prudent Use of Antibiotics
BSI	-	Blood Stream Infection
CI	-	Confidence Interval
CIP	-	Ciprofloxacin
COR	-	Crude Odds Ratio
ERHK	-	Eastern Regional Hospital Koforidua
NIT	-	Nitrofurantoin
SMART	-	Study for Monitoring Antimicrobial Resistance Trends
SXT	-	Trimethoprim-Sulfamethoxazole
USD	-	United State Dollar
UTI	-	Urinary Tract Infection
WHAIF	-	World Health-Care Associated Infections Forum
WHO	-	World Health Organization

DEFINITION OF KEY TERMS

Antimicrobial Resistance:

The ability of microbes to grow in the presence of a chemicals (drugs) that would normally kill them or limit their growth.

Culture:

Method of multiplying microbial organisms to determine type of organism and its abundance in a sample

Sensitivity Testing:

Laboratory techniques that help to determine which antibiotics are effective against a microbe.

Urinary Tract Infection:

Urinary tract infection is an infection in any part of your urinary system.

Uropathogen:

Any pathogen of the urinary tract.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

The emergence of Antimicrobial Resistance (AMR) poses significant threat to improving on the health outcomes of populations across the globe (Bernabé et al., 2017). AMR arises when microbes such as bacteria, viruses, fungi and parasites change in ways that render the drugs used to treat the infections they cause ineffective (WHO, 2017). Since the 1940s, the prevention and control of major infectious diseases of public health concern like tuberculosis, HIV, malaria, gonorrhoea and urinary tract infections (UTIs) have increasingly been affected by antimicrobial resistance. AMR has the potential of significantly reversing the progress that has already been made in the control of these diseases (Jindal, 2015). The lack of new antibiotics to replace old ones to which resistance has been developed further increases the challenges posed by AMR (Ventola, 2015).

The global increase in human population coupled with an increasing disease burden has made dependence on antibiotics inevitable. The absence of a proper monitoring and regulatory framework in the use of antimicrobial agents, inadequate infection control practices and limited resources in the diagnosis of infectious diseases have contributed to the worldwide development of AMR (World Health Organization, 2016). In low and middle-income countries especially in sub-Saharan Africa, inadequate policies have resulted in the irrational use and abuse of antibiotics in almost all settings where they are needed (Jindal et al., 2015).

The World Health Organization (WHO), in 2014, provided a comprehensive report on the global situation of AMR. The report focused on microbes causing diseases of public health concern. It also assessed the health and economic implications of AMR, surveillance

challenges and provided future directions for its prevention and control (World Health Organization, 2014).

In 2015, global leaders at the World Health Assembly authorized a global action plan to tackle AMR in the world (World Health Organization, 2015). This culminated into the first ever “African Conference on Antibiotic Use and Resistance” held in Ghana in March 2015 to publicize research information on AMR within the African sub-region.

Several studies in Ghana suggests the development of AMR and the need for containment (Christian et al., 2014; Newman, 2011; Tadesse et al., 2017). The first policy on AMR titled “Policy on Antimicrobial Use and Resistance for Ghana” was developed to provide direction and guidance for all stakeholders who are affected by or use antimicrobial agents. One of the key policy statements is to increase knowledge and evidence of AMR through surveillance and research. This is to be achieved through creating national monitoring systems for the use of antibiotics and surveillance of antimicrobial resistance to update policies (Ministry of Health, 2017).

The preliminary implementation period of the policy is from 2017 to 2021 through the Ghana National Action Plan on Antimicrobial Resistance. The action plan defines specific roles for all the major stakeholders (Ghana National Action Plan for Antimicrobial Use and Resistance Republic of Ghana, 2017).

As part of the implementation of the National Action Plan on AMR, a laboratory-based surveillance system has been set up to monitor the development and spread of AMR in the country. The surveillance system also aims to coordinate individual research findings into the national data management system on AMR to influence future actions in managing AMR in Ghana (Policy on Antimicrobial Use and Resistance, 2017). Continuous research on AMR

therefore contributes to the national pool of data and also updates information on AMR patterns at the local level for decision making on treatment strategies.

1.2 Problem Statement

UTIs are among the most common bacterial infections affecting about 150 million people worldwide every year (Khoshnood et al., 2017; Kibret & Abera, 2014). Complications such as pyelonephritis with sepsis, renal damage in children and frequent recurrences could arise from UTIs (Flores-Mireles, 2015). UTIs are normally treated with commonly available antibiotics and patients are expected to be cured within days of receiving treatment.

The misuse of antibiotics used to treat UTIs has led to the development of resistance among the major uropathogens in Ghana (Newman et al., 2011). Data from the Eastern regional hospital show a continuous increase in UTI cases over the past three years. Out-patient UTI cases rose from 3,757 in 2016 to 10,565 in 2018 whereas that of in-patients increased from 343 to 640 cases within the same period. Antibiotic resistance among uropathogens puts the increasing number of people with UTIs at risk of treatment failures.

Failure in treatment results in an increase in morbidity, complicated forms of UTIs and UTI associated mortality. The affected patient(s) may be put on treatment for longer duration with a rise in healthcare expenditure and loss of productive time. Generally, there is a negative impact on economic activity of people affected with huge social, public health and economic implications in the country.

In spite of a laboratory based surveillance programme of AMR in Ghana, the local resistance pattern of antibiotics used to treat UTIs at the Eastern Regional Hospital is not known hence underscores the need for this study to inform empirical therapy. This study therefore sought to examine the sensitivity pattern over the past five years in order to update knowledge for empirical therapy decision making at the hospital.

1.3 Justification

Urinary tract infections are one of the main reasons for the prescription and use of antibiotics. Patients suffering from drug resistant UTIs may be on treatment for longer duration with huge socio-economic consequences if an effective antibiotic is not selected for treatment. Knowledge on the various pathogens and their resistance profile is necessary to guide clinicians to accurately prescribe effective antibiotics locally. It will also help policy makers to have enough information for AMR policy formulation and implementation.

While several studies have focused on antibiotic resistance among various pathogens in Ghana, few have reported how resistance among uropathogens have changed over the years as hence the need for this study.

In the absence of this study, the amount of data available for national AMR surveillance would be limited. If this study is conducted however, clinicians in Ghana specifically in the Eastern Region will have better understanding of the spectrum and resistance patterns of antibiotics available for treating UTIs locally. This is likely to result in better choice of antibiotics for empirical therapy, reduction in treatment failures and economic burden on patients.

1.4 Conceptual framework

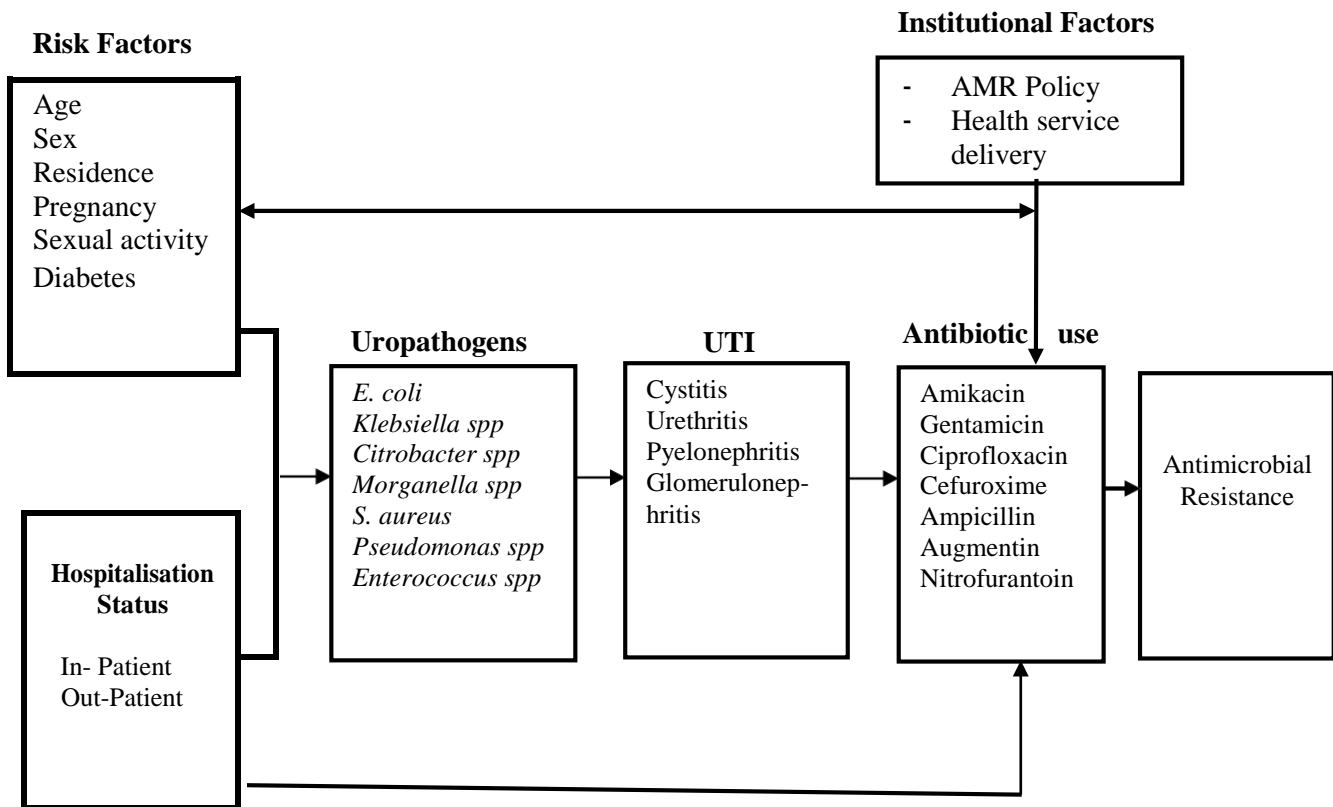


Figure 1.4: Conceptual framework of risk factors and uropathogens causing UTI and their inter-relationship with antibiotic resistance.

1.5 Narrative of Conceptual Framework

The prevalence of UTI is influenced by several factors including age, sex, pregnancy, hospitalization and exposure to urological procedures. These factors expose persons to particular uropathogens that cause UTI. UTIs are one of the major reasons for the prescription and use of antibiotics globally.

The use of antibiotics largely influences the susceptibility pattern of the various uropathogens. In an environment where antibiotics are overused or abused, there is high resistance developed by bacteria to the antibiotics.

Institutional factors such as access to drugs, presence of an AMR policy, proper diagnostic tools and availability of adequate prescribing staff also contribute to the way antibiotics are used. The presence and implementation of an AMR policy helps to monitor and regulate the use of antibiotics by consumers and healthcare delivery staff.

The interrelationship of these factors generally affects antibiotic susceptibility patterns of disease causing bacteria including uropathogens in countries and across the world.

1.5 Research Questions

1. What is the prevalence of Urinary Tract Infection among patients referred to the Eastern Regional Hospital Laboratory in Koforidua to diagnose UTI from 2014 to 2018?
2. What is the trend of the main bacteria isolates responsible for UTI among patients visiting the eastern regional hospital laboratory, Koforidua from 2014 to 2018?
3. What is the antimicrobial resistance pattern and associated factors among patients diagnosed with UTI at the Eastern Regional Hospital in Koforidua, Ghana?

1.6 General objective

To assess the resistance pattern of uropathogenic bacteria over the past five years and associated factors among patients diagnosed with UTI at the Eastern Regional Hospital, Koforidua.

