UNIVERSITY FOR DEVELOPMENT STUDIES

PREVALENCE OF URINARY TRACT INFECTIONS AND ANTIBIOTIC RESISTANCE OF UROPATHOGENS ISOLATED FROM PATIENTS IN THE TAMALE TEACHING AND CENTRAL HOSPITALS

BY

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DECLARATION

I, DAVID YEMBILLA YAMIK, declare that this thesis is the result of my own original work, with the exception of references to other people's works which have been duly acknowledged, no part of it has been presented for another degree in this University or elsewhere.

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ABSTRACT

Urinary Tract Infection (UTI) is an infection in any part of your urinary system, caused by the presence of bacteria in the urinary tract (UT). Data on the prevalence of urinary tract infections and multidrug resistance of uropathogens are limited in the Northern Region of Ghana. The aim of this research was to determine prevalence of UTI among patients and the resistance patterns of uropathogens isolated from patients in a secondary and tertiary health care hospital in the Northern Region of Ghana. A total of 736 clean catch midstream urine samples were collected from patients of all age groups attending the Tamale teaching hospital and the Tamale central hospital in a period of six months, April, 2018 to September, 2018 and uropathogen isolated in the Spanish laboratory complex of the University for Development Studies, Nyankpala by quantitative urine culture on Cysteine Lactose Electrolyte Deficient (CLED) medium. Bacteria isolates were identified by their morphology and standard biochemical tests. By the Kirby-Bauer disk diffusion method, antibiotic susceptibility test was also done on the uropathogens using fourteen (14) antibiotics. Statistical Package for Social Sciences (SPSS) version 20 was used to analyse the data. Urinary tract infection (UTI) at both the Tamale teaching hospital and the Tamale central hospital was 36.0% and 21.4%, respectively. There was significantly higher ($P \leq 0.05$) urinary tract infection (UTI) among females (80.5%) than males (19.5%). Coagulase negative *Staphylococcus* (CoNS), *S. aureus*, *E. coli*, *Serratia* spp. *Klebsiella* spp and *Enterobacter* spp. were the common organisms isolated. The highest UTI was recorded among the age group of 20-29 years at the Tamale teaching hospital (35.0%) and the Tamale central hospital (54.5%), with the overall mean age of 34.28±1.29. Sterile pyuria (SP) in this research was 67.9% and more predominant in

females (94.2%) than males (5.8%), with the mean age of the patients associated with sterile pyuria being 27.8±1.68. Asymptomatic bacteriuria (ASB) recorded at both the Tamale teaching hospital and the Tamale central hospital was 40.1% and 20.8%, respectively. Asymptomatic bacteriuria was significantly high (P≤ 0.05) among the age group 20-29 years with the overall mean age of 32.48±1.29. The highest multidrug resistance was observed with *S. aureus* (100.0%), *E. coli* (100.0%), *Enterobacter* spp *(*100.0%) and *Klebsiella* spp (100.0%). Uropathogens showed significantly high (P≤ 0.05) resistance to almost all the antibiotics tested. Therefore, there should be public education on consequences of misuse of antibiotics. Asymptomatic bacteria and sterile pyuria are conditions which must not be overlooked in the management of UTI infections in these hospitals owing to the high rates recorded among patients in this study.

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DEDICATION

This work is dedicated to God Almighty who made all things possible.

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CHAPTER ONE

INTRODUCTION

The urinary tract (UT) is the organ that collects and stores urine and releases it from the system (body). It is made up of many parts including the kidneys, ureters, bladder, urethra and other structures (Omonigho *et al*., 2001). Usually, diseases occur as a result of infections cause by pathogenic microorganisms, externally or internally of the body. Urinary Tract Infection (UTI) is a type of infection, involving the existence of microorganisms in the UT which is believed to be germ-free (Al-Badr & Al-Shaikh, 2013). This normally happens when bacteria move into and colonize the peri-urethral area. Patients with healthy UT are always affected as results of the movement of bacteria (uropathogens) to the bladder from the urethra and occasionally progress to the kidney.

Urinary tract infection is divided into two; that is, Symptomatic UTI which has visible symptoms of UTI and the asymptomatic UTI popularly known as asymptomatic bacteriuria (ASB) which has no symptoms of UTI.

Mostly the organisms that cause urinary tract infections are Gram negative bacteria such as *Escherichia coli*, *Proteus* species, *Klebsiella* species, *Enterobacter* species, *Citrobacter* species *Serratia* species and *Pseudomonas* species (Agyepong *et al*., 2018; Asafo-Adjei *et al*., 2018). *Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis*, *Citrobacter intermedius* and *Staphylococcus saprophyticus* are also frequently isolated (Chon *et al*., 2001; Ogbukagu *et al*., 2016).

Urinary tract infection is among the commonest infections ravaging the world population (Chang & Shortliffe, 2006; Kucheria *et al*., 2005) accounting for an estimated 23% of all

hospital acquired infections (Emmerson *et al*., 1996). It affects different categories of people including different age groups, male and female, and pregnant women (Chang & Shortliffe, 2006; Obiogbolu *et al*., 2009). Except in children where males predominate, urinary tract infection is common in females globally and mostly in young girls (Foxman, 2002). According to Al-Badr & Al-Shaikh (2013), about 50%–60% of women develop UTI during their life cycle, which accelerates at adolescence and remains high throughout their adult lives (Hantoosh *et al*., 2016).

Urinary tract infections are always treated with antibiotics or antimicrobials that act against the bacteria. But as a result of selective pressure due to the abuse of some of these antibiotics, the antibiotics select strains that are resistant to the antibiotics causing the resistant strains to multiply and spread over time thereby increasing the prevalence of multidrug resistant (MDR) organisms in urinary tract infections (Agyepong *et al*., 2018; Baral *et al*., 2012; Calbo *et al*., 2006). This resistance to one or more antibiotic agents in more than two antimicrobial classes is termed multidrug resistance.

Globally, knowledge of clinicians has shown the increasing incidence of antibiotic resistance to common antibiotics by uropathogens (Sweileh *et al*., 2018). Therapeutic options of urinary tract infection are few due to resistance to newer and more potent antimicrobials (Abbo & Hooton, 2014) thereby causing a great challenge in health care institutions.

1.1 Problem Statement

In many parts of the world, UTI is among the common bacterial infections that cause morbidity and mortality. Globally, about 150 million people are affected annually leading to a world income loss of about 6 billion US dollars through medication (Abbo & Hooton, 2014).

The issue is more prevailing in the less developed countries like Africa, accounting for not less than 250 million people affected annually (Getenet & Wondewosen, 2011). Urinary tract infection is high in Kumasi and Accra both in the Southern sector of the country (Agyepong *et al*., 2018; Gyansa-Lutterodt *et al*., 2014).

The emerging public health problem is antibiotic resistance among pathogens (Sharma *et al*., 2013). Globally, multidrug resistance is the major cause of debility and death. According to World Health Organization (WHO) (2018), it poses great threat to the prevention and treatment of bacterial infections.

Studies have shown that antibiotic resistant bacterial infections are high in developing countries (Bernabé *et al*., 2017) which may account for an increase in morbidity and mortality due to higher burden of bacterial infection, late presentation, limited access to diagnostics, unavailability of second line antibiotics, the inability to diagnose and the public sector relying solely on first line treatment (WHO, 2018).

There is a global concern of increasing resistance of uropathogens to antibiotics. While common blood stream pathogens only show low to moderate resistance to antibiotics, uropathogens show moderate to high rate of resistance to antibiotics that are commonly used including evidence of the emergence of cephalosporin resistance in West Africa

(Bernabé *et al.*, 2017). A research done in Equatorial Guinea shows that there are greater number of strains that are multidrug resistant (MDR) and extensively drug resistant (XDR) to the commonly used antibiotics (Shatalov, 2015). Akintobi *et al*. (2013) found that uropathogens are resistant to an extensive number of antibiotics in Nigeria.

Ghana is among the countries leading in antibiotic resistance of uropathogens in West Africa (Bernabé *et al*., 2017). A study conducted in Accra shows that uropathogens are resistance to a considerable number of antibiotics (Gyansa-Lutterodt *et al*., 2014).

A research conducted in Ghana revealed that multidrug resistance is high, with uropathogens dominating, therefore, calling for urgent attention (Opintan *et al*., 2015). There is also high multidrug resistance with bacterial isolates including uropathogens in Kumasi, the Southern sector of Ghana (Agyepong *et al*., 2018). Researches have also proven that multidrug resistance is high in Accra, also in the Southern sector of the country (Asafo-Adjei *et al*., 2018; Donkor *et al*., 2019). Research in the Northern region of Ghana has also shown that there is some level of multidrug resistance of uropathogens in malnourished children in the Tamale Teaching Hospital (Darkom, 2014).

1.2 Justification

Urinary Tract Infection may lead to many deaths since infections are gradually becoming more and more problematic to treat as a result of antibiotic resistance. Uropathogenic bacterial strains that are multidrug resistant are now high, with the emergence of new strains that are extensively drug resistant (XDR) to the available antibiotics (Shatalov, 2015). There is evidence of multidrug resistant uropathogens in Ghana (Opintan *et al*., 2015).

Research conducted by Gyansa-Lutterodt *et al*. (2014) in Accra shows that uropathogens are resistant to an extensive number of antibiotics. This is important for the re-directions of first and second line treatments for UTI in the future.

Effective antibiotic therapies may decrease treatment failure. Costs of treatment of UTI may be guided by knowledge of the prevalence and resistance characteristics of the uropathogens. According to Gyansa-Lutterodt *et al*. (2014), the changing pattern of urinary tract pathogens to antibiotics has been reported worldwide and knowledge of antibiotic susceptibility of the pathogens is necessary for proper medication. However, there is limited data describing multidrug resistance among uropathogens in Ghana. The few data available mostly depict the situation in the Southern sector of the country. This research therefore, sought to investigate the resistance patterns and multidrug resistance among uropathogens isolated from patients in a secondary and tertiary health care hospital in the Northern Region of Ghana.

1.3 Main Objective

- To investigate the occurrence of urinary tract infections and multiple drug resistant uropathogens among patients attending two major health care hospitals in Northern Region of Ghana.

1.4 Specific Objectives

- To determine the prevalence of urinary tract infections among patients in secondary and tertiary care hospitals.
- To assess the incidence of sterile pyuria among patients.
- To evaluate asymptomatic bacteriuria among patients.

- To identify multidrug resistant uropathogens among patient isolates.

1.5 Limitations of the Study

This study had some limitations including, detailed information such as gestational ages of pregnancy, and sexual activities which are considered a risk factor for developing UTI in patients could not be captured. This was because most patients in the study area did not feel comfortable giving out such information. Any attempt to persuade them normally led to their withdrawal from the study. But these limitations did not affect the purpose of the study which was to establish the prevalence of urinary tract infection, asymptomatic bacteriuria, multidrug resistance among uropathogens and sterile pyuria among patients in secondary and tertiary care hospitals.

Coagulase Negative *Staphylococcus* (CoNS) could not be speciated into *Staphylococcus sarprophyticus* and *Staphylococcus epidermidis* due to limited resources. However, this also did not affect the study in any way since CoNS is widely accepted.

One of the limitations was the inability to identify Extended-Spectrum Beta-Lactamase (ESBL) producing organisms from the isolates to help ascertain the isolates carrying the Beta Lactamase genes since this hydrolyses antibiotics like ampicillin rendering them useless and causes treatment failure due to limited resources. But this lapse did not affect the purpose of the study that is to establish multidrug resistance among uropathogens in secondary and tertiary care hospitals.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Urinary Tract Infection (UTI) is the invasion of the urinary tract by pathogens. This is among the common infectious diseases that affect people of all age groups and at different locations. These infections which are normally treated with antibiotics are becoming hard to cure because of antibiotic resistance as a result of selective pressure among uropathogens due to misuse and inappropriate exposure to antibiotics.