1.6.1 Specific objectives

1. To determine the proportion of Urinary Tract Infection among patients referred to the Eastern Regional Hospital laboratory in Koforidua to diagnose UTI from 2014 to 2018.
2. To assess the trend of the main bacteria isolates responsible for UTI among patients visiting the Eastern Regional Hospital laboratory, Koforidua from 2014 to 2018.
3. To determine the antimicrobial resistance pattern and associated factors among patients diagnosed with UTI from 2014 to 2018 at the Eastern Regional Hospital in Koforidua, Ghana.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Concept of Antimicrobial Resistance

Antimicrobial resistance (AMR) refers to the capacity of a microbe (bacteria, viruses and parasites) to prevent an antimicrobial agent (such as antibacterial, antivirals and anti-malarial) from destroying it. This renders standard treatments ineffective and infections may persist and be transmitted to other persons (WHO, 2017)

Antimicrobial drugs have been of immense help to the global fight against infectious diseases since their discovery. Penicillin was the first antibiotic to be discovered in 1928 by Sir Alexander Fleming. The discovery of antibiotics has led to major transformations in the treatment, management and control of infectious diseases. Millions of lives have been saved over these years leading to a significant improvement in human health and the quality of life in general across the world (Ventola, 2015).

Several classes of antibiotics have been developed since the first discovery was made. These new antibiotics have been used to treat various infections caused by bacteria, fungi, parasites and viruses. In less than a century of these significant achievements, the development of antimicrobial resistance (AMR) has been documented in almost all the classes of antibiotics. Much attention has been devoted to resistance in antibacterial agents due to the wide range and common nature of bacterial infections affecting humans across the globe.

Bacteria develop resistance through several mechanisms. These include preventing access of the antibiotic, removal of the antibiotic, destroying the drug, modifying the antibiotic, circumventing the effects of the antibiotic and changing the targets of the antibiotic.

Gram-negative bacteria have membranes that protect them from the external environment. The openings in these membranes can be adjusted to selectively prevent entry of antibiotics thereby rendering them ineffective against the bacteria. Another way bacteria develop resistance is to remove antibiotics that enter their cell by using pumps in the cell wall. *Pseudomonas aeruginosa* is an example of bacteria that shows resistance to several antibiotics (including beta-lactams and fluoroquinolones) using this approach (Kon & Rai, 2016).

Some bacteria also destroy the antibiotics to make them ineffective by using enzymes they produce. An example of such bacteria is *Klebsiella pneumoniae* which produce carbapenemases to breakdown carbapenem drugs and most other beta-lactam drugs. Other bacteria utilize enzyme inactivation to render antibiotics ineffective. This is done by producing enzymes to inactivate certain antibiotics. For example *Staphylococcus aureus* uses enzymes to produce compounds that bind to aminoglycosides to make them ineffective.

Some antibiotics are designed to interrupt metabolic processes necessary for the survival of the bacteria. Some bacteria acquire resistance to these antibiotics by developing alternate pathways to bypass these drug disruptions. Evidence suggests that *Staphylococcus aureus* bacteria uses this mechanism to bypass the drug effects of trimethoprim. Other antibiotics also function by targeting some specific parts of bacteria for destruction. By changing the structure of their target sites, some bacteria are able to avoid destruction by antibiotics thereby making them resistant to that particular antibiotic. For example *E. coli* bacteria can add a compound to the outside of the cell wall to prevent the drug colistin from recognizing and binding to it ("How Antibiotic Resistance Happens | CDC", 2019).

2.2 Global Prevalence of Antimicrobial Resistance

A project titled the Global Advisory on Antibiotic Resistance was initiated by the Alliance for the Prudent Use of Antibiotics (APUA) to compile data on AMR from several surveillance programmes across the globe. The project report cited the problem of AMR as affecting the treatment of all microbial diseases with bacteria such as *Staphylococcus aureus*, *Streptococcus pneumoniae*, and some strains of *Neisseria gonorrhoeae*, *Escherichia coli* strains and *Klebsiella* species being implicated in Europe, United States and South East Asia. This contributed to the declaration by the World Health Assembly in 2005 that AMR was a problem that needed urgent attention (Levy & Brien, 2005).

In a summary of key messages at the fourth biennial World Healthcare-Associated Infections Forum (WHAIF) held in June 2013 in France to address the rapid spread of AMR, the global situation on AMR was presented by several experts from over thirty countries. It was noted that about ninety percent of *Staphylococcus aureus* strains had developed resistance to penicillin in the United Kingdom. In the United States, almost all strains were penicillin resistant and fifty percent also resistant to methicillin (Huttner et al., 2013).

Data obtained from some member states of the World Health Organization (WHO) suggests that the proportion of commonly isolated bacteria *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus* showing resistance to specific antibacterial agents is more than 50% in most WHO member countries (WHO, 2014).

Some studies conducted in Europe have shown that common uropathogens demonstrate varying degrees of AMR against commonly prescribed antibiotics in Portugal, Italy, England, The Netherlands, and some areas in France, Spain, and Poland (Fluit et al, 2000; Linhares et al, 2013). In the United States, a study carried out to determine trends in antimicrobial activity of some antibiotics on urine isolates of *E. coli* (most common cause of UTIs) from female

patients over a seven year period showed resistant rates among the isolates to ampicillin, trimethoprim-sulfamethoxazole (SXT), ciprofloxacin and nitrofurantoin as (36.0-37.4% per year), (14.8-17.0%), (0.7-2.5%) and (0.4-0.8%) respectively (Karlowsky et al, 2002).

Across many regions in the United States, *Neisseria gonorrhoeae* has developed resistance to penicillin, tetracycline and fluoroquinolones and only susceptible to ceftriazone currently (Huttner et al., 2013). Another study conducted by Phouangsouvanh and colleagues in the Lao People's Democratic Republic to determine the antimicrobial susceptibility of *Neisseria gonorrhoeae* isolates revealed resistance to penicillin (by b-lactamase production), tetracycline and ciprofloxacin were 89.9%, 99.4% and 84.8%, respectively while all isolates were susceptible to ceftriaxone and spectinomycin (Phouangsouvanh, 2018).

2.3 Prevalence of Antimicrobial Resistance in Africa

In Africa, several studies have shown that AMR is on the rise. A systematic review by Tadesse and colleagues describes the general situation of AMR on data published from 2013–2016 on antibiotic drug sensitivity in Africa. They observed that the overall resistance to commonly used drugs, like amoxicillin and trimethoprim/sulfamethoxazole was 72.9% and 75% respectively. Also, a lesser level of resistance of *S. aureus*, *Klebsiella spp.*, *E. coli* and *S. pneumoniae* to carbapenems and fluoroquinolones was seen in all regions of Africa as related to the other antibiotic-bacterium groupings. In the same study, it was observed that *Klebsiella spp.* resistance to ciprofloxacin in West Africa was higher than in other regions. Resistance to the trimethoprim (33.9%–100%), ampicillin (7.9%–100%) and penicillin (0%–75%) was mostly high in all regions (Tadesse et al., 2017).

Commonly used antibiotics (ampicillin, penicillin, amoxicillin, gentamicin, ciprofloxacin, chloramphenicol and trimethoprim) for the treatment of common bacterial infections such as urinary tract infections (UTI), pneumonia, meningitis, blood stream infection (BSI) and

diarrhoea have been observed to demonstrate various degrees of resistance in West Africa as demonstrated by Bernabe et al (2017) in a systematic review and meta-analysis of antimicrobial resistance in West Africa. Among studies on blood stream infections, the general rates of AMR were observed for antimicrobials among Gram-negative bacteria as follows: ampicillin, 68.4%; chloramphenicol, 52.4%; trimethoprim/sulfamethoxazole (SXT), 54.7%; amoxicillin/clavulanic acid (AMC), 41.5%; and gentamicin, 37.2%. The most active antibiotics for Gram-negative BSIs were third- generation cephalosporins for which resistance was observed in 17.7% of isolates, and fluoroquinolones, 12.1% of isolates. This increasing trend of resistance was similar in bacteria responsible for meningitis, UTIs, pneumonia and diarrhoea in their study (Bernabé et al., 2017).

2.4 Urinary Tract Infections

Urinary tract infection (UTI) is a general term that describes any infection relating to any part of the urinary tract, namely the kidneys, ureters, bladder and urethra. The urinary tract can be separated into the upper (kidneys and ureters) and lower tract (bladder and urethra). Infections may include either only the lower urinary tract or both the upper and lower tracts. The infections can be caused by bacteria, fungi, virus and parasites. Some of the clinical symptoms of UTI include flank pain, fever, dysuria, urinary urgency and frequency (Tan, 2016).

UTIs are one of the most common bacterial infections diagnosed in health practice around the world (Nzalie et al, 2016). They are a major cause of morbidity in infant boys, older men and females of all ages. Factors such as age, gender, pregnancy, sexual activity, prostate enlargement in men are the main determinants of its frequency (Mohammed et al, 2016).

2.4.1 Pathogenesis of UTI

There are two main paths by which bacteria can enter and spread inside the urinary tract in humans. These are the ascending and hematogenous pathways. In the hematogenous route, organisms especially originating from the blood infect the parenchyma of the kidney. The kidney is mostly the site where abscesses occur in patients with bacteraemia. This is normally caused by gram positive bacteria such as *Staphylococcus aureus*. Gram negative bacteria do not normally infect the kidney by the haematogenous route.

Most UTIs occur by the ascending route. Majority of uropathogens originate from the rectal flora and invade the bladder through the urethra. In females, the urethra is short and is situated near to the vulvar and perineal areas. This makes invasion by rectal flora more likely hence the frequent development of UTIs among females. The development of infection depends on the particular microbe, the amount of the inoculum and host defenses. When the bacteria ascend into the bladder, they may proliferate and then pass up the ureters and then to the renal parenchyma (Sobieszczyk, 2018).

2.4.2 Categories of urinary tract infection

Clinically, UTIs are characterized as uncomplicated or complicated. Uncomplicated UTIs normally affect persons who are otherwise healthy and do not have any structural or neurological urinary tract abnormalities. These infections are further distinguished into lower UTIs (cystitis) and upper UTIs (pyelonephritis). Risk factors are connected with cystitis, include female gender, a previous UTI, sexual intercourse, vaginal infection, diabetes, obesity and genetic susceptibility (Lee et al., 2018).

Complicated UTIs are normally linked with factors that compromise the urinary tract or host immunity. Some of these factors include urinary obstruction, urinary retention initiated by neurological disease, immunosuppression, renal failure, renal transplantation, pregnancy and

the presence of foreign bodies such as calculi, indwelling catheters or other drainage instrument (Flores-Mireles et al, 2015).

2.4.2 Epidemiology of UTI

UTIs affect all persons, however the distribution varies with age and sex. Persons at increased risk for morbidity include neonates, pre-pubertal girls, young women, older men, individuals with structural abnormalities of the urinary tract and immunocompromised patients. In neonates, UTIs occur more often in males; thereafter they occur more frequently in girls and women. Infections occurring in preschool boys are normally associated with serious congenital abnormalities. It has also been shown that lack of circumcision predisposes young boys and infants to UTIs (Odoki et al., 2019).

UTs are rare in men less than 50 years of age and symptoms of dysuria (painful urination) are more commonly associated with sexually transmitted infection of the urethra or prostate. The incidence of UTIs in men increases after the age of 50 years and may be due to prostatic diseases and the use of instrumentation during hospitalization (Basseye et al, 2016).

Among young adults, the prevalence of UTIs increases in the female population. Up to 40% of women will experience a symptomatic urinary tract infection at some time during their life and many will have recurrent episodes. Pregnant women have a 4-10% prevalence of UTI which has been shown to increase the risk of premature delivery, fetal mortality and pyelonephritis in the mother. In the hospitalized patient, urinary tract infection may account for close to 50% of hospital-acquired infections and are a major cause of Gram negative bacteremia and mortality (Tenney et al., 2018)

2.4.3 Causative organisms of UTIs

The major causative bacteria for UTIs are gram negative bacteria and they account for about 80-85% of infections. The main organisms include *Escherichia coli* (*E. coli*), which is implicated in about 75.5-87% of UTI infections, *Klebsiella* species, *Citrobacter* spp, *Acitenobacter* spp, *Enterobacter* spp, *Providencia* spp, *Pseudomonas* spp, *Serratia* spp and *Proteus* species. Some gram positive bacteria that also cause UTIs are *Staphylococcus* and *Enterococcus* species (Akram, 2007; Mohammed et al., 2016).

In a study by Oli and colleagues in 2017 to determine the type and antibiotic susceptibility pattern of bacteria uropathogens isolated from female patients attending a teaching hospital in Nigeria, they found the major uropathogens to be *E. coli* (28.5%), *Staphylococcus aureus* (28.0%), *Salomonella* spp (28.0%) and *Pseudomonas aeruginosa* (20.5%) (Oli et al., 2017). Among paediatric patients of a tertiary hospital in Eastern India, Mishra et al in 2016 discovered *Enterococcus faecalis* and *Staphylococcus aureus*, *Citrobacter freundii*, *Enterobacter aerogenes*, *Escherichia coli*, *Klebsiella oxytoca*, *K. pneumoniae*, *Proteus vulgaris* and *Pseudomonas aeruginosa* as the main bacteria responsible for UTI among children from urine samples collected over an eighteen month period (Mishra, 2016). In another study at a Medical University in Iran, Khameneh and colleagues (2009) showed that out of 803 urine culture positive for bacteria growth, *E. coli* dominated with 75.83% followed by *Klebsiella* spp (5.83), *Proteus* spp and *Staphylococcus* spp. Other isolates responsible for UTI among the study subjects were Coagulase Negative *Staphylococcus*, *Citrobacter* spp, *Enterobacter* spp and *Pseudomonas aeruginosa*.

In Ghana, Prah and colleagues demonstrated the common organisms causing UTI among out-patients of the University of Cape Coast Hospital to be *E. coli*, *Staphylococcus saprophyticus*, *Enterobacter* spp *Klebsiella* spp and *Candida* spp (Prah et al., 2019). In another study at a referral hospital in Accra, Gyansah-Lutterodt and colleagues showed the predominant

organisms causing UTI among patients as *Coliforms* (44.2%) and *E. coli* (36.2%). Other organisms present were *Pseudomonas* spp (5.4%), *S. aureus* (4.5%), *Proteus* spp (1.3%), *Klebsiella* spp (1.3%) and *Providencia* spp (1.8%) (Gyansa-Lutterodt et al., 2014).

2.4.4 Treatment of Urinary Tract Infections

Presently, antibiotics are the main drugs of choice in the treatment of urinary tract infections. The choice of antibiotic therapy is normally guided by urine culture and sensitivity results. However, these tests are normally completed after three days and also not readily available in all health facilities. Hence, antibiotic treatment is typically started empirically before urine culture results become available (Karimian et al., 2017).

It is also recommended that the choice of antibiotic be done in reference with local antimicrobial sensitivity patterns in each area. Some of the groups of antibiotics commonly prescribed include aminoglycosides, carbapenems, cephalosporin, monobactams, nitrofurans, penicillins, quinolones, and sulfonamides (Linhares et al., 2013). In Ghana, the main recommended drugs of choice for treating complicated and uncomplicated UTIs include ciprofloxacin, nitrofurantoin and cefuroxime (Standard Treatment Guidelines, Ghana, 2017).

2.5 Prevalence of Antimicrobial Resistance among Uropathogens

The development of AMR among uropathogens has been widely demonstrated in various studies across the globe. These increasing rates of resistance threatens to increase disease burden, prolong illness and increase the cost of health service delivery.

In a study conducted by Karimian and colleagues to examine the antibiotic resistance of bacteria causing UTI among children in Iran, results showed that resistance to imipenem, cefotaxime and cephalexin was more dominant in persistent UTI cases as well as in patients who had used antibiotics before acquiring the UTI. Additionally, the study identified nitrofurantoin as a viable alternative for the treatment of multidrug-resistant uropathogens in

children with a febrile UTI (Karimian et al., 2017). Sibi (2014) showed that *Klebsiella oxytoca* strains isolated from the urine of pregnant women in India were resistant to cefotaxime and ceftriaxone. The study also revealed Cephalosporins and Quinolones to be effective against UTI causing organisms in pregnant women while antibiotic sensitivity testing revealed high resistance to penicillins (beta lactam group) by uropathogens (Sibi, 2014).

A study conducted by Lu et al. (2012) to monitor antimicrobial resistance trends surveyed gram negative bacteria causing UTI in Asia-Pacific region. The study showed that the level of antibacterial resistance among uropathogens was high in most countries in the region (China, Hong Kong, Taiwan, Malaysia, Philippines, Singapore and South Korea) with the exception of New Zealand. Over 85% of pathogens causing UTI were sensitive to antimicrobial agents used in testing in New Zealand (Lu et al., 2012).

In Africa, several studies have been conducted to show the varying uropathogenic profile and antibiotic resistance across the continent. In Ethiopia, Bitew and colleagues showed the overall antibiotic resistance rates of the gram-negative bacterial isolates ranged from 17.7% for piperacillin/tazobactam combination and 78.3% for ampicillin. High resistance levels of bacterial uropathogens for trimethoprim/sulfamethoxazole combination (66.3%) and tetracycline (62.3%) (Bitew et al, 2017).

In Libya, one study suggested a range of 10.5% to 64.5% of AMR shown by uropathogens isolated to various antibacterial agents (Kibret & Abera, 2014) while another study in Ethiopia demonstrated high resistance rates of 85.6%, 88.9%, 76.7% to erythromycin, amoxicillin and tetracycline respectively (Mohammed et al., 2016).

Duffa in 2018 demonstrated in Ethiopia the susceptibility of bacteria isolated from urine to some commonly prescribed antibiotics. In their study, *Acinetobacter* spp. was completely resistant to gentamicin (GN), trimethoprim-sulfamethoxazole (SXM), and augmentin (AMP).

Enterococcus species showed resistance of 71.4% to chloramphenicol (C) and 85.7% to both SXM and erythromycin. *S. aureus* was 100% sensitive to almost all antibiotics. Multidrug resistance to more than two antibiotics was seen in 73.7% of the bacterial isolates (Duffa et al, 2018).

In West Africa, specifically, in low and middle income countries, Bernabé et al (2017) found after the isolation of bacteria from urine samples of both inpatients and outpatients that urinary tract pathogens in West Africa showed varying degrees of resistance to commonly prescribed antibiotics. The analysis showed AMR among in-patients with UTIs to third-generation cephalosporins. Moreover, ciprofloxacin (a fluoroquinolone) was moderately active against *E. coli*, *Klebsiella* spp. and *P. aeruginosa* isolated from inpatients' urine specimen and was extremely active in that of outpatients. Their findings suggested that fluoroquinolones were a better choice in the treatment of UTIs (Bernabé et al., 2017).

In a study to determine the prevalence and antibiotic resistance patterns of UTI at the university of Port Harcourt teaching hospital in Nigeria, the commonest isolates were *Escherichia coli* (32.8%), *Staphylococcus aureus* (17.2%), and *Klebsiella* spp. (16.4%). About 93.8% of isolates were resistant to tetracycline, 92.2% to the Co-trimoxazole, and 86.7% to Nalidixic acid. *Pseudomonas* spp. isolates were also resistant to the fluoroquinolone (Wariso, 2010).

Moroh et al (2014) conducted a retrospective analysis of a twelve year data on urine sample in Abidjan and results showed that *Escherichia coli* was the predominant species (28.7%), followed by *Staphylococcus aureus* (17.4%), and *Klebsiella pneumoniae* (14.9%), and *Enterobacter aerogenes* (10%). These bacteria accounted for 71% of UTI diagnoses over the study period. Resistance investigations to antibiotics showed high rates of resistance to amoxicillin (78.9%), tetracycline (76.4%), and trimethoprim/sulfamethoxazole (77.9%). Cefotaxime and netilmicin respectively demonstrated 13.9% and 3.1% of bacterial resistance.

Generally, it was observed in the study that bacterial resistance increased over time for all antibiotics except chloramphenicol (Moroh et al., 2014).

In Ghana, a laboratory-based surveillance on AMR conducted in the year 2015 revealed increasing trends of resistance to commonly used antimicrobial agents believed to cure various bacterial infections. According to the study, urine was the most common clinical specimen cultured in clinical laboratories in Ghana. Urine isolates formed 38.6% of pathogens isolated. Sensitivity testing revealed high levels of resistance to ciprofloxacin which is the recommended antibiotic for treating UTIs Ghana (Opintan et al., 2015).

Also, Gyansa-Lutterodt et al (2014) showed antibiotic resistance in their study to determine the prevalence and antibiotic sensitivity pattern of uropathogens among patients referred to the Ghana Police Hospital's Laboratory. Uropathogens isolated were highly sensitive to nitrofurantoin and gentamicin. The bacteria showed varying degrees of resistance to common antibiotics used in the treatment of uncomplicated UTI such as ciprofloxacin (Gyansa-Lutterodt et al., 2014). Furthermore, Boye et al. (2012) showed the high incidence of UTI among pregnant women in Cape Coast. The bacteria isolated showed variable sensitivity patterns to gentamicin, tetracycline, amikacin, ampicillin and erythromycin. The highest sensitivity was seen against gentamicin and the lowest against erythromycin. All the isolated bacteria were resistant to amikacin and penicillin.

2.6 Factors influencing the antimicrobial resistance among patients diagnosed with UTI

2.6.1 Age, Sex and Residence

A number of studies have shown the association between demographic characteristics and antimicrobial resistance among patients with urinary tract infections.

Karlowsky and colleagues (2011), in a yearly Canadian National Surveillance study (CANWARD), tested 2,943 urinary culture pathogens for antimicrobial sensitivity from the

year 2007 to 2009. They found out that there was a significant association between increased age and resistance to ciprofloxacin. Their study also demonstrated an association with resistance to two or more frequently recommended oral antibiotics (amoxicillin-clavulanate, ciprofloxacin, nitrofurantoin, and SXT). They also showed that the percentage of isolates resistant to amoxicillin (AMC), ciprofloxacin (CIP), nitrofurantoin (NIT) and trimethoprim-sulfamthoxazole (SXT) varied by gender. Among females, the percentage resistance was AMC (4.3%), NIT (2.9), CIP (17.2), SXT (20.8) while that of males was AMC (3.3%), NIT (7.9%), CIP (27.2%), SXT (26.3%) (Karlowisky et al., 2011).

These findings were consistent with a previous study conducted in the United States by Sahn et al (2001). They showed that among females, the percentage of multiple drug resistant *E. coli* resistant to ampicillin, cephalothin, nitrofurantoin, SXT, and ciprofloxacin were 38.6%, 14.3%, 0.8%, 18.7% and 3.2% respectively. That of males also were 39.3%, 18.5% 1.4% 20.1% and 7.6% respectively (Sahn, 2001). In a joint modelling of resistance to six antimicrobials in Canada (2019), Soucy and colleagues showed that male sex was a consistent risk factor for antibiotic resistance to *Escherichia coli*. They also showed that resistance trends were higher in more densely populated urban areas compared with less densely populated areas which is suggestive of increased use in densely populated areas (Soucy et al., 2019).

2.6.2 Hospitalization status

The hospitalization status referring to whether a patient is an Out-patient or In-patient (on admission) is known to influence disease patterns and consequently resistant patterns among various uropathogens. While some infectious diseases such as UTIs are acquired from the community, they may also be acquired from the hospital due to some procedures such as catheterization that patients are exposed to.

Some studies have examined how hospitalization status influences resistance to antibiotics used to treat uropathogens. In 2013, McGregor showed significant differences in resistance pattern of *E. coli* to Ciprofloxacin and Nitrofurantoin between In-patients and Out-patients (McGregor et al., 2013). In-patients are also a consistent risk factor for resistance to antibiotics (Soucy et al., 2019). In Botswana (2013), Renuart and colleagues also demonstrated that uropathogens from In-patient urine samples were more likely to exhibit resistance to co-trimoxazole compared to Outpatient samples (Renuart et al., 2013).

CHAPTER THREE

3.0 METHODS

3.1 Research Design

A retrospective cross-sectional study design was employed to review records of urine culture and antibacterial sensitivity results of patients referred to the bacteriology laboratory at the Eastern Regional Hospital in Koforidua, Ghana from 2014 to 2018.

3.2 Study Area

The study was carried out at the Bacteriology unit of the Clinical Laboratory Department of the Eastern Regional Hospital located in Koforidua, Ghana.