The effect is worse in low resource developing countries due to inadequate facilities and capital to manage UTIs caused by antibiotic resistant strains of uropathogens. Reports of increasing resistance of uropathogens to antibiotics have become a global concern (WHO, 2018).

2.2 Etiology of Urinary Tract Infections

Bacterial pathogens are the main cause of many human diseases, externally or internally of the body. UTI involves the existence of microorganisms in the urinary tract (UT) (Al-Badr & Al-Shaikh, 2013).

Mostly, it is caused by Gram negative bacteria such as *Escherichia coli*, *Proteus* species, *Klebsiella* species, *Enterobacter* species, *Serratia* species and *Pseudomonas* species (Agyepong *et al.*, 2018; Chon *et al.*, 2001). *Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, Citrobacter intermedius* and *Staphylococcus saprophyticus* are most at times isolated (Chon *et al.*, 2001; Ogbukagu *et al.*, 2016).

A research done by Agyepong *et al*. (2018) shows that *Proteus mirabilis, Klebsiella pneumoniae, Enterobacter* spp., *Acinetobcter baumannii, E. coli, Yersinia* spp., *Burkholderia cepacia, Pasteurella* spp., *Salmonella enterica, Vibrio* spp., *Pseudomonas aeruginosa, Citrobacter koseri, Chromo bacterium violaceum, Pantoea* spp., *Serratia* spp., *Providencia rettgeri, Cadecea lapagei, Sphingomonas paucimobilis* and *Aeromonas* spp., are mostly obtained from urine analysis.

A prospective study of febrile children by Adjei & Opoku (2004) had a similar trend of results. They indicated that up to about 30% of urine samples had bacterial growth with Gram negative bacilli dominating the other organisms and *Escherichia coli* and *Proteus* spp., accounting for more than 50% of the total bacteria isolates. But, *Escherichia coli* alone can account for about 80% of uropathogens recovered from acute uncomplicated infected patients, followed by *Staphylococcus saprophyticus* which ranges from 10% to 15% (Ronald, 2002) with *Enterobacter* spp., *Klebsiella* spp., *Proteus* spp., and *Enterococci* occasionally causing pyelonephritis and uncomplicated cystitis (Ronald, 2002).

According to Bouza *et al*. (2001), *E. coli, Enterococci, Candida, Klebsiella, Proteus* as well as *P. aeruginosa* are the predominant uropathogens associated with nosocomial UTI in Europe.

Gram positive bacteria such as *Staphylococcus aureus* has also been isolated in Kumasi, Ghana (Adjei & Opoku, 2004). Ojo & Anibijuwon (2010) reported that *E. coli, Proteus* spp., *Klebsiella* spp., *Staphylococcus* spp., *Streptococcus* spp. as well as *Pseudomonas* spp. are the dominant uropathogens obtained from patients in Nigeria.

A study in Nigeria on UTI male patients suffering from sterility indicated that *Staphylococcus aureus* can be the dominant uropathogen (14.0%), followed by *Chlamydia trachomatis* (11.4%), *E. coli* (4.3%), *Mycoplasma genitalium* (4.0%) and *K. aerogenes* (4.0%) (Ibadin *et al*., 2012). Others are *Staphylococcus saprophyticus, P. aeruginosa*, *Proteus mirabilis* with 2.7% each, *P. vulgaris* (2.1%), *Treponema pallidum* (2.1%), *Wulchereria bancrofti* (0.9%) and *Schistosoma haematobium* (0.3%) (Ibadin *et al*., 2012).

Zeyaullah & Kaul (2015) stated that *Enterobacteriaceae* are the predominant pathogens among the causative organisms of UTI in Saudi Arabia, followed by Gram positive *cocci*. However, according to Janyenga *et al*. (2015), 18.9% of the UTI cases are due to *Escherichia coli* making it the most common organism isolated in Windhoek-Namibia, as compared to *Proteus mirabilis*, *Enterococcus faecalis* and *Klebsiella pneumonia*. The prevalence of *Escherichia coli* can be as high as 55.5% as compared to 23.2%, 4.5%, 3.2%, 2.6% and 8.4% for *Klebsiella pneumonia*, *Proteus mirabilis*, *Pseudomonas* species, *Enterobacter* species and *Enterococcus faecalis*, respectively in Equatorial Guinea (Shatalov, 2015).

High (64.9%) prevalence of uropathogenic *E. coli* was also observed in the United States of America (Sanchez *et al*., 2016). A study in Paris, France indicated that the rate of UTI can be as high as 75.2% with *E. coli* representing about 82.8% of all bacterial species (Rossignol *et al*., 2016).

According to Mahato *et al*. (2018), *E. coli* (67.87%), *Klebsiella* (14.01%) and *Pseudomonas* (13.77%) are the predominant uropathogens isolated in Eastern Nepal. It

has also been established by Asafo-Adjei *et al*. (2018) and Donkor *et al*. (2019) that *E. coli* can be 33.3% and 48.4%, respectively higher among uropathogens in Accra, Southern Ghana. Agyepong *et al*. (2018) also proved that isolates of uropathogens like E. coli (34.5%) and *Klebsiella pneumoniae* (24.6%) can dominate among the uropathogens in the Southern sector of the Ghana.

Generally, Gram negative bacteria are more predominant in UTI cases and can serve as a guide during diagnoses and medication of suspected UTI among patients (Agyepong *et al.*, 2018; Asafo-Adjei *et al.*, 2018; Donkor *et al*., 2019). However, Gram positive bacteria can sometimes dominate among uropathogens (Ibadin *et al*., 2012).

2.2.1 Factors Affecting Etiology of Urinary Tract Infection

According to Ronald (2002), factors like spinal cord injury, age, diabetes and catheterization affect the etiology of UTI. Patients with spinal cord injury (SCI) and catheterization develop UTIs with uropathogens that form thick biofilms on the bladder wall making these infections difficult to eradicate.

Ageing is linked to change in immune function, an increasing number of medical conditions and exposure to nosocomial pathogens putting the elderly at an increased risk for developing infection (High *et al*., 2010).

Patients with diabetes have some defects in their immune systems such as impaired neutrophil function, decreased T-cell-mediated immune response, low levels of prostaglandin E, thromboxane B2, leukotriene B4 (Boyko & Lipsky, 1995), incomplete emptying of bladder due to autonomic neuropathy, poor metabolic control (Boyko *et al*., 2005; Fünfstück, Nicolle *et al*. , 2012) as well as higher glucose concentration in the

urine resulting in urinary colonization by pathogenic microorganisms (Boyko *et al*., 2005; Boyko & Lipsky, 1995).

2.2.1.1 Spinal Cord Injury, Diabetes, or Catheterization

Organisms associated with UTI among patients with diabetes include *Klebsiella* spp., Group B *streptococci*, and *Enterococcus* spp., as well as *E. coli*. Higher glucose concentration in urine allows urinary colonization by these uropathogenic microorganisms (Boyko *et al*., 2005; Boyko & Lipsky, 1995).

According to O'gara & Humphreys (2001), patients with chronic indwelling catheters are always associated with coagulase negative *Staphylococci* (CoNS). CoNS adhere to the surface of the catheter through the formation of complex biofilm matrix in which they embed themselves (Mack *et al*., 2007; O'Gara & Humphreys, 2001; Qin *et al*., 2007) making it difficult to eradicated because of their entrenchment in this microbial biofilm matrix (Souli & Giamarellou, 1998). *E. coli*, *Proteus mirabilis* and *Pseudomonas* spp. infections are always associated with patients who have spinal cord injuries (Ronald, 2002).

2.2.1.2 Age of the Person

Many studies have shown that uropathens can be isolated from any age group of individual. According to Zeyaullah & Kaul (2015), *Klebsiella* and *Escherichia coli* infections are associated with the age group of 20-49 years with *Pseudomonas* infections predominant in children and the elderly (less than 20 years and greater than 50 years) in Saudi Arabia. Also, *E. coli* was isolated from the age group of 1 to 20 years in Yemen (Salwa & Maher, 2014). It has also been established that in community-acquired

infection, *Salmonella* Typhi can be found in elderly patients (greater than 60 years) in Saudi Arabia (Alzohairy & Khadri, 2011).

S. aureus was isolated from the age group between 21 and 40 years with *Streptococci*, *P. aeruginosa* isolated between the age of 31 and 40 years and above in Yemen (Salwa & Maher, 2014). The same study indicated that the prevalence of *Klebsiella pneumonia* can decrease as much as 13.3% from age 1 year to 20 years and from there increase to 24.4% at age 30 years with *Candida* spp. mostly isolated from the age group above 40 years. However, *Proteus vulgaris* is normally uncommon in the age group between 1 and 10 years and 21 and 30 years (Salwa & Maher, 2014).

2.3 Factors Contributing to Urinary Tract Infections

Cross infections from partners, socioeconomic conditions like educational status and presence of co-wives and human activities relating to personal hygiene are some of the contributory factors of urinary tract infection (Badran *et al*., 2015). Age, gender, insulin autoantibody, excretion of albumin and blood sugar are also some of the risk factors of UTI (He *et al*., 2018). Increase in glucose concentration can lead to urinary colonization by pathogenic microorganisms (Boyko *et al*., 2005; Boyko & Lipsky, 1995).

Ageing is associated changes in immune function, exposure to nosocomial pathogens and an increasing number of medical conditions that put the elderly at an increased risk for developing infection (High *et al*., 2010). Urinary tract infections (UTIs) affect women than men, though the occurrence in elderly men and women is comparably the same. The main risk factors of UTI in young women are sexual intercourse and the use of spermicidal contraceptives (Harrington & Hooton, 2000). Anatomic and physiologic

factors, such as obstructing lesions and estrogen deficiency are significant UTI risk determinants associated with age (Harrington & Hooton, 2000).

2.3.1 Virulence Factors

Virulence is how the pathogens manage to colonize their host and cause harm to it by parasitic relationship. A review conducted by Kucheria *et al*. (2005) to discuss current ways in understanding how relations between pathogens, like the uropathogenic *Escherichia coli* and the host lead to infection, revealed that some of these bacteria such as *E. coli* have a wide range of virulence factors that stimulate colonisation and infection of the urinary tract.

Contamination of the urinary tract from the rectal area and various enhanced virulence factors specific for colonization and invasion of the urinary epithelium can also cause urinary tract infection (Kabew, Abebe, & Miheret, 2013).The intensity of urinary tract infection is associated with the equilibrium of the virulence of the bacteria and host immunity (Köves & Wullt, 2016).

Possession of fimbriae with adhesive tips, bacterial capsule including lipopolysaccharide (LPS), and production of toxins such as haemolysin and colony necrotizing factors are the virulence factors most commonly associated with these organisms (Kucheria *et al*., 2005). These make them very capable of colonising their host thereby causing infections indicating that infections can be reduced with the reduction of these structures.

2.3.2 Pregnancy

According to Mccormick *et al*. (2008), urinary tract infections during pregnancy are common and are related to most maternal and perinatal illness and death. At pregnancy,

the development of urinary tract infection is associated with motionlessness of urine in the ureters, which restricts urination, with an increased post-void outstanding urine volume, vesicoureteral reflux, and increased urinary pH (Krcmery *et al*., 2001). Pyelonephritis is more common in pregnant women especially during the second trimester of pregnancy (Hill *et al*., 2005) as a result of increasing mechanical compression by the expanding uterus (Minardi *et al*., 2011).