The Eastern Regional Hospital was established in 1926 to provide comprehensive secondary level in-patient and out-patient healthcare service. It is a secondary level referral health facility and also a referral center for the entire district hospitals in the Eastern region. The hospital also serves as the main health facility for people living in the New Juabeng municipality with over 180,000 inhabitants.

It has ten (10) wards and 280 to 300 bed capacity. (Eastern Region Analytical Report, 2018).

There are several departments at Eastern Regional Hospital of which the Clinical Laboratory department is included. Other departments include the Out-patient department, Surgical Wards, Prenatal and Postnatal wards, Children's ward, Neonatal Intensive Care Unit (NICU), Dental Department, Physiotherapy and Optometry Departments. In the year 2018, the facility saw an OPD attendance of 237,870 and admitted 21,014 patients (DHMIS, 2019).

The Clinical Laboratory Department provides reliable laboratory services for patients to support clinicians for diagnosis and monitoring of patients' treatment outcomes. It is subdivided into the Bacteriology Unit, Parasitology Unit, Haematology Unit, Serology Unit,

3.3 Study Population

This was a records review. The study included all clinical laboratory records of patients suspected of UTI and referred to the Bacteriology Unit at the Eastern Regional Hospital in Koforidua, Ghana, for confirmation between the years 2014 to 2018. The period was selected in order to provide a comprehensive amount of recent laboratory data for evaluation.

3.4 Study Variables

The variables in this study included dependent variable and independent variables. The dependent variable was antimicrobial resistance among patients diagnosed with UTI at the Eastern Regional Hospital in Koforidua, Ghana. The independent variables were Sex of patient, age of patient, urinary tract infection status, uropathogens isolated, type of ward and hospitalization status of patient (as shown in Table 3.1).

Table 3.1: Summary of Variables used in the Study

Variables	Operational Definitions	Indicator	Variable type	Source of data
Dependent Variable				
Antimicrobial resistance	Documented resistance to antibiotics used to treat UTI	Resistant or Sensitive to antibiotics used to treat UTI	Categorical	Records review
Independent variables				
Age	Age of patient in years	Age at last birthday	Continuous	Records review
Sex	Biological sex of patient	Male or Female	Categorical	Records review
Urinary Tract Infection status	Bacteriologically confirmed UTI using culture	Bacteria growth or No bacteria growth	Categorical	Records review
Uropathogen	Bacteria isolated from culture as cause of UTI	Type of bacteria isolated from urine culture	Categorical	Records review
Hospitalisation status	Location of patient in the hospital	In-patient or Out-patient	Categorical	Records review

3.5 Sampling Method

This study utilized a census of total laboratory records available on patients tested for UTI at the Bacteriology Unit of the Eastern Regional Hospital in Koforidua, Ghana from the year January 2014 to December 2018. The sample included all laboratory data that met the inclusion criteria.

3.6 Inclusion and Exclusion Criteria

3.6.1 Inclusion Criteria

1. All records of patients in the Urine Culture and Sensitivity testing records book at the Bacteriology Unit of the Eastern Regional Hospital Laboratory.
2. All patient records of Urine Culture and Sensitivity from January 2014 to December 2018.

3.6.2 Exclusion Criteria

1. All records of UTI caused by other uropathogens apart from bacteria was excluded from the study.
2. Laboratory records of Urine culture and sensitivity tests with incomplete data was excluded from the study.
3. Urine culture results that indicated mixed bacteria growth were excluded from the study since they are considered as a contamination making the result invalid.

3.7 Source of Data and Data Collection

The data collected were located in the Bacteriology Unit of the Clinical Laboratory Department of the Eastern Regional Hospital. In the Bacteriology Unit, the data were archived in a shelf containing all Culture and Sensitivity records. The data were in the upper section of the shelf designated as Urine Culture and Sensitivity result.

A data extraction form (Appendix I) was designed to cover all relevant information from the lab records. It had sections on patients' demographic characteristics, bacteria isolates responsible for UTI, source of urine specimen, culture and sensitivity result.

3.8 Quality Control

3.8.1 Pre- Data collection

The principal investigator was assisted by four intern laboratory scientists who had received training in the extraction of data from the lab records. Pre-testing of the data extraction tool was done at the Bacteriology unit of the Tetteh Quarshie Memorial Hospital at Mampong as a quality control measure for the study. The data extraction forms did not permit entry of names of patients but rather specimen identification numbers to be captured to assist in data cleaning and validation processes. The extracted data sheets were reviewed on a daily basis for completeness and allocated unique serial numbers to avoid double entry.

3.8.2 Post- Data collection

The extracted data were randomly checked with original records to validate entered data. Information derived from patients records were kept in secret files and made only accessible to the principal investigator.

3.9 Data processing and Analysis

The data gathered from the medical records were cleaned, coded, and entered into a Microsoft excel 2010 spreadsheet and exported into STATA version 15. Statistical tools namely time graphs, percentages, frequency tables, and cross tabulations were used to describe the data. Chi-square test was used to assess the association between UTI and various independent variables. Both bivariate and multivariable logistic regression analysis was used to assess predictors of antimicrobial resistance for three most sensitive antibiotics and the most resistant antibiotics.

Odds ratios were reported with their 95% Confidence Intervals. Statistical significance was determined at p-value of < 0.05 .

3.10 Ethical Consideration

Ethical clearance was obtained from the Ethical Review Committee of the Ghana Health Service. Ethical Approval number was **GHS-ERC: 036/05/19** (Appendix II)

Permission to the Eastern Regional Hospital and Laboratory Department was granted by the Eastern Regional Director of Health Services, the Medical Director of the Eastern Regional Hospital and Head of Laboratory Services before data collection.

CHAPTER FOUR

4.0 RESULTS

4.1 Distribution of variables at study site

Out of 14568 records of urine culture and sensitivity recorded from January 2014 to December 2018, 12655 (86.9%) met the criteria to be included in the study. Out of 12655 records used in the study, 2234(17.7%) were recorded in 2014, 2081(16.4%) in 2015, 1868(14.8%) in 2016, 3045(24.1%) in 2017 and 3427(27.0%) in 2018 (as shown in Table 4.1)

4.1.1 Distribution of participants by sex

Most of the cases eligible for inclusion in the study were females 8280, (65.43%) (as shown in Table 4.1)

4.1.2 Distribution of participants by age.

The ages of the cases selected into the study range from 4 weeks to 100 years with the median age being 25 years. Majority of the cases fall within 19 to 45 years of age, 5807 (45.89%) followed by those within the age bracket of 2 to 5 years, 1824 (14.41%). The least recorded age group is those within 13 to 18 years, 555 (4.39%) (As shown in Table 4.1).

4.1.3 Distribution of cases by hospital location

Majority of the cases included in the study were from the Out-patient department, 8663(68.46%) followed by the kids ward which represent 12.64% of selected participants. Majority of the units that referred cases to the laboratory to test for UTI were units that catered specifically for females and children (Antenatal Clinic, Gynaecology Unit, Female Ward, Children's Ward and Neonatal Intensive Care Unit) (as shown in Table 4.1).

Table 4.1: Distribution of study characteristics

Study characteristic	Frequency N=12,655	Percentage (%)
Sex		
Female	8,280	65.4
Male	4,375	34.6
Age groups		
<1	1,096	8.7
2-5	1,824	14.4
6-12	1,297	10.3
13-18	555	4.4
19-45	5,807	45.8
46-60	1,051	8.3
Above 60	1,025	8.1
Hospital location		
Out-patient Department	8,663	68.5
Antenatal clinic	796	6.3
Gynaecology unit	858	6.8
Female ward	172	1.4
Male ward	109	0.9
Children's ward	1,600	12.6
Neonatal Intensive care	90	0.7
Emergency unit	329	2.6
Other units*	38	0.3
Year of attendance		
2014	2,234	17.6
2015	2,081	16.4
2016	1,868	14.8
2017	3,045	24.1
2018	3,427	27.1

Other units*: Urology, Ant-retroviral clinic

4.2 Distribution of reported cases of UTI

4.2.1 Overall reported cases of UTI from 2014 to 2018

The overall proportion of UTI from 2014 to 2018 was 2,573 (20.3%) out of 12,655 people. As seen in figure 4.2, UTI cases rose significantly from 398 (17.8%) in 2014 to 757 (28.4%) in 2018.

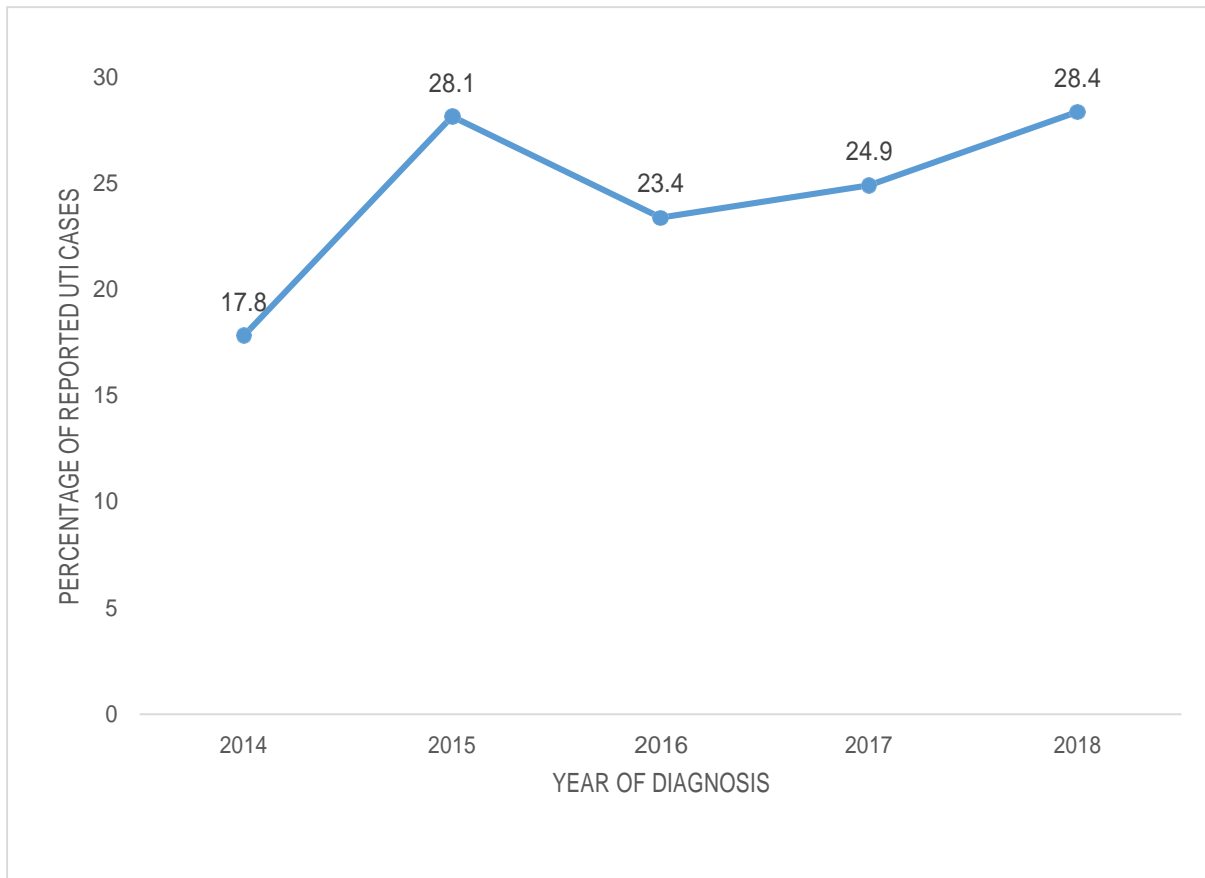


Figure 4.2 Pattern of UTI cases from 2014 to 2018

4.2.2 Distribution of UTI by sex.

Out of 2573 cases of UTI, majority were females 2060 (80.06%). Proportions of UTI varied significantly ($p < 0.05$) between Male and Females in the study subjects (as shown in Table 4.2).

4.2.3 Distribution of UTI by age categories.

Out of 2,573 UTI cases, 42.32% (1,089/2,573) representing the majority of cases were among the 19-45 age category. This is followed by those above 60 years of age 14.65% and then children aged 1 and below. The age group with the least number of UTI cases is those between 13 and 18 years (as shown in Table 4.2).

4.2.4 Distribution of UTI by hospitalization status and hospital units

Most of the UTI cases, 74.04%, occurred from Out-patient settings though this was not statistically significant ($p > 0.05$) when compared with number of cases occurring from In-patients. When stratified into the individual hospital units, 68.09% (1,752/2,573) being majority of the cases were Out-patients followed by Children's' ward 9.06% (233/2,573). The least number of UTI cases were from Male ward and other units which contributed 0.93% and 0.51% of UTI cases respectively. Variations in UTI cases among the various hospital units were statistically significant ($p < 0.05$) (Table 4.2).

Table 4.2 Distribution of UTI cases by study characteristics

Study characteristics	UTI	No UTI	Pearson Chi-square	
	N=2573 n (%)	N=10082 n (%)	χ^2	p-value
Sex				
Male	513 (19.9)	3,862 (38.3)	305.75	0.0001
Female	2,060 (80.1)	6,220 (61.7)		
Age categories				
</=1	310 (12.1)	786 (7.8)	356.53	0.001
2-5	273 (10.6)	1,551 (15.4)		
6-12	143 (5.6)	1,154 (11.5)		
13-18	97 (3.8)	458 (4.5)		
19-45	1,089 (42.2)	4,718 (46.8)		
46-60	284 (11.0)	767 (7.6)		
Above 60	377 (14.7)	648 (6.4)		
Hospitalization status				
In-patient	668 (25.9)	2,528 (25.1)	0.8554	0.355
Out-patient	1,905 (74.1)	7,554 (74.9)		
Hospital Unit				
OPD	1,752 (68.1)	6,911(68.5)	95.20	0.001
Antenatal Clinic	153 (5.9)	643 (6.4)		
Gynaecology Unit	228 (8.9)	630 (6.3)		
Female Ward	60 (2.3)	112 (1.1)		
Male Ward	24 (0.9)	85 (0.8)		
Kids Ward	233 (9.1)	1,367 (13.5)		
NICU	31(1.2)	59 (0.6)		
Emergency Unit	79 (3.1)	250 (2.5)		
Other Units*	13 (0.5)	25 (0.3)		
Year of Diagnosis				
2014	398	2,234	21.17	0.001
2015	457	1,624		
2016	354	1,514		
2017	607	2,438		
2018	757	2,670		

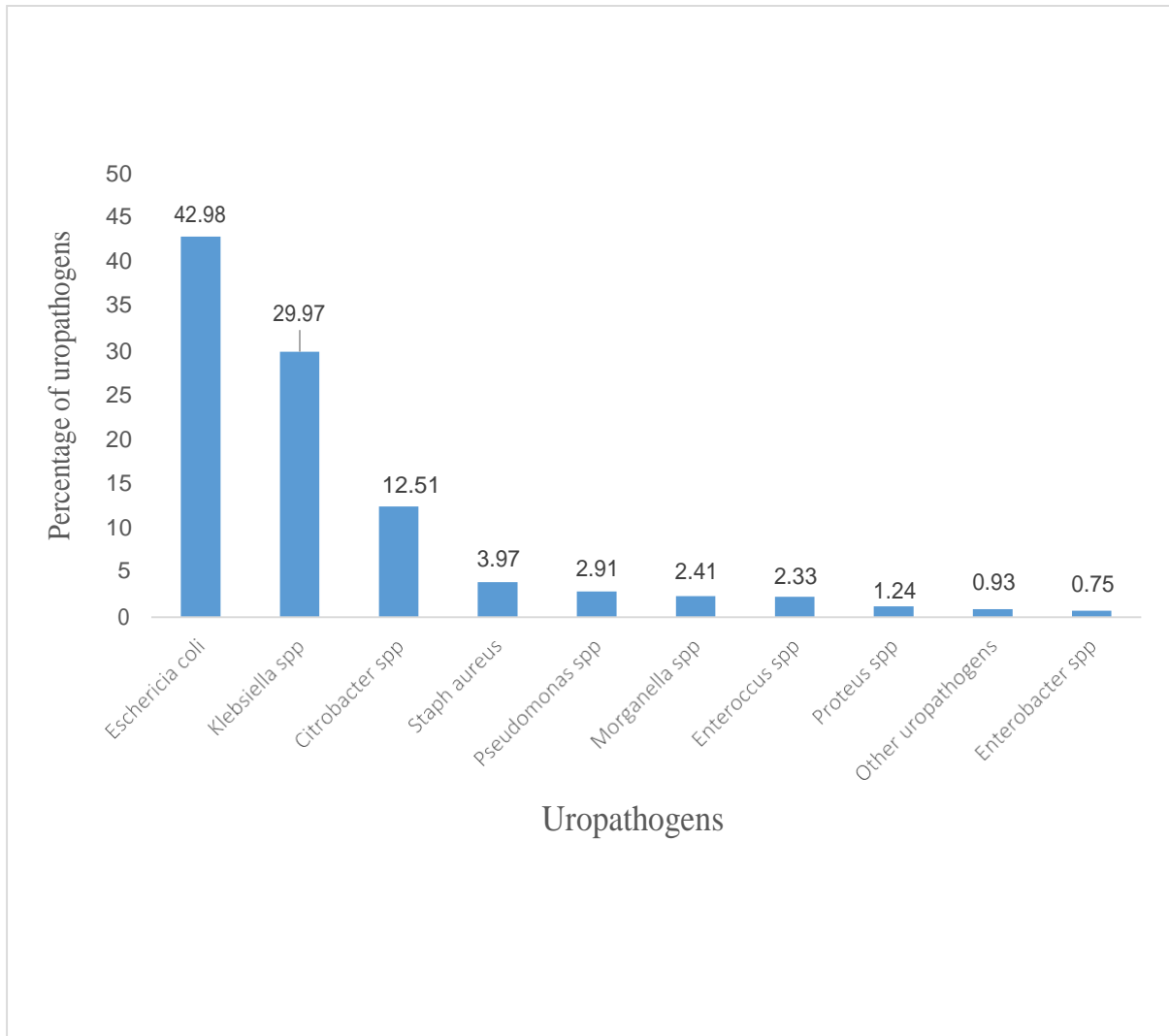
OPD: Out-patient department, NICU: Neonatal Intensive Care Unit

Age categories adopted from (Mohammed et al., 2016)

4.3 Distribution of Uropathogens

Out of 2,573 uropathogens isolated as cause of UTIs over the five year period (2014-2018), fourteen (14) different uropathogens were reported. *Escherichia coli*, 1,106 (42.98%),

Klebsiella spp 771(29.97%) and *Citrobacter* spp 322 (12.51%) represented the majority of isolates. The least reported isolates were *Proteus* spp, *Enterobacter* spp and those grouped as Other uropathogens (Figure 4.3a). The numbers of the three major uropathogens have been increasing over the years (Figure 4.3b).



Other uropathogens: *Acinetobacter* spp (6), *Providencia* spp (8), *Serratia* spp (4), *Non-hemolytic Streptococcus* (4) *Coagulase negative Staphylococcus* (2)

Figure 4.3a Percentage distribution of Uropathogens

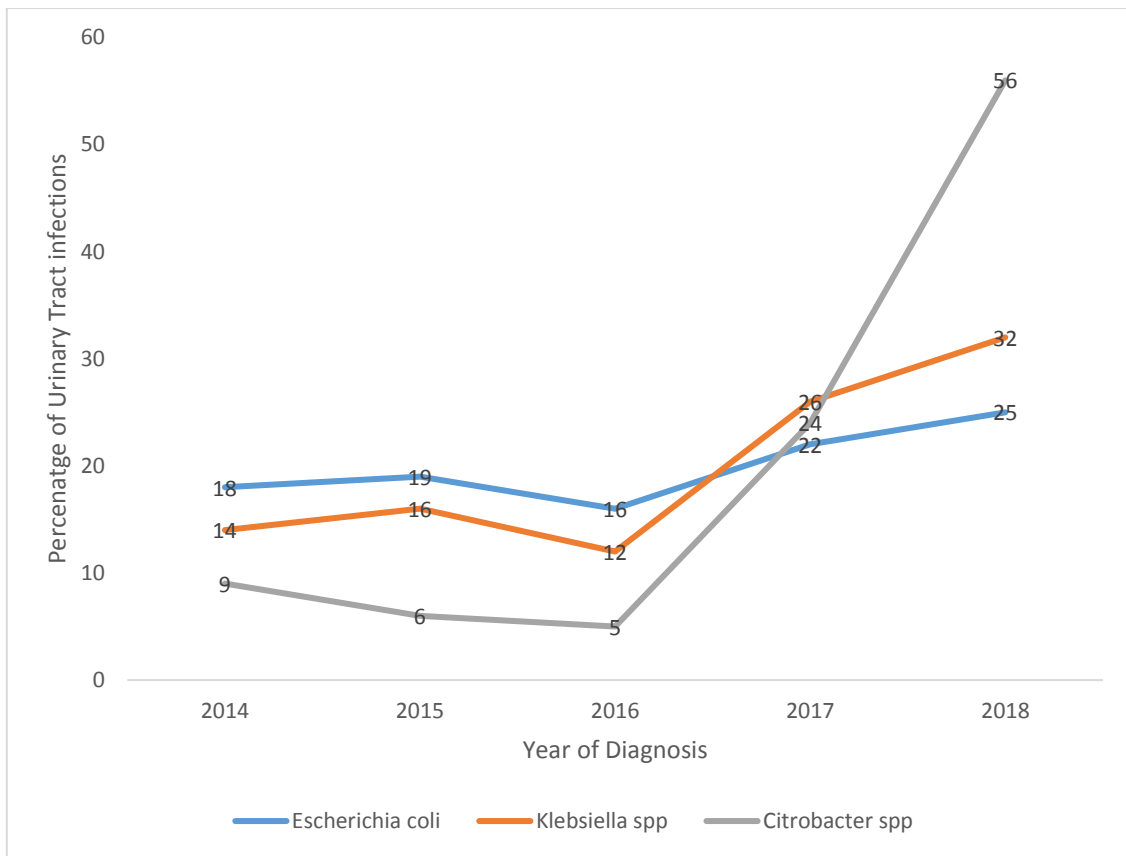


Figure 4.3b Trendline of three main uropathogens from 2014 to 2018

4.3.1 Distribution of uropathogens by sex

Escherichia coli, *Klebsiella* spp and *Citrobacter* spp are the most dominant uropathogens in both sexes. However, the frequencies of uropathogens are higher in females than males. The proportion of individual isolate remains almost the same in both sexes (Shown in Table 4.3.1).

Table 4.3.1 Distribution of uropathogens by sex

Uropathogens	Female	Male	Total
	N=2,060	N=513	N=2,573
	n (%)	n (%)	n (%)
<i>Escherichia coli</i>	923 (44.8)	183 (35.7)	1,106 (42.9)
<i>Klebsiella spp</i>	605 (29.4)	166 (32.4)	771 (29.9)
<i>Citrobacter spp</i>	242 (11.8)	80 (15.6)	322 (12.5)
<i>Proteus spp</i>	25 (1.2)	7 (1.4)	32 (1.2)
<i>Morganella spp</i>	49 (2.4)	13 (2.5)	62 (2.4)
<i>Pseudomonas spp</i>	51 (2.5)	24 (4.7)	75 (2.9)
<i>Staphylococcus aureus</i>	85 (4.1)	17 (3.3)	102 (3.9)
<i>Enterococcus spp</i>	49 (2.4)	11 (2.1)	60 (2.3)
<i>Enterobacter spp</i>	13 (0.6)	6 (1.2)	19 (0.7)
Other uropathogens*	15 (0.7)	6 (1.2)	24 (0.9)

**Acinetobacter spp* (6), *Providencia spp* (8), *Serratia spp*(4), *Non-hemolytic Streptococcus* (4) *Coagulase negative Staphylococcus*(2)

4.3.2 Distribution of uropathogens by age categories

Generally, the majority of UTI were caused by *Escherichia coli*, *Klebsiella spp*, and *Citrobacter spp* across all age categories. In the age categories below five (5) *Klebsiella spp* is the predominant uropathogen while *Escherichia coli* is responsible for UTI among age groups with adults (above 19 years). *Enterobacter spp* is not recorded to have caused any infection among the age categories ≤ 1, 6-12, 13-18 and 46-60 (as shown in Table 4.3.2).