History of diabetes, recurrent urinary tract infection, and abnormal anatomy of the urinary tract increase the risk of developing urinary tract infection during pregnancy (Golan *et al*., 1989).

During pregnancy, the immune system undergoes modifications, favouring embryo growth (Mccormick *et al*., 2008). Researchers suggest that the immune response is modified from a cell-mediated to a humoral response. This mechanism does not solely rely on the recognition of cell-surface major histocompatibility complex (MHC) proteins, resulting in less efficient responses to the bacterial cell surface proteins and possibly enabling pathogenicity. These changes can allow uropathogens to infiltrate, proliferate and ascend proximally and cause problems during pregnancy (Mccormick *et al.*, 2008).

Boye *et al*. (2014) stated that pregnant women (between 15 and 32 years) are mostly affected in Cape Coast. Ashshi *et al*. (2014) discovered that the factors that are associated with UTI among pregnant women can also be as a result of advanced age, multiparity, low educational level, as well as unsatisfactory personal hygiene.

Moreover, diabetic condition, using certain contraceptives and using panties made of silky materials are among the influencing factors. Refat *et al*. (2017) also stated that

factors associated with UTI during pregnancy are previous UTI history, unhealthy urination habits, maternal anemia, an increase in sexual intercourse, child spacing (less than two years), poor hygienic practices, inadequate socioeconomic conditions, suboptimal nutritional habits, and constipation. According to Donkor *et al*. (2019), pregnancy remains the main factor of UTI in Accra.

Urinary tract infection presents a serious health problem to pregnant women which is attributed to many risk factors. UTI in women can be reduced when the above factors are prevented. Particularly, diabetic conditions should be avoided or controlled in order to decrease the risk of UTI in pregnant women.

2.3.3 Alteration of Vaginal Flora

The dominant vaginal flora are *Lactobacilli* (Minardi *et al*., 2011). In the reproductive age, the vagina of women is highly acidic with an approximate pH of 3.8 to 4.2 (Ekanom *et al*., 2012) restricting pathogenic growths by low vaginal pH (Al-Saadi & Al-Windawi, 2003; El-Nahi, 2012). The acidity is believed to be as a result of the breakdown of glycogen by *Lactobacillus* in the vagina walls to lactic acid *(*Ekanom *et al*., 2012).

Access of uropathogens to uroepithelial cells can be restricted by cell wall remains of *Lactobacillus* species (Larsen & Monif, 2012). However, after menopause, vaginal pH is around 2.2 to 3.8 higher (Caillouette *et al*., 1997) since the amount of glycogen liberated from vaginal cells is influenced by fluctuation in estrogen concentration.

Estrogen is almost nonexistent after menopause, thus accounting for the reduced acidity of vaginal fluid at these times (Al-Saadi & Al-Windawi, 2003) thereby altering vaginal flora which may lead to urinary tract infection. Partial treatments and reappearance of

genitourinary tract infection lead to a shift in the local flora from the predominant *lactobacilli* to *coliform* uropathogens facilitating urinary tract infections by these microorganisms (Minardi *et al*., 2011).

These factors may account for why most literature report urinary tract infections among old women.

2.3.4 Sex of the Person

Most of the uropathogens are recorded from females. However, prevalence of uropathogens also occur in men with the exception of *Candida albicans* infection in their urinary tract which may be as a result of men not being its natural host. Unlike men, the condition most women experience much later in life is vaginal atrophy (Freedman, 2008). It is defined as permanent involution of the mucous membranes and tissues of the vagina following the drop in estrogen level that commonly occurs in women during menopause (Freedman, 2008). The Proliferation of *Lactobacillus* in the vaginal epithelium stimulated by estrogen causes the vagina pH to reduce, thereby restricting colonisation of *Enterobacteriaceae* in the vagina (Minardi *et al*., 2011).

However, at menopause, the vagina pH is always higher than those observed during the fertility period (Freedman, 2008) as a result of low estrogen levels (Miller, 2005; El-Nahi, 2012). This leads to alkalization of the vagina causing colonisation by enteric microorganisms and thereby facilitating urinary tract infections (Miller, 2005; El-Nahi, 2012).

In addition to the nonexistence of estrogens, decrease in size of vaginal muscles in older women resulting in collapse of the ligaments holding the uterus, pelvic floor, and bladder,

results in prolapse of the internal genitalia increasing the risk for urinary tract infections (Minardi *et al*., 2011). In older women, the deterioration in the functional status of vaginal tissues is the main factor for the development of recurrent urinary tract infections (Nicolle, 1997).

Unlike men who have a longer urethra, the shorter urethra of women and the nearness of the urethra to the anus and vaginal introitus sometimes lead to the incidence of symptomatic infection (Hooton *et al*., 1999; Levinson, 2010; Minardi *et al*., 2011).

These show that in general, females are more prone to UTI and if there are plans to eradicate it, more women should be targeted.

2.3.5 Sexual Activity

One of the risk factors of urinary tract infections is sexual activity (Mccormick *et al*., 2008). About 75% to 90% of bladder infections in young sexually active women are caused by sexual activity (Nicolle, 2008), with the risk of infection associated with frequent sexual intercourse. Intercourse can injure the uroepithelium of the distal urethra (Mccormick *et al*., 2008) resulting in increased bacterial colonisation. According to Lema (2015), multiple sex partners is one of the risk factors associated with UTI in young women.

The occurrence of symptomatic urinary tract infection is associated with sexual intercourse, diaphragm spermicide and recent relationship (Scholes *et al*., 2000). Also, the use of condom has been linked to an increased risk of urinary tract infection, but this effect may be due to trauma (Scholes *et al*., 2000). Uropathogenic *E. coli* is more likely to be transmitted between sex partners during sexual activity (Foxman *et al*., 2002).

Reinfection by *coliform* bacteria from the vaginal reservoir can occur following sexual activity.

According to Michael & Adenike (2016), Coagulase negative *Staphylococcus* are always normal flora of the urogenital area at puberty, which may invade the urinary tract during sexual activity particularly in females.

2.4 Risk Levels of Urinary Tract Infections

There are different levels of risks associated with UTI among different conditions in different category of people (Table 2.1).

Table 2. 1: Risk Levels of Urinary Tract Infections

Category of people	Risk Factors	Risk level
Men	Older men who experience prostatitis (inflammation of the prostate) are in a higher risk group. Chronic conditions, some medications, problems with incontinence people using bladder catheters. Men can get UTIs, particularly if they have trouble with urine flow. A small number of young men may get a UTI usually as a result of a sexually transmitted disease.	High
Babies and children	Malnourishment	Moderate
Women	The short and straight urethra, changes in their hormonal levels, some are more likely to get an infection during certain times in their menstrual cycle, such as just before a period. During pregnancy, the drainage system from the kidney to the bladder widens so urine does not drain as quickly. In older women, the tissues of the urethra and bladder become thinner and drier with age as well as after menopause or a hysterectomy, use of spermicide jelly or diaphragm for contraception, have had a new sexual partner in the last year (an increase in sexual activity may trigger symptoms of a UTI in some women), had their first UTI at or before 15 years of age, have a family history of repeated UTIs,	Highest
Diabetic patient	People with diabetes have the highest risk of contracting UTIs due to high glucose (sugar) content in their urine, which provides an ideal breeding ground for bacteria as well as the diabetes also changing the body's defence system making it harder to fight a UTI. As the duration and severity of diabetes increases, susceptibility to UTIs increases.	Increased

Sources: (Darkom (2014) and KidneyHealth (2015)

2.5 Prevalence of UTIs

According to Alanazi (2018), urinary tract infection (UTI) is a grave health problem affecting millions of people yearly. Urinary tract infection affects different classes of people such as different age groups, male and female and pregnant women (Chang & Shortliffe, 2006; Obiogbolu *et al*., 2009) causing a great health threat in the world particularly in the developing countries. According to Bahadi *et al*. (2010) urinary tract infection (UTI) is a common problem of pregnancy.

2.5.1 Influence of Sex on Prevalence of Urinary Tract Infection

Urinary tract infection is not the same in different sexes and will always differ from each other as reported by many researchers. According to Al-Haddad (2005), 30% of women suffer from UTI in Yemen. Iregbu *et al*. (2013) indicated that urinary tract infection in females is 2% higher as compared to males in Nigeria. The same trend of results was found by Ogbukagu *et al*. (2016) in the same country which shows that females can be 4% more infected than males with the prevalence percentages of 52% (females) and 48% (males).

A total of 140 midstream urine samples analysed by Salwa & Maher (2014) to investigate the prevalence of UTI among males and females indicated that UTI can be as high as 74.3%, with the prevalence in females 32.8% higher than males in Saudi Arabia. However, isolates recovered from male patients can be 1% higher than isolates from female patients and can be as high as 50.5% and 49.5% respectively in Kumasi, the Southern part of Ghana (Agyepong *et al*., 2018). Also with the rate of UTI (11.3%) observed in Eastern Nepal, female show higher prevalence (70.53%) than male (29.47%)

(Mahato *et al*., 2018). However, Otajevwo (2013) found a higher prevalence of UTI in male outpatients (58.3%) than in the female outpatients (41.7%) in Midwestern Nigeria.

Most pregnant women (70%) may develop glycosuria and this, in combination with physiological amino acid urea at pregnancy and a low urine osmolality favour bacterial growth (Mccormick *et al.*, 2008). However, approximately 5% of non-pregnant women can be affected compared with pregnant women (Akintobi *et al*., 2013). Urinary tract infections recur in 4 to 5% of pregnancies (Mccormick *et al*., 2008).

Except in children where males predominate, urinary tract infection is more common in females globally (Foxman, 2002). According to Jenson & Baltimore (2006), nearly 5% of girls and 1% of boys have a UTI by 11 years of age. Prevalence of UTI in female can be as high as 65% in Nigeria (Ojo & Anibijuwon, 2010).

According to Al-Badr & Al-Shaikh (2013), about 50–60% of women develop UTI in life (Hantoosh *et al*., 2016). Research done in the Northern region of Ghana showed that 71.4 % of urinary tract infected group are males and 28.8% are females (Darkom, 2014).

2.5.2 Prevalence of Urinary Tract Infection in Different Age Groups of People

A study done in Northern America revealed that urinary tract infections affect 2.4% to 2.8% of children every year (Chang & Shortliffe, 2006). Iregbu *et al*. (2013) noted that the highest percentage of urinary tract infections are found in the age group below one year (46%) and above 57 years (32%) in Nigeria, with 2.6% higher among adults as compared to children. Also, the prevalence of UTI in children was reported as 17.6% in Beira, Mozambique (Meeren *et al*., 2013). Research done in the Northern region of

Ghana indicated that 49 (27.2%) out of 180 children has urinary tract infections (Darkom, 2014).

However, similar research by Ogbukagu *et al*. (2016) in Nigeria showed that in both sexes, the highest incidence of UTI can be found among the age group of 26 to 38 years which disputes most researches that the aged and children are the most susceptible.

According to Agyepong *et al*. (2018), the highest prevalence of UTI is from age group of ≥60 years (24.5%) followed by < 10 years (24.0%) and the least can be observed within the age group of 10–19 years (9.5%) with a mean patient age of 35.95 ± 27.11 years in the Southern part of the country which in a way confirms the findings of Iregbu *et al*. (2013 and Meeren *et al*. (2013).