Table 4.3.2 Distribution of uropathogens by age categories

Uropathogens	Age categories						
	</=1	2-5	6-12	13-18	19-45	46-60	Above 60
	N=310 n (%)	N=273 n (%)	N=143 n (%)	N=97 n (%)	N=1089 n (%)	N=284 n (%)	N=377 n (%)
<i>Escherichia coli</i>	106 (34.2)	75 (24.2)	55 (38.5)	42 (43.3)	481 (44.2)	153 (54.0)	194 (51.5)
<i>Klebsiella spp</i>	130 (41.9)	115 (42.1)	44 (30.8)	29 (30.0)	295 (27.1)	69 (24.3)	89 (23.6)
<i>Citrobacter spp</i>	48 (15.5)	52 (19.1)	26 (18.2)	10 (10.3)	119 (10.9)	25 (8.8)	42 (11.1)
<i>Proteus spp</i>	4 (1.3)	0 (0.0)	4 (2.8)	1 (1.0)	15 (1.4)	1 (0.4)	7 (1.9)
<i>Morganella spp</i>	5 (1.6)	5 (1.8)	2 (1.4)	1 (1.0)	28 (2.6)	12 (4.2)	9 (2.4)
<i>Pseudomonas spp</i>	3 (0.9)	7 (2.6)	1 (0.7)	4 (4.1)	35 (3.2)	9 (3.2)	16 (4.2)
<i>Staph aureus</i>	7 (2.3)	6 (2.2)	7 (4.9)	9 (9.3)	59 (5.4)	8 (2.8)	6 (1.6)
<i>Enterococcus spp</i>	6 (1.9)	7 (2.6)	4 (2.8)	1 (1.0)	29 (2.7)	5 (1.8)	8 (2.1)
<i>Enterobacter spp</i>	0 (0.0)	2 (0.7)	0 (0.0)	0 (0.0)	15 (1.4)	0 (0.0)	2 (0.5)
Other uropathogens*	1 (0.3)	4 (1.5)	0 (0.0)	0 (0.0)	13 (1.2)	2 (0.7)	4 (1.1)

**Acinetobacter spp* (6), *Providencia spp* (8), *Serratia spp*(4), *Non-hemolytic Streptococcus* (4) *Coagulase negative Staphylococcus*(2)

4.3.3 Distribution of Uropathogens by Hospitalization status

Most of the isolates recorded in the study were from the Out-patient Department. *Escherichia coli*, *Klebsiella spp* and *Citrobacter spp* were the most prevalent uropathogens in both In-patients and Out-patients.

Table 4.3.3 Distribution of uropathogens by hospitalization status

Uropathogens	Hospitalization status		
	Out-patient N=1905 n (%)	In-patient N=668 n (%)	Total N=2573 n (%)
<i>Escherichia coli</i>	864 (45.3)	242 (36.2)	1106 (42.9)
<i>Klebsiella spp</i>	533 (28.0)	238 (35.6)	771 (29.9)
<i>Citrobacter spp</i>	231 (12.1)	91 (13.6)	322 (12.5)
<i>Proteus spp</i>	21 (1.1)	11 (1.7)	32 (1.2)
<i>Morganella spp</i>	46 (2.4)	16 (2.4)	62 (2.4)
<i>Pseudomonas spp</i>	51 (2.7)	24 (3.5)	75 (2.9)
<i>Staphylococcus aureus</i>	81 (4.3)	21 (3.2)	102 (3.9)
<i>Enterococcus spp</i>	46 (2.4)	14 (2.1)	60 (2.3)
<i>Enterobacter spp</i>	15 (0.8)	4 (0.6)	19 (0.7)
Other uropathogens*	17 (0.9)	7 (1.1)	24 (0.9)

**Acinetobacter spp* (6), *Providencia spp* (8), *Serratia spp*(4), *Non-hemolytic Streptococcus* (4)
Coagulase negative Staphylococcus(2)

4.4 Antimicrobial Resistance Pattern

The highest percentage resistance (100%) is recorded for *Proteus spp* to tetracycline and the lowest resistance (3.1%) is recorded for *Proteus spp* to Amikacin. Seven (7) out of the eleven (11) antibiotics, Nalidixic acid, Ampicillin, Tetracycline, Co-trimoxazole, Pipimedic acid, Gentamicin, and Cefuroxime have their resistances ranging between 46.7% (*Pseudomonas spp* to Pipimedic acid) to 100% (*Proteus spp* to tetracycline).

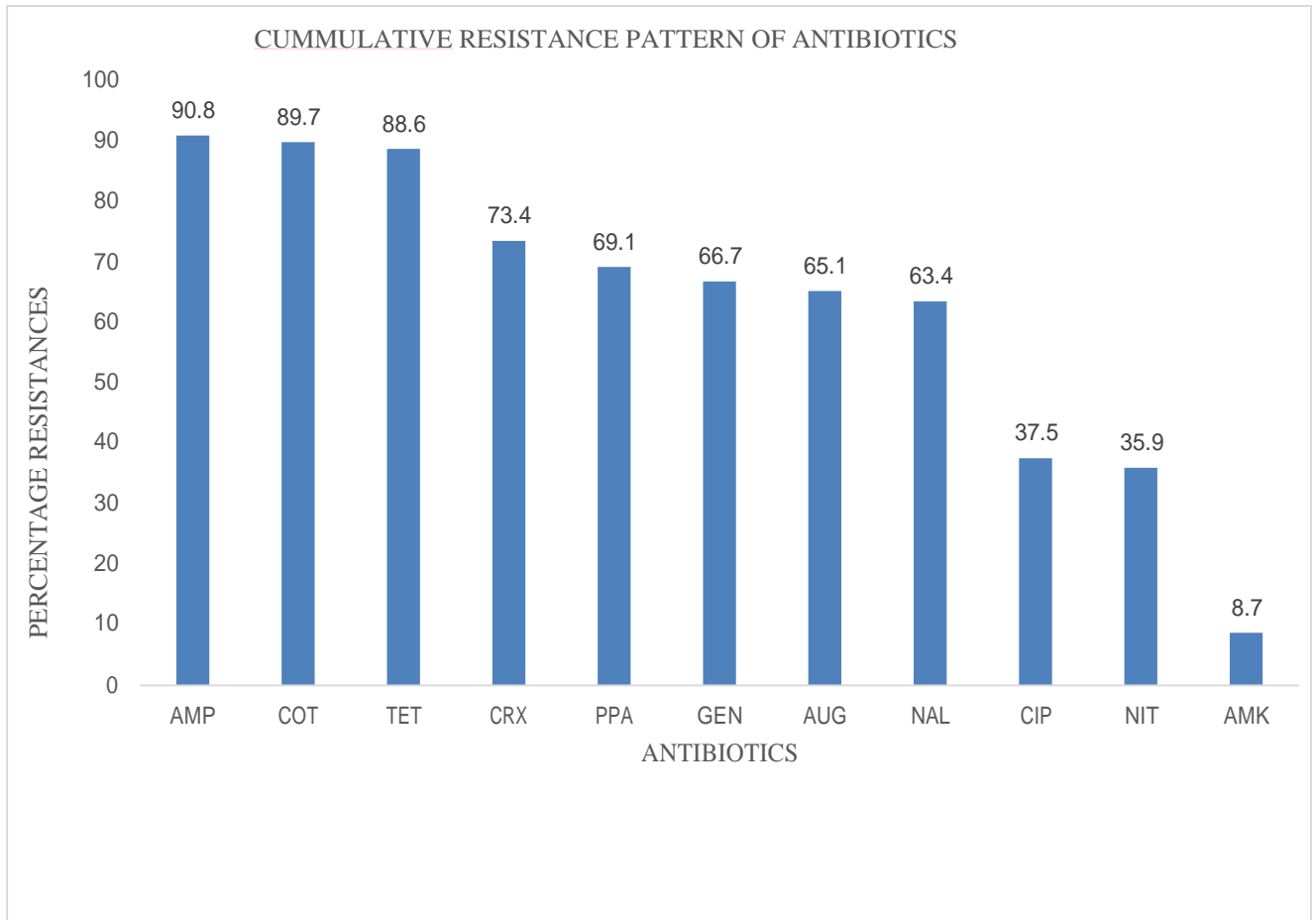
The resistance of three (3) antibiotics, Nitrofurantoin, Ciprofloxacin and Amikacin range between 3.1% (*Proteus spp* on Amikacin) and 65% (*Proteus spp* to Nitrofurantoin). The least resistant antibiotic Amikacin has resistance ranging from 3.1% (*Proteus spp* on Amikacin) to 35% (*Enterococcus spp* on Amikacin). The percentage resistance of the most resistant antibiotic, Ampicillin, ranges from 83.3% (*Enterococcus spp* to Amikacin) to 96.9% (*Proteus spp* to Ampicillin) (as shown in Table 4.4.1).

Table 4.4.1 Frequency and percentage distribution of antimicrobial resistance of uropathogens among antibiotics used in the study.

Uropathogens (Total number)	ANTIBIOTICS										
	NIT	NAL	AMP	TET	COT	PPA	GEN	CRX	CIP	AMK	AUG
	N=2573 n (%)										
<i>Escherichia coli</i> (1106)	192(17.7)	775(70.0)	1010(91.3)	1002(90.5)	1007(91.0)	791(71.5)	693(62.7)	762(68.9)	454(41.0)	86(7.8)	726(65.6)
<i>Klebsiella spp</i> (771)	433(56.2)	439(56.9)	694(90.0)	681(88.3)	695(90.0)	523(67.8)	570(73.9)	630(81.7)	268(34.8)	62(8.0)	539(69.9)
<i>Citrobacter spp</i> (322)	176(54.7)	191(59.3)	297(92.2)	279(86.6)	278(86.3)	233(72.4)	202(62.7)	247(76.7)	107(33.2)	29(9.0)	229(71.1)
<i>Proteus spp</i> (32)	21(65.6)	16(50.0)	31(96.9)	32(100.0)	30(93.8)	20(62.5)	19(59.4)	21(65.6)	8(25.0)	1(3.1)	11(34.4)
<i>Morganella spp</i> (62)	27(43.5)	40(64.5)	57(92.0)	58(93.5)	56(90.3)	43(69.3)	46(74.2)	47(75.8)	24(38.7)	3(4.8)	42(67.7)
<i>Pseudomonas spp</i> (75)	35(46.7)	40(53.3)	70(93.3)	65(86.7)	68(90.7)	35(46.7)	53(70.7)	62(82.7)	23(30.7)	9(12.0)	57(76.0)
<i>Staph aureus</i> (102)	8(7.8)	63(61.8)	87(85.3)	82(80.4)	91(89.2)	60(58.8)	62(60.9)	56(54.9)	29(28.4)	8(7.8)	27(26.5)
<i>Enterococcus spp</i> (60)	10(16.7)	39(65.0)	50(83.3)	51(85.0)	51(85.0)	40(66.7)	45(75.0)	37(61.7)	32(53.3)	21(35.0)	24(40.0)
<i>Enterobacter spp</i> (19)	9(47.4)	16(84.2)	17(89.5)	15(78.9)	16(84.2)	15(79.0)	11(57.9)	9(47.4)	7(36.8)	1(5.3)	8(42.0)
<i>Other uropath</i> * (24)	12(50.0)	13(54.2)	22(91.7)	15(62.5)	17(70.8)	17(70.8)	15(62.5)	18(75.0)	12(50.0)	3(12.5)	13(54.2)
Cumulative resistance	923(36.0)	1632(63.4)	2335(90.8)	2280(88.6)	2309(89.7)	1777(69.1)	1716(66.7)	1889(73.4)	964(37.5)	223(8.7)	1676(65.1)

NIT: Nitrofurantoin NAL: Nalidixic acid AMP :Ampicillin TET: Tetracycline COT: Co-trimoxazole PPA: Pipimedic acid GEN: Gentamicin CRX: Cefuroxime CIP: Ciprofloxacin AMK: Amikacin AUG: Augmentin

From figure 4.4.2, Ampicillin, Co-trimoxazole and Tetracycline represent the most resistant antibiotic with cumulative percentage resistance of 90.8%, 89.7% and 88.6% respectively. Ciprofloxacin, Nitrofurantoin and Amikacin are the least resistant out of the eleven (11) antibiotics used in the study with resistance of 37.5%, 35.9% and 8.7% respectively.



NIT: Nitrofurantoin NAL: Nalidixic acid AMP: Ampicillin TET: Tetracycline COT: Co-trimoxazole PPA: Pipimedic acid GEN: Gentamicin CRX: Cefuroxime CIP: Ciprofloxacin AMK: Amikacin AUG: Augmentin

Figure 4.4.1 Cumulative resistance pattern of antibiotics used in the study

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The odds of resistance to Co-trimoxazole and Tetracycline are significantly increased with the various uropathogens. *Escherichia coli* has 4.0 times increased odds of resistance to Co-trimoxazole (AOR=4.0, CI=1.61, 9.94) and 5.82 times increased odds of resistance to Tetracycline (AOR=5.82, CI=2.47, 13.72) and this is statistically significant at $p < 0.05$ (as shown in Table 4.5.1).

Statistically significant ($P < 0.05$) increased odds of resistance to Co-trimoxazole (AOR=3.73, CI=1.49, 9.33) and Tetracycline (AOR=4.86 CI=2.05, 11.50) is observed in *Klebsiella* spp. In *Citrobacter* spp, the odds of resistance is increased by 2.63 folds to Co-trimoxazole (AOR=2.63, CI=1.03, 6.73) and 4.20 folds to Tetracycline (AOR=4.20, CI=1.72, 10.26). The odds of resistance of Co-trimoxazole in *Proteus* spp is increased by 6 folds (AOR=6.06, CI=1.12, 32.69) and this is statistically significant at $p < 0.05$.

Co-trimoxazole resistance has 3.67 increased odds of being *Morganella* spp UTI (AOR= 3.67 CI=1.08, 12.43) and tetracycline resistance has 8.62 times increased odds of being *Morganella* spp infection (AOR=8.62, CI=2.32, 32.02) and this is statistically significant at $p < 0.05$. Resistance to Co-trimoxazole among *Pseudomonas* spp is increased by 3.88 folds (AOR=3.88, CI=3.31, 1.12) and that of tetracycline is increased by 3.81 times (AOR=3.81 CI=1.31, 11.05). Resistance to Tetracycline shows 3.53 increased odds of being *Enterococcus* spp UTI (AOR= 3.53, CI=1.18, 10.54). All these are statistically significant at $p < 0.05$ (shown in Table 4.5.1).

Persons below 12 years of age have reduced odds of resistance to Co-trimoxazole and Tetracycline while persons above 13 years have increased odds of resistance to tetracycline. This is however not statistically significant ($p > 0.05$) (Table 4.5.1)

Table 4.5.1 Logistic regression showing association between the three most resistant antibiotics with study variables.

Variables	ANTIBIOTICS					
	AMPICILLIN		COTRIMOXAZOLE		TETRACYCLINE	
	COR	AOR	COR	AOR	COR	AOR
Sex						
Female	Ref	Ref	Ref	Ref	Ref	Ref
Male	1.01(0.72,1.42)	0.91(0.63, 1.30)	0.91(0.67, 1.25)	0.94(0.67, 1.31)	0.94(0.69, 1.27)	1.04(0.76, 1.44)
Uropathogen						
Other uropathogens	Ref	Ref	Ref	Ref	Ref	Ref
<i>Escherichia coli</i>	0.96 (0.22, 4.13)	0.93 (0.21, 4.01)	4.19 (1.69, 10.34)**	4.00(1.61, 9.94)**	5.78(2.45, 13.53)***	5.82(2.47, 13.72)***
<i>Klebsiella spp</i>	0.82 (0.19, 3.56)	0.77 (0.19, 3.37)	3.77 (1.51, 9.37)**	3.73(1.49, 9.33)**	4.54(1.93, 10.67)***	4.86(2.05, 11.50)***
<i>Citrobacter spp</i>	1.08 (0.24, 4.86)	1.02 (0.23, 4.60)	2.60 (1.02, 6.63)*	2.63(1.03, 6.73)*	3.89(1.60, 9.45)**	4.20(1.72, 10.26)**
<i>Proteus spp</i>	2.82 (0.24, 33.04)	2.79 (0.24, 32.77)	6.18 (1.15, 33.15)*	6.06(1.12, 32.69)*	-----	-----
<i>Morganella spp</i>	1.04 (0.19, 5.74)	1.02 (0.18, 5.64)	3.84 (1.14, 12.99)*	3.67(1.08, 12.43)*	8.7(2.35, 32.16)**	8.62(2.32, 32.02)**
<i>Pseudomonas spp</i>	1.23 (0.23, 7.03)	1.29 (0.23, 7.14)	4.00 (1.24, 12.95)*	3.88(3.31, 1.12)*	3.9(1.35, 11.27)*	3.81(1.31, 11.05)*
<i>Staphylococcus aureus</i>	0.53 (0.11, 2.47)	0.53 (0.11, 2.48)	3.41 (1.16, 10.03)*	3.31(1.12, 9.71)*	2.46(0.94, 6.43)	2.47(0.94, 6.51)
<i>Enterococcus spp</i>	0.45 (0.09, 2.25)	0.44 (0.09, 2.18)	2.33 (0.75, 7.22)	2.32(0.75, 7.2)	3.40(1.14, 10.10)*	3.53(1.18, 10.54)*
<i>Enterobacter spp</i>	0.77 (0.10, 6.06)	0.81 (0.10, 6.40)	2.20 (0.48, 9.99)	2.22(0.49, 10.14)	2.25(0.57, 8.93)	2.18(0.55, 8.70)
Age categories						
</=1	Ref	Ref	Ref	Ref	Ref	Ref
2-5	0.91(0.49, 1.68)	0.91 (0.49, 1.68)	0.61 (0.37, 1.03)	0.64(0.38, 1.08)	0.84(0.53, 1.33)	0.91 (0.56, 1.45)
6-12	0.87(0.42, 1.81)	0.86 (0.41, 1.79)	0.65(0.35, 1.20)	0.64(0.34, 1.20)	0.94(0.53, 1.67)	0.94 (0.52, 1.68)
13-18	0.70(0.32, 1.52)	0.68 (0.31, 1.50)	1.10(0.49, 2.51)	1.05(0.46, 2.41)	1.19(0.59, 2.42)	1.26 (0.61, 2.60)
19-45	0.70(0.44, 1.16)	0.67 (0.41, 1.09)	0.87(0.57, 1.35)	0.86(0.55, 1.36)	1.29(0.88, 1.89)	1.38 (0.92, 2.07)
46-60	0.83(0.46, 1.50)	0.78 (0.43, 1.42)	1.13(0.63, 2.01)	1.07(0.60, 1.94)	1.51(0.90, 2.54)	1.50 (0.88, 2.56)
Above 60	0.81(0.47, 1.40)	0.76 (0.43, 1.32)	0.91(0.54, 1.52)	0.90(0.53, 1.51)	1.36(0.85, 2.17)	1.35 (0.84, 2.18)
Hospitalization status						
Out-Patient	Ref	Ref	Ref	Ref	Ref	Ref
In-patient	0.92(0.69, 1.25)	0.89(0.66, 1.21)	0.95(0.71, 1.26)	0.99(0.74, 1.32)	0.98(0.74, 1.29)	1.04(0.79, 1.38)

COR= Crude Odds Ratio, AOR= Adjusted Odds Ratio Ref: Reference category p-value<0.05=*, p-value<0.01=**, p-value<0.001=*** --=missing

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Among uropathogens, *Proteus* spp showed 69.0% reduced odds of resistance to Ciprofloxacin (AOR=0.31, CI=0.10, 0.99). This was statistically significant at $p<0.05$

Resistance to Nitrofurantoin had 91.0% and 80.0% reduced odds of being *Staphylococcus aureus* UTI (AOR=0.09 CI=0.03, 0.26) and *Enterococcus* spp (AOR=0.2 CI=0.07, 0.57) respectively and this was statistically significant at $p<0.05$.

Among age categories, the odds of resistance to nitrofurantoin was reduced by 32% among persons aged 16-49 years (AOR=0.68 CI=0.5, 0.91). This was statistically significant at $p<0.05$. The odds of resistance to Ciprofloxacin was increased by 2.47 times and 2.53 times among persons aged 46-60 (AOR= 2.47 CI=1.76, 3.51) and above 60 years of age (AOR=2.53 CI=1.83, 3.47) respectively. These were statistically significant at $p<0.01$.

Resistance to Ciprofloxacin was increased by 26.0% among in-patients (AOR=1.26 CI=1.05, 1.53) and this was statistically significant at $p<0.05$.

Table 4.5.2 Logistic regression showing association between the three least resistant antibiotics and study variables.

VARIABLES	ANTIBIOTICS					
	AMIKACIN		NITROFURANTOIN		CIPROFLOXACIN	
	COR	AOR	COR	AOR	COR	AOR
Sex						
Female	Ref	Ref	Ref	Ref	Ref	Ref
Male	1.14(0.82, 1.60)	1.02 (0.71, 1.45)	1.5 (1.24, 1.84)	1.20 (0.95, 1.51)	0.96 (0.78, 1.17)	0.91(0.73, 1.14)
Uropathogen						
Other uropathogens*	Ref	Ref	Ref	Ref	Ref	Ref
<i>E. coli</i>	0.59 (0.17, 2.02)	0.58 (0.17, 2.0)	0.21 (0.09, 0.47)***	0.21 (0.09, 0.47)	0.70 (0.31, 1.56)	0.66 (0.29, 1.50)
<i>Klebsiella spp</i>	0.61 (0.18, 2.11)	0.58 (0.17, 2.02)	1.28 (0.57, 2.89)	1.22 (0.54, 2.77)	0.53 (0.24, 1.20)	0.55 (0.24, 1.26)
<i>Citrobacter spp</i>	0.69 (0.19, 2.46)	0.67 (0.19, 2.38)	1.21 (0.53, 2.76)	1.16 (0.50, 2.67)	0.50 (0.22, 1.14)	0.52 (0.22, 1.21)
<i>Proteus spp</i>	0.23 (0.22, 2.32)	0.22 (0.02, 2.33)	1.91 (0.65, 5.64)	1.84 (0.62, 5.48)	0.33 (0.11, 1.03)	0.31 (0.10, 0.99)*
<i>Morganella spp</i>	0.36 (0.07, 1.90)	0.35 (0.07, 1.90)	0.77 (0.30, 1.98)	0.77 (0.30, 2.00)	0.63 (0.24, 1.63)	0.58 (0.22, 1.52)
<i>Pseudomonas spp</i>	0.95 (0.24, 3.85)	0.93 (0.23, 3.78)	0.88 (0.35, 2.20)	0.83 (0.33, 2.09)	0.44 (0.17, 1.13)	0.40 (0.15, 1.03)
<i>Staph aureus</i>	0.60 (0.15, 2.43)	0.61 (0.15, 2.53)	0.09 (0.03, 0.25)***	0.09 (0.03, 0.26)***	0.40 (0.16, 0.99)	0.42 (0.17, 1.05)
<i>Enterococcus spp</i>	3.77 (1.01, 14.12)*	3.81 (1.01, 14.34)*	0.20 (0.07, 0.57)**	0.20 (0.07, 0.57)**	1.14 (0.44, 2.95)	1.19 (0.46, 3.11)
<i>Enterobacter spp</i>	0.39 (0.04, 4.07)	0.42 (0.04, 4.40)	0.90 (0.27, 3.00)	0.97 (0.29, 3.25)	0.58 (0.17, 1.99)	0.64 (0.18, 2.10)
Age categories						
<=1	Ref	Ref	Ref	Ref	Ref	Ref
2-5	0.89 (0.52, 1.52)	0.85 (0.49, 1.46)	0.90 (0.65, 1.25)	0.83 (0.58, 1.18)	0.98 (0.68, 1.40)	0.96 (0.67, 1.38)
6-12	0.55 (0.25, 1.17)	0.52 (0.24, 1.14)	0.68 (0.45, 1.02)	0.75 (0.48, 1.17)	1.24 (0.81, 1.89)	1.22 (0.80, 1.87)
13-18	0.93 (0.44, 1.97)	0.96 (0.45, 2.05)	0.71 (0.45, 1.13)	1.02 (0.60, 1.72)	1.26 (0.77, 2.05)	1.28 (0.78, 2.10)
19-45	0.66 (0.43, 1.10)	0.64 (0.41, 1.00)	0.52 (0.40, 0.67)***	0.68 (0.50, 0.91)*	1.32 (1.0, 1.7)	1.29 (0.97, 1.72)
46-60	0.75 (0.43, 1.30)	0.76 (0.43, 1.33)	0.52 (0.37, 0.72)***	0.76 (0.52, 1.10)	2.51 (1.79, 3.52)***	2.47 (1.76, 3.51)**
Above 60	0.88 (0.54, 1.44)	0.87 (0.53, 1.45)	0.70 (0.52, 0.96)*	0.98 (0.70, 1.38)	2.48 (1.80, 3.41)***	2.53 (1.83, 3.47)**
Hospitalization status						
Out-Patient	Ref	Ref	Ref	Ref	Ref	Ref
In-patient	1.05 (0.77, 1.43)	1.05 (0.76, 1.44)	1.54 (1.29, 1.85)	1.36 (1.11, 1.65)	1.12 (0.93, 1.34)	1.26 (1.05, 1.53)*