2.5.3 Global Prevalence of Urinary Tract Infections

A study done in Northern America revealed that urinary tract infections affect 2.4% to 2.8% of children every year (Chang & Shortliffe, 2006). In the United State of America, the incidence of urinary tract infection has been increased by 52% between 1998 and 2011 (Simmering *et al*., 2017). According to August & Rosa (2012), a prevalence of 21.15% in women in Panamanian

Urinary tract infection (UTI) is one of the frequent clinical bacterial infections, accounting for nearly 25% of all infections in Saudi Arabia (Al-Badr & Al-Shaikh, 2013). A study done in Yemen showed that out of 140 urine samples collected for analysis, 104 (74.3%) had UTI (Salwa & Maher, 2014).

According to a global report, the prevalence rate of urinary tract infections ranges from 6% to 37% in children alone in less developed countries (Uwaezuoke, 2016), an alarming

situation. According to He *et al*. (2018), the prevalence of UTI is 11.2% in China. In the United Kingdom, A prevalence of 21% was recorded among adults over a period of ten years (Ahmed *et al*., 2018).

2.5.4 Prevalence of Urinary Tract Infection in Africa

Urinary tract infection is predominant in the less developed countries like Africa, accounting for not less than 250 million people affected annually (Getenet & Wondewosen, 2011). A study done in Nigeria indicated that out of 6763 urine samples, 885 (13.1%) were positive for uropathogens (Iregbu *et al*., 2013), which is 6.9% lower than what was found by Al-Badr & Al-Shaikh (2013) in Saudi Arabia. A prevalence of 25% was also reported in Abidjan in Ivory Coast (Moroh et al., 2014)

A study done in Ethiopia showed that the overall prevalence of UTIs in both symptomatic and asymptomatic patients is 15.8% (Getu, 2015). A study also done in Nigeria indicated that out of 3000 urine samples examined, 528 (17.6%) uropathogens were isolated (Ogbukagu *et al*., 2016) indicating a marginal increase (2.1%) in Nigeria from 2013 to 2016. The prevalence of urinary tract infections ranges from 6% to 37% in children alone in the less developed countries (Uwaezuoke, 2016).

A study in Ethiopia revealed 90.1% prevalence of urinary tract infection (Seifu & Gebissa, 2018). Urinary tract infection is ranked third among Human Acquired Infections (HAIs) in Ghana, recording a prevalence of 2.2% higher than respiratory tract infections (Labi *et al*., 2019) with the secondary and tertiary health institutions predominating in terms of prevalence (Labi *et al*., 2019). A study done at the Komfo Anokye Teaching Hospital in the Ashanti region of Ghana found 34.5% prevalence of UTI caused by Gram negative bacteria (Agyepong *et al*., 2018). According to Labi *et al*.

(2019), the prevalence of urinary tract infection in Southern and the Northern part of Ghana is 18.5%.

Urinary tract infection is a common problem among university students in Northern Ethiopia with a prevalence of 21.1% (Gebremariam *et al*., 2019) Also, the rate of UTI is estimated to be 10.1%-76.6% in Accra, Ghana (Asafo-Adjei *et al*., 2018; Donkor *et al*., 2019).

2.6 Sterile Pyuria

Sterile pyuria is the occurrence of leucocytes in the urine without any symptoms of urinary tract infection. It is comparatively, a common problem with different causes met often in all health care facilities, though there is limited information to suggest the estimated prevalence in hospitals (Rees & Manley, 2015).

2.6.1 Causes of Sterile Pyuria.

The causes of sterile pyuria are urinary tract infection, bladder cancer, genito-urinary tuberculosis, sexually transmitted infection (especially chlamydia), interstitial cystitis, *schistosomiasis*, post-menopausal atrophic vaginitis / trigonitis, renal disease sarcoidosis, balanitis, lupus, kawasaki disease, prostatitis, ketamine abuse, cyanotic congenital heart disease, appendicitis or diverticulitis, renal calculi and non-urological infections (pneumonia) (Rees & Manley, 2015).

2.6.2 Prevalence of Sterile Pyuria

A study in India found 28.8% prevalence of sterile pyuria among females (Awasthi *et al*., 2012). Out of the 74% cases with pyuria, sterile pyuria was 28.1% with negative urine cultures in the United State of America (Shipman, *et al*., 2018).

Sterile pyuria is common among women than men because of pelvic infection a factor, which is more associated with women (Hooker *te al*., 2014). According to Alwall & Lohi (1973), Sterile pyuria is a common condition, and population based studies show that 13.9% of women and 2.6% of men are affected. However, Sterile pyuria can be present in up to 46% of males with genitourinary tuberculosis (GU-TB) (Garcia *et al*., 2010).

The rate of sterile pyuria in acute appendicitis and sterile pyuria in acute diverticulitis can be estimated at 87.5%, and 72.7%, respectively (Chan *et al*., 2014).

Specific populations have a higher risk of this condition; for example, the frequency of detection of sterile pyuria was 23% among inpatients in one study (excluding those with urinary tract infection) (Hooker *et al*., 2014). There is a higher prevalence in immunosuppressed patient such as in human immunodeficiency virus (HIV) infection or organ transplant recipients (Newby *et al*., 2014).

2. 7 Asymptomatic Bacteriuria

Patients with positive urine cultures who lack symptoms of a urinary tract infection are termed asymptomatic bacteriuria which is more common in some patient populations. The prevalence increases with age (Hines *et al*., 2014) as well as sexual activity in young women, patients with impaired urinary voiding or indwelling urinary devices. Socioeconomic conditions and sexual behavior are some of the factors that cause asymptomatic bacteriuria (Mittal & Wing, 2005).

2.7.1 Prevalence of Asymptomatic Urinary Tract Infections

Asymptomatic urinary tract infections can be as high as 15% in males and 10.7% in females, which is lesser than symptomatic urinary tract infection in terms of prevalence (Salwa & Maher, 2014).

The prevalence of asymptomatic bacteriuria is reported to be 5-8% in the Southern sector of Ghana (Labi *et al*., 2015; Turpin *et al*., 2007) which is lower than the prevalence of asymptomatic bacteriuria reported in Cape Coast (56.5%) also in the Southern sector of Ghana (Boye *et al*., 2014). Also, about 8.47% prevalence of asymptomatic bacteriuria was reported in India (Awasthi *et al*., 2012). Below is a table showing a summary of the prevalence of asymptomatic bacteriuria among various patient populations (Table 2.2).

Table 2. 2: Prevalence Pattern of Asymptomatic Bacteriuria

Population	**Prevalence, %**	**Average %**
Healthy, premenopausal women	1.0-5.0	3.0
Pregnant women	1.9-9.5	5.7
Postmenopausal women aged 50-70	2.8-8.6	5.7
Diabetic patients		
Women	9.0-27	18
Men	0.7-11	9
An elderly person in the community (≥70 yrs.)		
Women	10.8-16	13.4
Men	3.6-19	11.3
An elderly person in a long-term care facility		
Women	25-50	37.5
Men	15-40	27.5
Patients with spinal cord injuries Intermittent catheter use	23-89	56
Sphincterotomy and condom catheter in place	57	57
Patients undergoing hemodialysis	28	28
Patients with indwelling catheter use		
Short-term	9-23	16
Long-term	100	100

Source: Hines *et al*. (2014)

2.8 Antibiotic Resistance in UTI

Urinary tract infections are treated with antibiotics or antimicrobials, which act against the bacteria. Examples include; Amikacin, Ampicillin, Ampicillin/sulbactam, Cefepime, Cefuroxime, (parenteral), Ceftriaxone, Cephalothin, Ciprofloxacin, Levofloxacin, Ertapenem, Gentamicin, Imipenem, Meropenem, Nitrofurantoin, Piperacillin/tazobactam, Tobramycin Ampicillin, Oxacillin, TMP/SMX (Bactrim), Daptomycin, Linezolid and Vancomycin.

The emerging public health problem is antibiotic resistance among pathogens (Sharma *et al*., 2013). Selective pressure, due to the abuse of some of these antibiotics allows the antimicrobials to select strains that are resistant to the antimicrobials causing the resistant strains to multiply and spread over time thereby increasing multidrug resistant (MDR) organisms in urinary tract infections (Agyepong *et al*., 2018; Baral *et al*., 2012; Calbo *et al*., 2006). Biofilm is the slimy, porous substance produce by microorganism as a mechanism to prevent antibiotics from reaching the organisms thereby forming high resistance to most antibiotics (Minardi *et al*., 2011). Traditionally many of the features of the pathogens connected with UTI are now changing primarily because of antimicrobial resistance (Ronald, 2002). Resistance to one or more antibiotic agents in more than two antimicrobial classes is termed multidrug resistance (Magiorakos *et al*., 2012).

There are many cases of antibiotic resistance to the commonly used antibiotics by uropathogens in both developed and the developing countries (Sweileh *et al*., 2018) limiting therapeutic options to UTI due to the resistant of the uropathogens to newer and more potent antibiotics (Abbo & Hooton, 2014; Howard *et al*., 2003).

There is a global concern of increasing resistance of uropathogens to antimicrobials. Uropathogens demonstrate moderate to high rate of resistance to commonly used antibiotics including evidence of the rise in cephalosporin resistance (Bernabé *et al*., 2017).

There is high rate (40%-72%) of antibiotic resistance of uropathogens in Europe (Bouza *et al.*, 2001). Uropathogenic *E. coli* show resistance to amoxicillin, trimethoprim/sulfamethoxazole, ciprofloxacin, cefotaxime and nitrofurantoin in Paris France (Rossignol *et al.*, 2016). However, uropathogens like *E. coli* have as high as 100 % susceptibility to antibiotics like carbapenems at Anhui Provincial Hospital in China (Ren *et al*., 2016).

A study by Ogbukagu *et al*. (2016) proved that uropathogenic *Staphylococcus aureus* is sensitive to cephalexin, penicillin V, erythromycin and gentamycin while *Pseudomonas aeruginosa* show resistance to all of these antibiotics in Anambra State, Nigeria. While uropathogeic *Escherichia coli* and *Klebsiella* spp. resist all the antibiotics except gentamicin, *Citrobacter intermedius*, is resistant only to cephalexin and erythromycin in primary health centres in Anambra State, Nigeria (Ogbukagu *et al*., 2016).

In most of the Asian Countries, uropathogens show high resistance to broad spectrum antibiotics such as fluoroquinolones (>39%), cephalosporins (>42%) with amikacin and imipenem proving more effective (Choe *et al*., 2017). Resistant level of uropathogens can be as high as 94.4%, 84.5%, 80.0%, 79.0%, 71.3%, 57.5% and 1.5% to ampicillin, trimethoprim and sulfamethoxazole, cefuroxime and Axetil, cefuroxime, cefotaxime, cefoxitin and erytapenem respectively of 89.5% of the bacterial uropathogens in Kumasi,

Southern Ghana (Agyepong *et al*., 2018). However, 100% susceptibility of uropathogens to cefuroxime can be observed, with the sensitivity level of these uropathogens to nitrofurantoin, and amoxicillin clavulanic acid recording more than 65% (Adjei & Opoku, 2004). All the Gram negative bacteria show poor sensitivity to cotrimoxazole and ampicillin in the Southern sector of Ghana (Adjei & Opoku, 2004). Janyenga *et al*. (2015) found that the common uropathogenic organisms are resistant to amoxicillin and cotrimoxazole in Windhoek-Namibia

According to Iregbu *et al*. (2013), about 3% of *Klebsiella* spp., 11% of *E. coli* and 17% of *P. aeruginosa* are resistant to imipenem in Nigeria. Antibiotic resistance is high (>80%) among uropathogen in children in Beira, Mozambique (Meeren *et al.*, 2013).

About 85.7% of *Pseudomonas* are resistant to ampicillin and tetracycline (Darkom, 2014) at the Tamale Teaching Hospital in the Northern region of Ghana. Commonly used antimicrobials such as ampicillin, tetracycline, chloramphenicol, and sulfamethoxazole are now ineffective (>70%) against Gram negative and Gram positive isolates in Ghana (Opintan *et al*., 2015). Studies conducted in Nigeria, Uganda and Tanzania also found similar results (Andabati & Byamugisha, 2010; Dada-Adegbola & Muili, 2010; Moyo *et al*., 2010).

Research has shown that some uropathogens are susceptible to some antibiotics; Akintobi *et al*. (2013) revealed that out of the many antibiotics, amikacin and nitrofurantoin can be most effective than cefuroxine. Gentamicin as well as cefipime, ofloxacin and Piperacillin/tazobactam (piptaz) are also effective antibiotics against bacteria isolated from urine (Boye *et al*., 2014; Janyenga *et al*., 2015). Low level of resistance to

piperacilin/tazobactam, amikacin and imipenem was observed by Shatalov (2015) in Equatorial Guinea.

A study done in the Ashanti region of Ghana reported that uropathogens show high resistance to ampicillin, sulfamethoxazole, cefuroxime and cefotaxime with resistance percentages of 94.4%, 84.5%, 79.0%, and 71.3%, respectively but low resistance to ertapenem, meropenem and amikacin with resistance percentages of 1.5%, 3% and 11%, respectively (Agyepong *et al*., 2018).

2.8.1 Factors Contributing to the Emergence of Antibiotic Resistance

The natural situation in antibiotic resistance is as a result of the microbes being overexposed to antibiotic due to overuse or inappropriate usage of an antibiotic (Prestinaci *et al*., 2016). The older antibiotics (trimethoprim/sulfamethoxazole ampicillin, tetracycline, and chloramphenicol) are cheap and can easily be afforded be people instead of seeking medical attention from health a facility, and their continue usage (wrongly) in both humans and animals contribute to the high resistance levels (Opintan *et al*., 2015).

Plasmid-mediated enzyme is the sole cause of resistance in Gram negative bacteria (Livermore, 2008). A research conducted in Korea also indicates that age, renal abnormalities, previous UTI and current hospitalization can lead to antibiotic resistance among Gram negative isolates that are associated with UTI (Yun *et al*., 2017). The contributory factors for antibiotic resistance can also be attributed to gender, UTI from health facilities, urinary catheter, previous UTI and antibiotic treatment (Gomila *et al*., 2018).

The resistance of uropathogens to commonly available antibiotics may be linked to their recurrent prescription in hospitals, their easy accessibility in the community without prescription and their low cost making them subject to abuse (Agersew & Chandrasekhar, 2013).

These might also be due to irrational and unnecessary use of antibacterial agents. The consequence of this could lead to the emergence of multidrug resistant bacterial strains. In recent studies, most of the isolated pathogens show MDR to two and more antibacterial agents tested (Getachew *et al*., 2012). Below (Figure 2.1) are some sectors that contribute to the development of antibiotic resistance. These sectors are also interconnected.

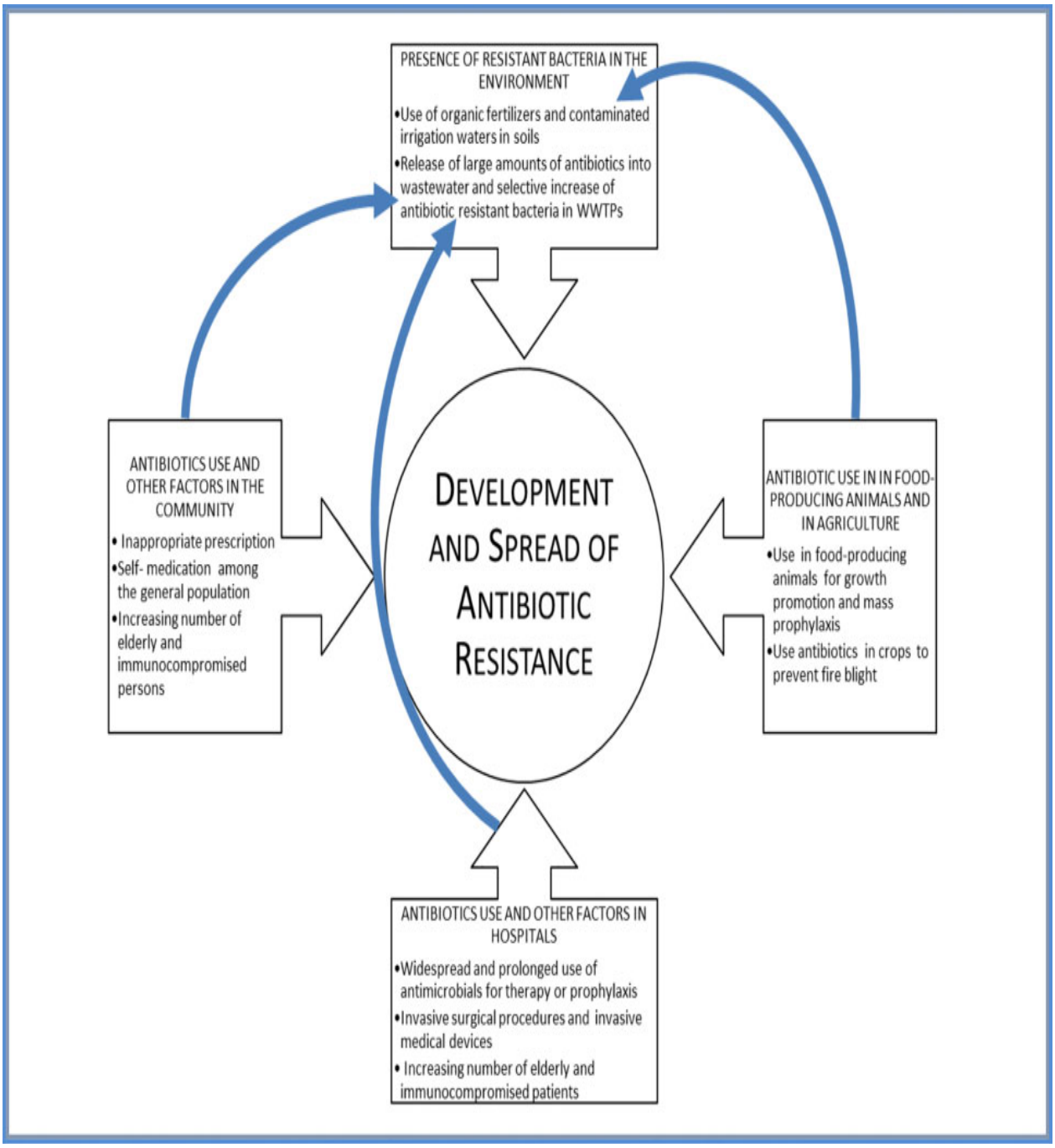

Figure 2. 1: Factors Involved in the Spread of Antibiotic Resistance in Different Sectors

Source: Prestinaci *et al.* (2016)

2.8.1.1 Antibiotics Use in Food and Animal Production and in Agriculture

A large quantity of antibiotic use occurs outside the field of human medicine. Antimicrobial use in aquaculture as growth promotors and for the treatment and prevention of disease is probably a main cause of the general problem of resistance (Marshall & Levy, 2011).

There has been a limitations on the use of antibiotics in plant and agriculture in countries like Europe and in USA owing to the worry that the use of antibiotic in agriculture might increase the frequency of antibiotic resistance genes in bacteria living on plant surfaces and the subsequent transfer of that genes into clinically important bacteria (Stockwell & Duffy, 2012). However, we can not say the same when it comes to Africa and particularly Ghana where there is little regulation on the use of antibiotics

2.8.1.2 The Environment and the Spread of Resistance

Soil is considered a reservoir of antibiotic resistance genes, since most antibiotics are derivative of soil microorganisms that are essentially resistant to the antibiotics produced (Prestinaci *et al*., 2016) . In addition, water contaminated with faecal microorganisms and organic fertilizers used on food crops may disseminate drug resistant bacteria in the soil since it is a major way of bacterial dissemination between different environmental sections (Prestinaci *et al*., 2016).

Some available data show that antibiotic resistant bacteria and antibiotic resistant genes can be detected in wastewater samples because the conditions in wastewater treatment plants are favourable for the proliferation of resistant bacteria. Several studies have reported high concentrations of tetracycline and sulphonamide resistant bacteria and

sulphonamide resistant genes in wastewater treatment plants in the last decade (Bouki *et al*., 2013; Novo *et al*., 2013).

2.8.1.3 Antibiotic Resistance Associated with other Factors in the Hospital

Inappropriate use of antibiotics is caused by over prescription by medical practitioners, even in the absence of appropriate indications. Over-prescription especially when the clinical picture of bacterial or viral etiology is alike is caused by uncertainty diagnoses. According to Tagoe & Attah (2010), several varying factors such as social circumstances, geographical region and existing health care systems can influence antibiotic use and misuse in various parts of the world.

Research has shown that broad-spectrum antibiotics are always prescribed by many doctors to patients assumed cannot wait for a full diagnosis or are likely to not return because of transportation cost or time (Van der Geest, 1991). Inappropriate prescribing of antibiotics has also been attributed to many causes including people who insist on antibiotics, physicians who simply prescribe them as they feel they do not have time to explain why they are not necessary, physicians who do not know when to prescribe antibiotics or else are careful for medico-legal reasons and those who just prescribe for economic reasons (Ronsmans *et al*., 1996).

The widespread use of antibiotics both inside and outside of medicine has been found to play a momentous role in the emergence of resistant bacteria (Goossens *et al*., 2005) whilst the volume of antibiotic prescribed is the major factor in increasing rates of bacterial resistance rather than compliance with antibiotics (Pechère, 2001).

2.8.1.4 Antibiotic Resistance Associated with other Factors in the Community

Self medication can be defined as the use of drugs to treat self diagnosed disorders or symptoms, or the recurrent or continued use of a prescribed drug for chronic or recurrent disease or symptoms (Kunin, 1978). Self medication with antibiotics constitute a major form of unreasonable use of medicine and can cause significant effects such as resistant microorganisms, treatment failures, increase in treatment cost, prolonged hospitalization periods and increase in morbidity (Goossens *et al*., 2005; Nathwani & Davey, 1992; WHO, 2000).

Self medication varies from one location to another. For instance, a higher prevalence of 19% self medication with antibiotics was reported in Southern Europe in comparison with northern Europe (3%) and central Europe (6%) (Prestinaci *et al*., 2016).

Studies have also shown that self medication with antibiotics is generally predominant in the developing world (Skliros *et al*., 2010; WHO, 2000). In some countries of Africa, 100% of antimicrobial use is without prescription (Morgan *et al*., 2011).

The prevalent trend of self medication in the developing world has been associated with several factors, particularly, lack of access to health care, poor regulatory practices, availability of antibiotics as over the counter drugs and the relatively higher prevalence of infectious diseases (Ebert, 2007; Friedman & Whitney, 2008; Vila & Pal, 2010). Self medication with antimicrobials is common in many areas of world, particularly in developing countries with loose regulatory systems where antibiotics are sold over the counter drugs(Prestinaci *et al*., 2016). One of the documented predictors of self medication is level of education (Awad *et al*., 2005; Sapkota *et al*., 2010).

High prevalence (70%) of self medication was reported in Accra which was attributed to inexpensive compared to medical care in the hospital, delays in medical care in hospitals (Donkor *et al*., 2012). In Ghana, a wide range of antibiotics are available on the market and acquiring drugs over the counter is a very common practice, facilitating self medication which is thought to be highly prevalent in the Ghanaian community (Feglo & Adu-Sarkodie, 2016; Van den Boom *et al*., 2010). Misuse of antibiotic was also observed in the Tamale teaching hospital in the Northern Region of Ghana with a prevalence of 62.40% (Garcia-Vello *et al*., 2020). This means that antibiotic resistance of urinary tract infections can be prevented with proper observations of these above-mentioned factors.

2.8.2 Impacts of Antibiotic Resistance

In as much as the impact of antibiotic resistance is less known in Africa and for that matter Ghana as a result of limited documentation, in the developed countries like Italy mortality and public health cost is always the issue (Prestinaci *et al*., 2016). Research conducted by Centres for Disease Control (2013) and ECDC/EMEA (2009) shows that there is a high prevalence of multidrug resistant bacteria strains that cause many infections and deaths annually. Some *Staphylococcal* species have shown some level of multidrug resistance and causing infections up to 60-70%. Methicillin resistant *S. aureus* has been observed in the neonatal units in New York (Patel & Saiman, 2010) which can sometimes be difficult or impossible to treat (Stoll *et al*., 2010) causing loss of lives and resources required for treatments.

This leads to an increase in the cost of medical care as a result of purchasing more expensive antibiotic such as second line and third line drugs as well as specialist, sophisticated medical equipment, longer time in hospitals, and procedures in handling

urinary tract infections (Prestinaci *et al*., 2016) and loss of productivities. The cost of remedying antibiotic resistance infections is estimated to be high in Europe (ECDC/EMEA., 2009) and the US (CDC, 2013) as a result of direct health care costs and loss of productivity.

Resources are limited in Africa, Ghana and northern Ghana to be precise. Therefore, the earlier the pragmatic approaches through the availability of information regarding antibiotic and multidrug resistance, the better in terms of saving resources for other developmental projections.

2.8.3 Prevalence of Multidrug Resistance

Globally, multidrug resistance is the major cause of debility and death. The prevention and treatment of bacterial infections are now facing serious challenges (WHO, 2018). Studies have proven that many of the uropathogens are resistant to two or more classes of antibiotics.

A study in Nigeria in 2006 shows that *Escherichia coli* and *Klebsiella* species are 100% and 66.7% sensitive to ofloxacin and to ciprofloxacin, respectively but resistant to cotrimoxazole, amoxicillin and clavulanic-acid potentiated amoxicillin (Ibadin *et al*., 2006). A study in northern Ghana shows that about 91% of *E. coli* isolates from patients are resistant to ampicillin, 76% to sulfamethoxazole and 46% to chloramphenicol (Djie-Maletz *et al*., 2008).

A similar study shows that uropathogens are generally low sensitive to most antibiotics commonly in use, like co-trimoxazole (40%), tetracycline (25%), chloramphenicol (33%) and ampicillin (40%) in Nigeria (Nwadioha *et al*., 2010).

A study in Brazil in the year 2012 revealed that *E. coli* is responsible for cases of significant bacteriuria (76.56%) and are resistant to trimethoprim/sulphsmethsoxazole (34.69%) and fluoroquinolones (21.42%) (Luiz *et al.*, 2012)

Among significant bacterial growth, up to about 41.1% of uropathogens are MDR in Nepal (Baral *et al*, 2012). While the most prevailing organism, *E. coli* shows 38.2% MDR, the second most common organism, *Citrobacter* spp is about 72.7% MDR. However, a combination of antibiotics (piperacillin and tazobactam), (ceftazidime and clavulanic) alongside with amikacin, imipenem can be more effective in treating UTI (Mehta *et al*., 2012). In Chandigarh, *E. coli* shows a higher (70-95%) rate of resistance towards commonly used antibiotics except for nitrofurantoin (4%) that is still active against uropathogens (Mehta *et al*., 2012). Urinary tract infection associated with multidrug resistant *E. coli* remains the common cause of febrile illness in North-Western Tanzania (Msaki *et al*., 2012).

A related finding was reported in Nepal by Sharma *et al*., (2013) with a descending order of antibiotic effectiveness from nitrofurantoin, ciprofloxacin, ofloxacin, and cephalexin respectively. Akintobi *et al*. (2013) found that all the uropathogens are resistant to antibiotics such as cefuroxine, amikacin and nitrofurantoin with ciprofloxacin, amoxicillin, cotrimaxozole and norfloxacin being as high as about 70-95% ineffective in treating uropathogens in Nigeria. Some uropathogens show a high rate of resistance to ampicillin and amoxicillin (93.5%), co-trimoxazole (83.9%), and tetracycline (80.6%) (Agersew *et al*., 2013).

According to Hines *et al*. (2014), about 75% of Gram positive bacteria are resistant to oxacillin and TMP/SMX (bactrim) while 25% of them, mostly S *aureus* are resistant to Ampicillin and *Pseudomonas aeruginosa*, *Enterococcus faecium* mostly less susceptible to most of the antibiotics

A study in Ethiopia also showed a high percentage of resistance to ampicillin (90%), tetracycline (100%) and co-trimoxazole (80%) (Getu, 2015). In Ethiopia, Multidrug resistance was seen in 96 % of the uropathogens (Getu, 2015). This might be due to the fact that many antibiotics are easily available for self-medication and they are being used indiscriminately. Shatalov (2015) pointed out that *E. coli* and *K. pneumoniae* possess high resistance to ampicillin (100%), trimethoprim/sulfamethoxazole (95%-100%), amoxicillin/clavulanic acid (74%-100%) whereas *K. pneumoniae* shows high resistant to gentamicin (86.2%), cefuroxime (85.7%) and ceftriaxone (81.3%) in Equatorial Guinea.

Also in Ghana, older drugs such as chloramphenicol, trimethoprim-sulfamethoxazole, ampicillin and tetracycline, are not effective (80%) against uropathogens (Opintan *et al*., 2015). However, isolates show resistance levels of 50% for injectable such as amikacin and gentamicin, particularly for Gram negative isolates. Resistance profiles for the third generation cephalosporins and quinolones such as nalidixic acid and ciprofloxacin are high (50%) across all the middle sectors of Ghana (Opintan *et al*., 2015). In the Gram positive uropathogens, cefoxitin resistance is 50% in the Northern and Southern sectors of Ghana, but almost 100% for the middle sectors of Ghana (Opintan *et al.*, 2015).

There is high multidrug resistance (14%-54.2%) among Gram negative uropathogens in South and Eastern Europe, Turkey and Israel (Gomila *et al.*, 2018). A research in China

reported that *E. coli* is the leading pathogenic microorganism isolated from UTI patients under diabetes treatment with UTIs of which 50% are multidrug resistant (He *et al*., 2018). The rate of multidrug resistance in eastern Nepal is 39.5%, 63.16% and 56.9% for *E. coli, Pseudomonas* and *Klebsiella*, respectively (Mahato *et al*., 2018).

High (89.5%) multidrug resistance is observed in bacterial isolates in Kumasi, Southern Ghana, from 53.8% to 100.0% with *Enterobacter* spp., *P. aeruginosa* and *Acinetobacter* spp. (Agyepong *et al*., 2018). Also high (80.1%) multidrug resistance among uropathogens was observed in Accra, Southern Ghana (Donkor *et al*., 2019).

It means that most uropathogens show high levels of resistance to many antibiotics implying therapeutic options can be a problem in future.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study Area

Samples were collected from the Tamale Teaching Hospital and the Tamale Central Hospital, and processed in the Spanish laboratory complex of the University for Development Studies Nyankpala in the Northern Region of Ghana.

Tamale Teaching Hospital which is now an 800 bed capacity is a referral hospital (tertiary health care hospital) located in the Northern Region of Ghana, that provides health services to the three northern regions of Ghana and cooperates with the University for Development Studies to offer undergraduate and graduate studies in medicine, nutrition and nursing.

The Tamale Central Hospital which is a 186 bed capacity is a secondary health care facility that supports the Tamale Teaching Hospital in providing health services to people of the Tamale metropolis and its surroundings.

Both hospitals are located in the Tamale metropolis. It is positioned at the center of the Northern Region, Ghana. It shares borders with the Sagnarigu District to the West and North, Mion District to the East, Central Gonja to the South-West and East Gonja to the South (Figure 3.1). It has a land size of 646.90180/sqkm and is positioned between latitude 9º16^{1} and 9º 34^{1} North and longitudes 0º 36^{1} and 0º 57^{1} West (Ghana Statistical Service, 2010).

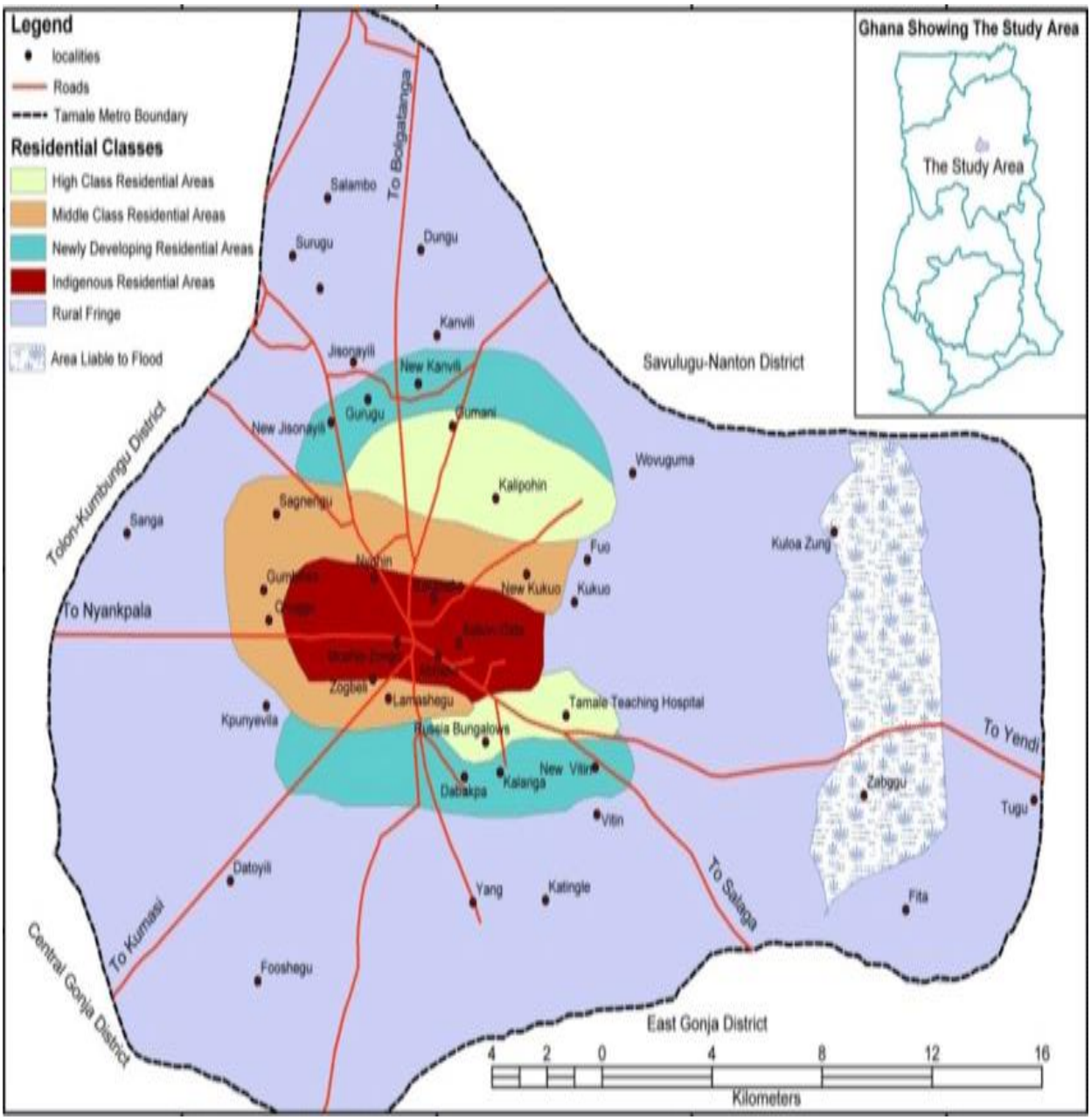

Figure 3. 1: Map of Tamale Metropolis

Source: Denteh, *et al.* (2018).

3.2 Determination of Sample Size

The fisher formula as described by (Tibyangye, 2013) was used to calculate the sample size (n). According to Labi *et al*. (2019), the prevalence of UTI in Ghana is 18.5%, and that in the Tamale Teaching Hospital (TTH) is 27.2% (Darkom, 2014). Therefore, considering the prevalence of 27.2% for the formula below,

$n = Z^2QP / I^2$

Where n = Sample size,

Q = 100-P

Z=Level of significance (1.96) for confidence interval of 95%.

P =Prevalence of UTIs in northern Ghana at 27.2% (according to TTH annual report) I = margin of error of setting a significance level of 0.05 (i.e. 5%).

$n = (1.96^2*(100-27.2))\ 27.2/5^2$

n =304

However, a total of 736 patients were sampled for uropathogens isolation for the purpose of this work and to minimize error because of the heterogeneous nature of the sampling subjects.

3.3 Experimental Design

This was a cross sectional survey that was carried out from 16th April, 2018 to 10th September, 2018.

3.4 Sample Collection

A total of 736 urine samples were collected from patients attending the Tamale Teaching and the Tamale Central hospitals. The study subjects included patients of all age groups and sex attending these hospitals.

Clean catch midstream urine samples were collected from patients into sterile screw capped universal containers. The samples were labeled, transported in an ice chest containing ice packs to the Spanish laboratory complex and plated within two to three hours of collection, to ensure maximum recovery of the organisms.

3.5 Sample Culturing

Sample culturing was done according to Mwaka *et al*. (2011). A Cysteine Lactose Electrolyte-Deficient agar (CLED) plate was divided into four. A loop-full (0.001 ml) of urine was inoculated onto each quadrant of CLED plate by the streaking method (Plate 3.1) and it was incubated at 37±2°C for 18-24hours (hrs). After the period of incubation, colonies were counted and those that showed significant growth identified. Significant microbial growth was characterized by microbial count greater than $1x10^5$ CFU/ml.

Plate 3. 1: Plating

3.6 Microbial Identification

Identification was done by routine procedures which included morphological characteristics on the CLED agar plate (Plate 3.2).

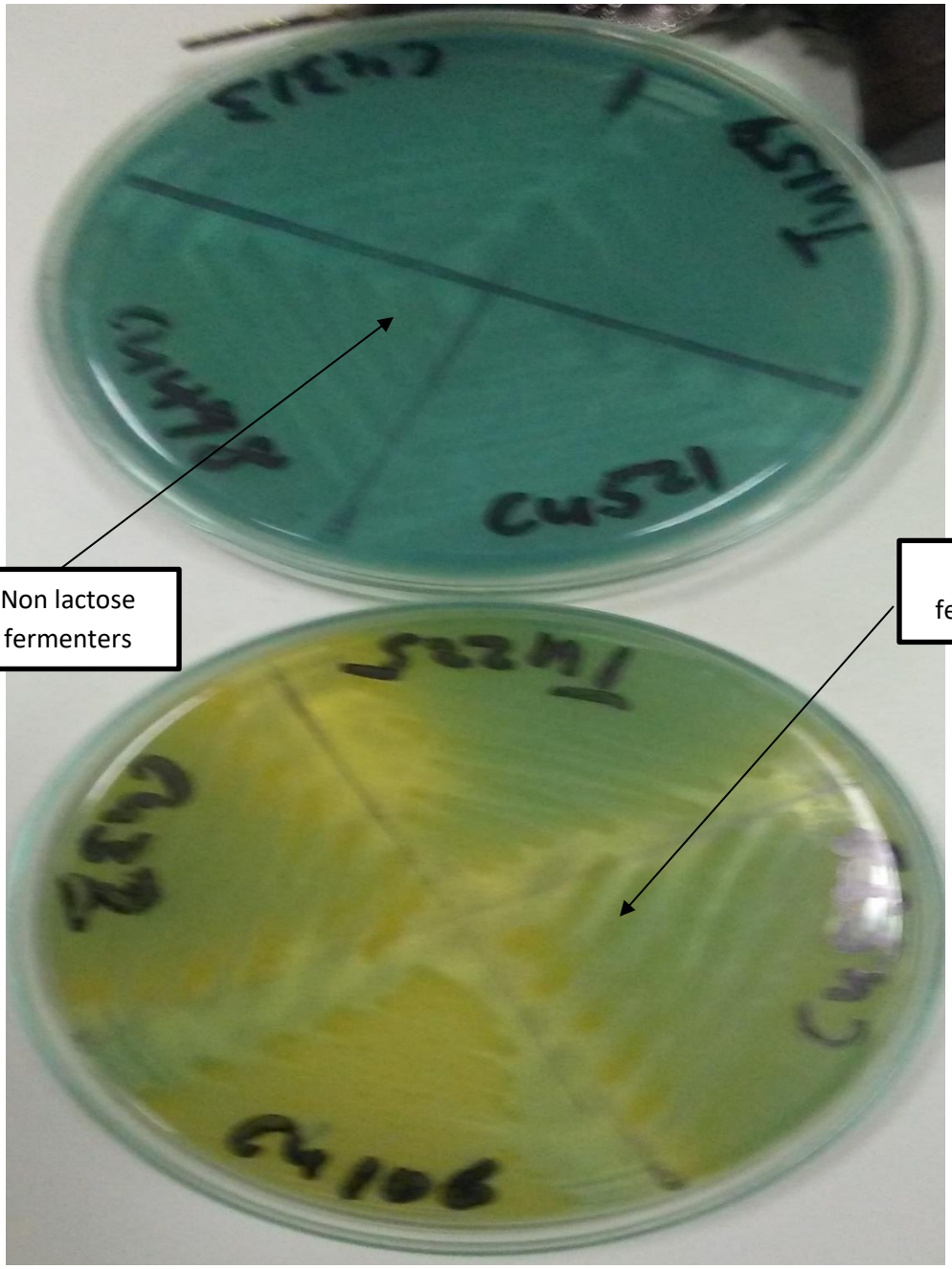

Plate 3. 2: Morphology of Colonies on CLED

This is colony morphology on CLED agar plates showing uropathogens that can ferment lactose component in the CLED agar.

3.7 Urine Microscopy

About 5 mL of sufficiently mixed urine sample was centrifuged at 3000 rpm for 10 min. A drop of the sediment was placed on a glass slide and covered with a cover slipped and observed under the microscope for detection of pus cells, red blood cells, casts and crystals. The occurrence of 10 or more pus cells/high-power field (HPF) was indicative of pyuria. Sterile pyuria in this study was defined as samples scoring 10 or more pus cells but recorded no growth on CLED plates after 24hrs of incubation.

3.8 Gram Staining

Gram staining was used for the first stage of microbial identification and the stained slides were observed under oil immersion (100x) using a Bright field microscope (Plate 3.5).

3.8.1 Smear Preparation

A loop of colonies was dissolved in distilled water on a glass slide. It was then passed swiftly through flame to fix the colonies on the slide. It was allowed to cool before applying stain.

3.8.2 Gram Staining Procedure

The air-dried, heat-fixed smear of cells was flooded with crystal violet staining reagent for 3 minutes (Plate 3.3). The slides were washed in a gentle and indirect stream of tap water. The slides were flooded with the mordant, Gram's iodine for 2 minutes. The slides were washed in a gentle and indirect stream of tap water. The slides were flooded with

decolorizing agent (Acetone-alcohol decolourizer) for 10 seconds. It was washed with water. The slides were flooded with counterstain, safranin for 30 seconds. The slides were washed in a gentle and indirect stream of tap water. The slides were put on an absorbent paper and was air dried (Plate 3.4) before it was observed with an electronic microscope (Plate 3.5).

Plate 3. 3: Gram Staining

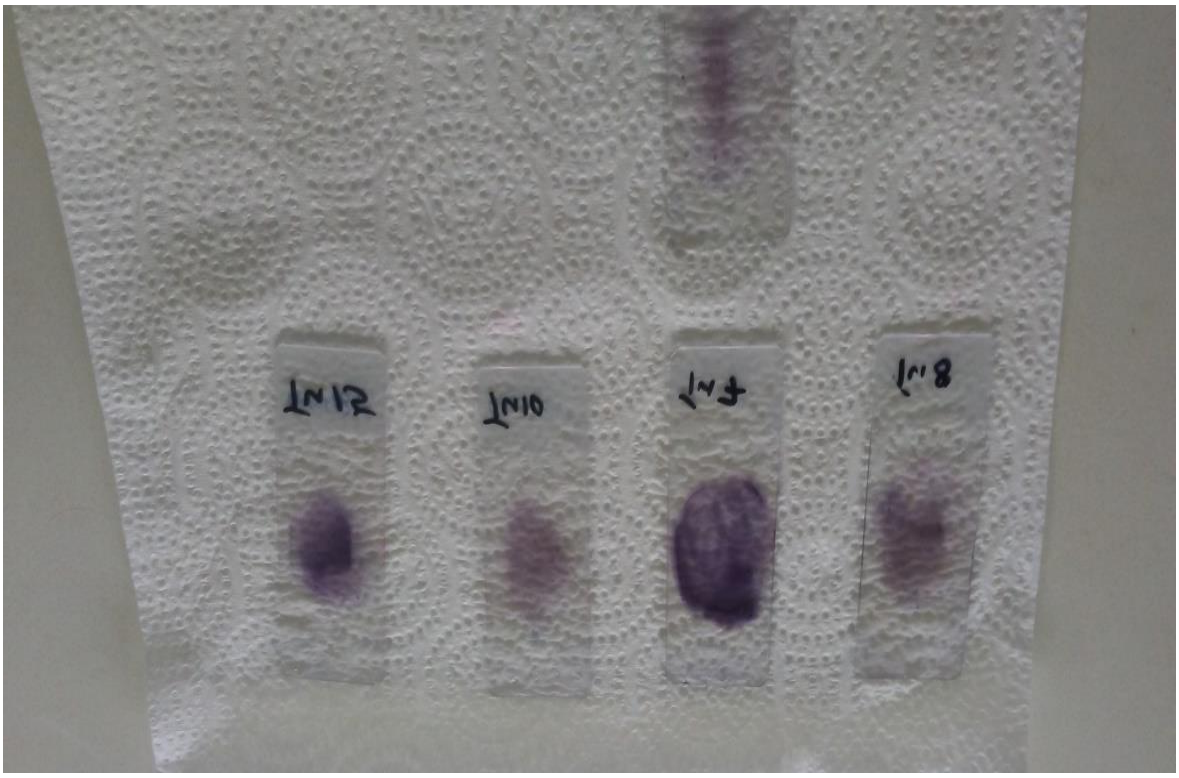

Plate 3. 4: Air Dried Gram Stained Slides

Plate 3. 5: Observing Gram Stained Slides with a Microscope

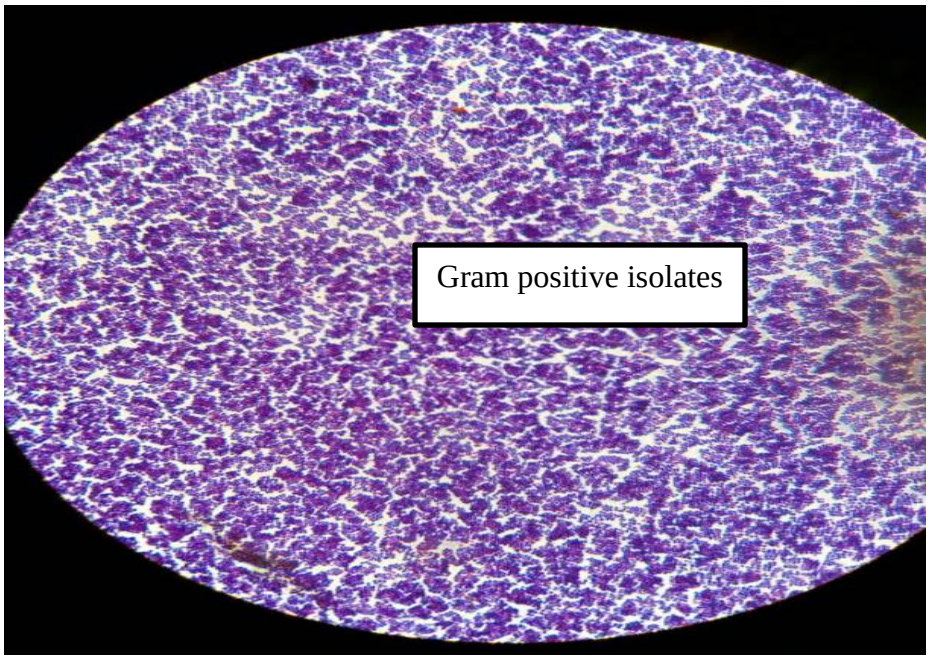

Plate 3. 6a: Microscopy Results of Gram Positive Isolates

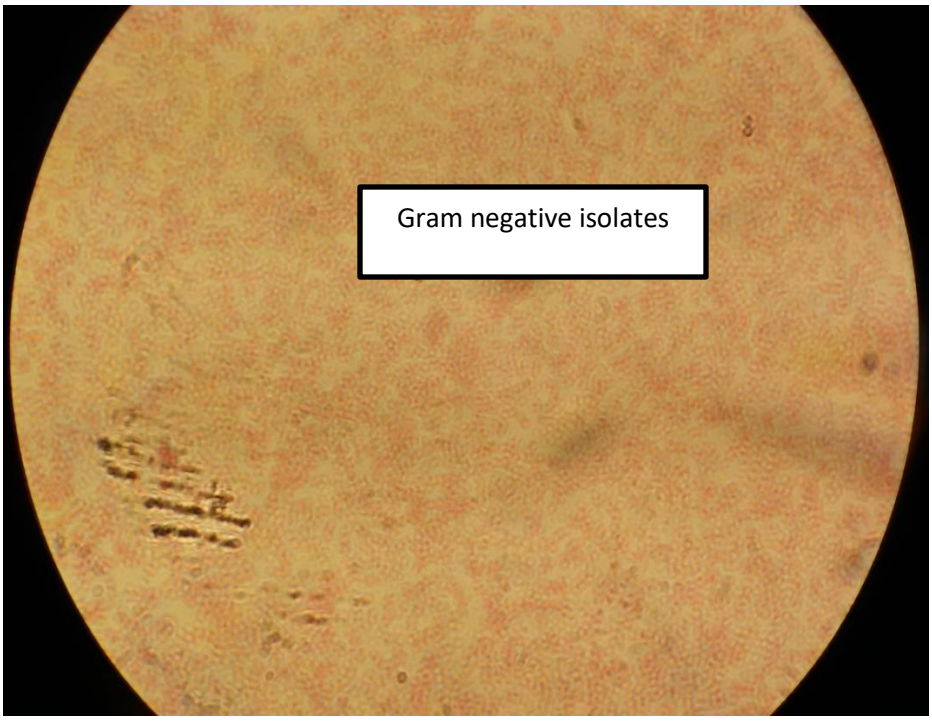

Plate 3. 6b: Microscopy Results of Gram Negative Isolates

3.9 Preparation of Pure Culture

A loop full of the colonies was streaked on nutrient agar and it was incubated at 37 ±2 ^{0}C for 18 to 24hrs to obtain pure culture for the biochemical tests.

Microbial colonies were also characterized biochemically and serologically according to Cheesbrough (2006).

3.10 Identification of Gram Positives

3.10.1 Catalase Test

This test was used to differentiate those bacteria that release the enzyme catalase, such as *Staphylococci*, from non-catalase producing bacteria such as *Streptococci*.

A loop (plastic) full of the 24hrs Gram positive pure colonies was placed on a glass slide. A drop of hydrogen peroxide (3%) was added to the colonies on the slide using a dropper. Catalase positive strains produced bubbles in 5 seconds (Plate 3.7).

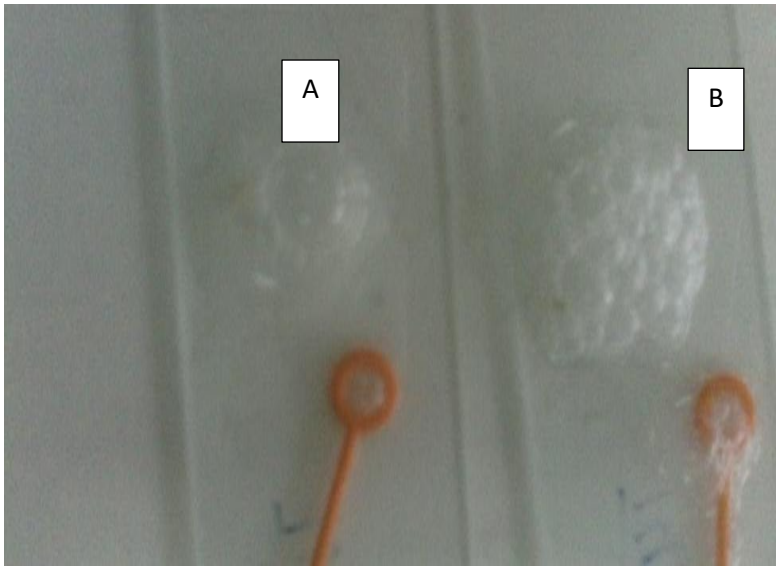

Plate 3. 7: Catalase Test

A= Catalase Negative

B= Catalase Positive

3.10.2 Coagulase Test

This test was used to identify *S. aureus* which releases the enzyme, coagulase. Coagulase causes plasma to clot by changing fibrinogen to fibrin.

A loop full of saline solution was placed on a slide. A loop full of 24hrs Gram positive pure colonies were dissolved in the saline solution on the slide. With a dropper, 2 to 3 drops of serum were added and swung for 30 seconds. Coagulase positive isolates were identified by the formation of lumps (agglutination) in the serum on the glass slide (Plate 3.8).

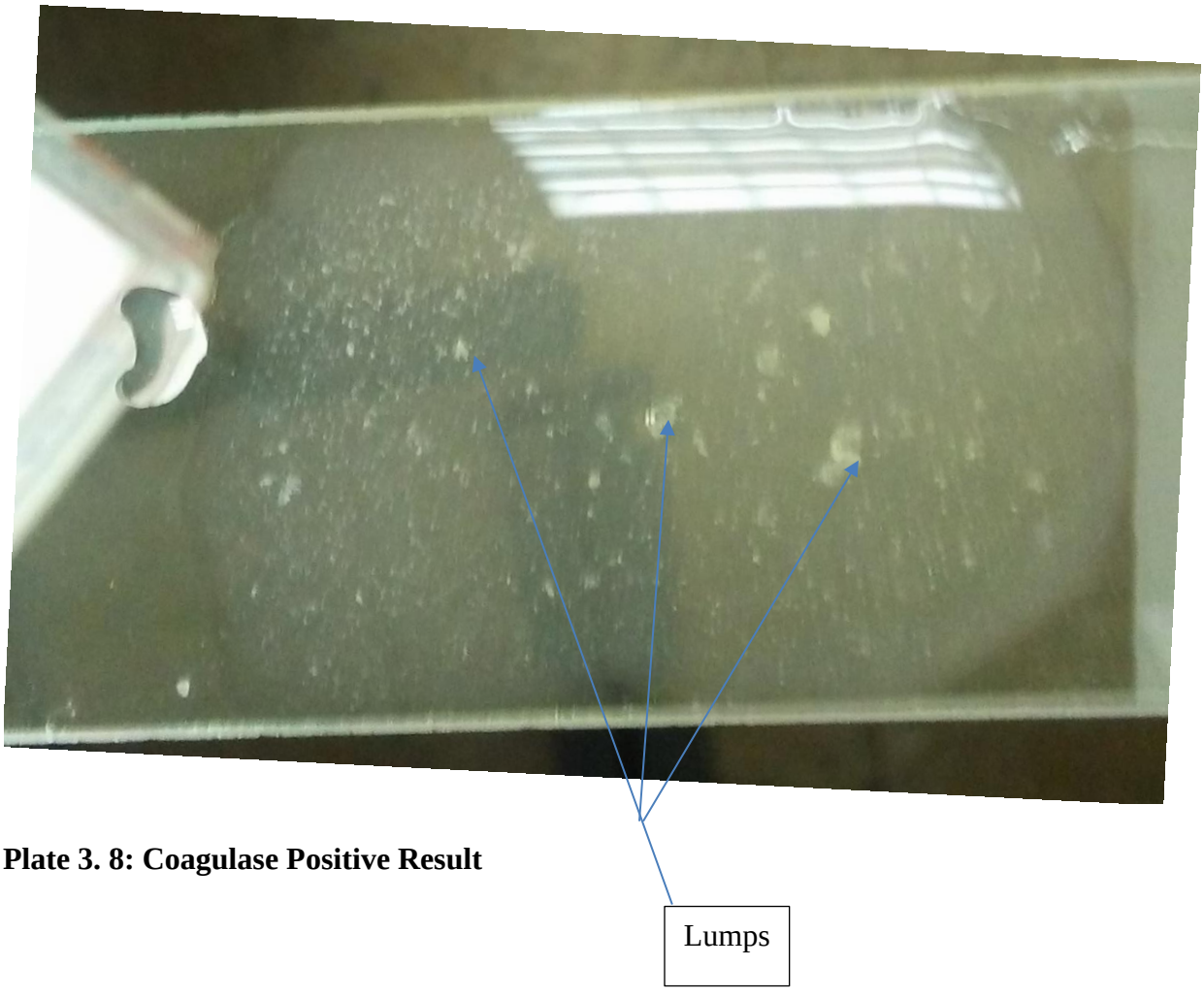

Plate 3. 8: Coagulase Positive Result

3.10.3 Haemolysis Test

A 24hrs pure colonies of catalase and coagulase negative strains of Gram positive cocci, were streaked on blood agar using an inoculation loop and incubated at 37 ±2 ^{0}C for 18 to 24hrs, to ascertain if the organism was β, α or γ haemolytic, thus to differentiate the *Streptococcus* spp. (Plate 3.9).