COR: Crude Odds Ratio AOR: Adjusted Odds ratio Ref: reference category, Other uropathogens: *Acinetobacter spp*, *Serratia spp*, *Providencia spp*, Non-hemolytic Streptococcus p-value<0.05=*, p-value<0.01=**, p-value<0.001=***

CHAPTER FIVE

5.0 DISCUSSION

5.1 Prevalence of Urinary Tract Infections

The overall proportion of UTI in this study was 20.3% among patients who reported to the Bacteriology Unit over the five year period. Though some studies have reported findings comparable to this in Ghana and other countries, these studies differed in study designs making comparisons difficult (Bitew, 2017; Gyansa-Lutterodt et al., 2014; Linhares et al., 2013; Mollick, 2016; Odoki et al., 2019). Among the urine samples sent to the Bacteriology Unit for testing, confirmed cases of UTI increased significantly by 10.6% ($p < 0.05$) over the five year period. This could have accounted for the increased Out-patient attendance over the years under review. The observed increment in UTI cases is clinically relevant for decision making in health service delivery at the Eastern Regional Hospital. The absence of an epidemic Alert threshold for UTIs may hinder public health decisions to implement appropriate interventions for UTI control among the public in Koforidua and neighbouring towns.

UTI was significantly higher among females ($p < 0.05$). This is not surprising as UTI is more common in females and is comparable to other studies reporting higher incidence in females (Anuli et al., 2016; Gyansa-Lutterodt et al., 2014; Prah et al., 2019; Reu et al, 2018). The high incidence of UTI in females is explained by the fact that the female urethra is susceptible to colonization due to its close proximity to the anus which allows access to the bladder. Poor vaginal hygiene, sexual intercourse and use of contraceptive are also contributory factors. Additionally, hormonal changes such as menopause and estrogen loss are responsible for the high prevalence of UTI in older women. However, men become more prone to UTIs after 50 years of age, when they are more likely to develop prostate complications due to loss of prostate

fluid. Enlarged prostate gland can also impede and slow the flow of urine, hence risk the risk of UTI (Basseye et al., 2016). This finding, in clinical practice, is necessary to inform gender based interventions for prevention and control of UTI among patients.

The occurrence of UTI varied significantly across age categories in this study ($p < 0.05$). About 40% of reported UTI cases occurred among the 19-45 age categories. The least percentage prevalence (3.8%) occurred among persons aged 13-18 years. This is expected and is in agreement with findings by Mohammed in Libya who used similar age categories (Mohammed et al., 2016). Varying age categories among studies, however, makes it difficult for comparison across studies. Most of UTI cases (42.3%) occurring between 19-45 year groups could be explained by the fact that majority of them are females in their reproductive years where pregnancy and frequent sexual activity are predisposing factors to UTI.

Surprisingly, children below 5 years accounted for about 20% of the overall confirmed cases of UTI over the period studied. Among paediatric patients, some urological structural abnormalities may explain the high UTI prevalence (Eisenberg, 2018). Clinically, it is important to investigate this occurrence at the Regional Hospital to inform therapeutic interventions.

5.2 Distribution of Uropathogens

This study identifies *Escherichia coli*, *Klebsiella* spp, and *Citrobacter* spp to be the most dominant bacteria isolates causing UTIs with increasing trends over the years. These uropathogens are common to several studies though their frequencies differ across studies. The prevalence of *Escherichia coli* and *Klebsiella* spp as the leading cause of UTI among patients examined is not surprising as this is supported by several other studies in Ghana, Africa and globally (Khameneh & Afshar, 2009; Moroh et al., 2014; Odoki et al., 2019; Opintan et al., 2015; Prah et al., 2019; Rodrigues et al., 2016). However, the emergence of *Citrobacter* spp as

one of the leading causes of UTI among the study subjects is worth looking into as this is not previously known in published surveillance data. For example, the Standard Treatment Guidelines of Ghana does not list *Citrobacter* spp as a major uropathogen (Standard Treatment Guidelines, 2017).

Klebsiella spp was found to be the most dominant uropathogen in children less than 5 years and *Escherichia coli* dominating among adults respectively. Differences in gut microbiota may account for this variation of uropathogens among children and adults.

5.3 Antimicrobial Resistance Pattern and associated factors

There is generally high antimicrobial resistance pattern among uropathogens identified. Ampicillin, Co-trimoxazole and Tetracycline being the oldest antibiotics were identified as the three most resistant antibiotics with cumulative percentage resistance ranging between 88% and 91%, Amikacin, Nitrofurantoin and Ciprofloxacin were found to be the three least resistant antibiotics to uropathogens identified in the study with their percentage resistances as Amikacin (8.7%), Nitrofurantoin (35.9%) and Ciprofloxacin (37.5%). These results are consistent with laboratory based surveillance on AMR conducted in Ghana (Opintan et al., 2015). These findings also reflects that found in Libya where Amikacin to be the least resistant to uropathogens and Ampicillin to be the most resistant (Mohammed et al., 2016). In Ethiopia, Kibret and colleagues (Kibret, 2014) found uropathogens to be susceptible to nitrofurantoin as detected in this study. However, their evidence that Gentamicin demonstrates low resistance to uropathogens contrasts findings in this study where resistance to gentamicin is 66.7%.

It is expected that the oldest antibiotics (Ampicillin, Co-trimoxazole, Tetracycline) will show the high levels of resistance as they have been used for longer periods allowing resistance to develop overtime. Though Nitrofurantoin is an old antibiotic, its limited use due to potential damage to kidneys of patients has contributed to the low resistance shown. Amikacin is

available only injectable form. This may account for its low usage hence the least resistance as patients do not easily resort to injections as a form of treatment. Ciprofloxacin is the recommended drug for first-line treatment of UTI in Ghana and is available in oral formulation hence the increased use in recent times. It is possible that significant resistance to Ciprofloxacin may be seen over time if necessary measures are not put in place to ensure rational use.

The study finds no significant association between antimicrobial resistance and the sex of a patient. This observation is in contrast to findings by other authors who identify male sex to be associated with increased resistance to antibiotics among uropathogens (Bailey, 2013; Sahm, 2001; Soucy et al., 2019). This may be explained by the low prevalence of UTI among men found in this study hence the low usage of antibiotics that contributed to negligible antibiotic resistance.

Most of the uropathogens identified in the study showed significantly increased resistance to Co-trimoxazole and Tetracycline. Interestingly, only *Enterococcus* spp is significantly associated with increased Amikacin resistance and this is worth investigating.

The study identifies increasing age to be positively associated with ciprofloxacin resistance. This finding upholds previous research (Adam et al., 2013; Fasugba et al., 2016; Sahm et al., 2001). This finding is not surprising because in Ghana, oral ciprofloxacin is recommended as the first line treatment for uncomplicated UTI and intravenous (IV) ciprofloxacin is indicated as the first line treatment for complicated UTI (Standard Treatment Guidelines, 2017). As identified in this study, adults represent the majority of persons with UTI hence the likelihood of overuse and abuse of ciprofloxacin and consequently the development of resistance.

In-patients were identified as a positive predictor of resistance for ciprofloxacin. The overuse of intravenous ciprofloxacin to treat complicated forms of UTI in healthcare settings may contribute to its positive association with ciprofloxacin resistance.

These findings are necessary to inform the rational antibiotic use to reduce progression to therapeutic dead ends where no antibiotic may be available to treat infections.

5.5 Limitations

1. The occurrence of some amount of missing data as a result of poor documentation may have been a limitation to the study.
2. The absence of other demographic variables such as educational level, employment details, residence and ethnic background in the archived laboratory data limited the ability of the researcher to examine factors contributing to increased prevalence in UTI over the years in the study.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATION

6.1 CONCLUSION

This study showed that about 20% of persons who reported to the Bacteriology Unit of the Eastern Regional Hospital were confirmed of Urinary Tract Infection over the five year period with increasing trends. A generally high proportion of these UTI cases were children and females. This finding is important in planning and targeting UTI preventive and control measures in the Eastern Region and beyond.

This study identifies *Escherichia coli*, *Klebsiella* spp and *Citrobacter* spp as the main causative organisms of UTI among the study subjects with increasing trends over the years. The pattern of resistance show a generally high resistance of uropathogens to the antibiotics used in the study. Ampicillin, Co-trimoxazole and Tetracycline were the three most resistant antibiotics. Amikacin, Ciprofloxacin and Nitrofurantoin were found to have adequate sensitivity to uropathogens isolated. This study therefore supports the use of Ciprofloxacin, Nitrofurantoin and Amikacin for the treatment UTIs at the hospital.

Increasing age and In-patient or hospitalizations were observed to positively influence antibiotic resistance especially with respect to ciprofloxacin in the study.

These findings are significant in updating information on the choice of antibiotic for empirical therapy in managing Urinary Tract Infections and also serve as surveillance information for AMR control at the Eastern Regional Hospital and in the country.

6.2 RECOMMENDATIONS

To the Eastern Regional Hospital

1. The hospital Public Health Unit should examine the rising trend of Urinary Tract Infections at the hospital in order to develop and implement strategies for prevention and control in the New Juabeng municipality and beyond.
2. The hospital should routinely audit the use of antibiotics especially ciprofloxacin among In-patients and the adult patients to minimize the development of resistance.

To the Ghana Health Service

1. To educate the general public on antimicrobial resistance and the rational use of antibiotics through its Health Promotion Unit.
2. Support health facilities in the country to conduct antimicrobial stewardship programmes through training and supportive supervision.

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APPENDIX II: ETHICAL CLEARANCE

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

In case of reply the number and date of this Letter should be quoted.



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9th July, 2019

MyRef: GHS/RDD/ERC/Admin/App/19/288
Your Ref. No.

Fred Gbadago
University of Ghana
School of Public Health
Legon

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

GHS-ERC Number	GHS-ERC 036/05/19
Project Title	A Five-Year Retrospective Study of Antimicrobial Sensitivity Pattern of Patients Diagnosed with Urinary Tract Infection at the Eastern Regional Hospital, Koforidua
Approval Date	9 th July, 2019
Expiry Date	8 th July, 2020
GHS-ERC Decision	Approved

This approval requires the following from the Principal Investigator

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report after completion of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.
- Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....
Dr. Cynthia Bannerman
(GHS-ERC CHAIRPERSON)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra

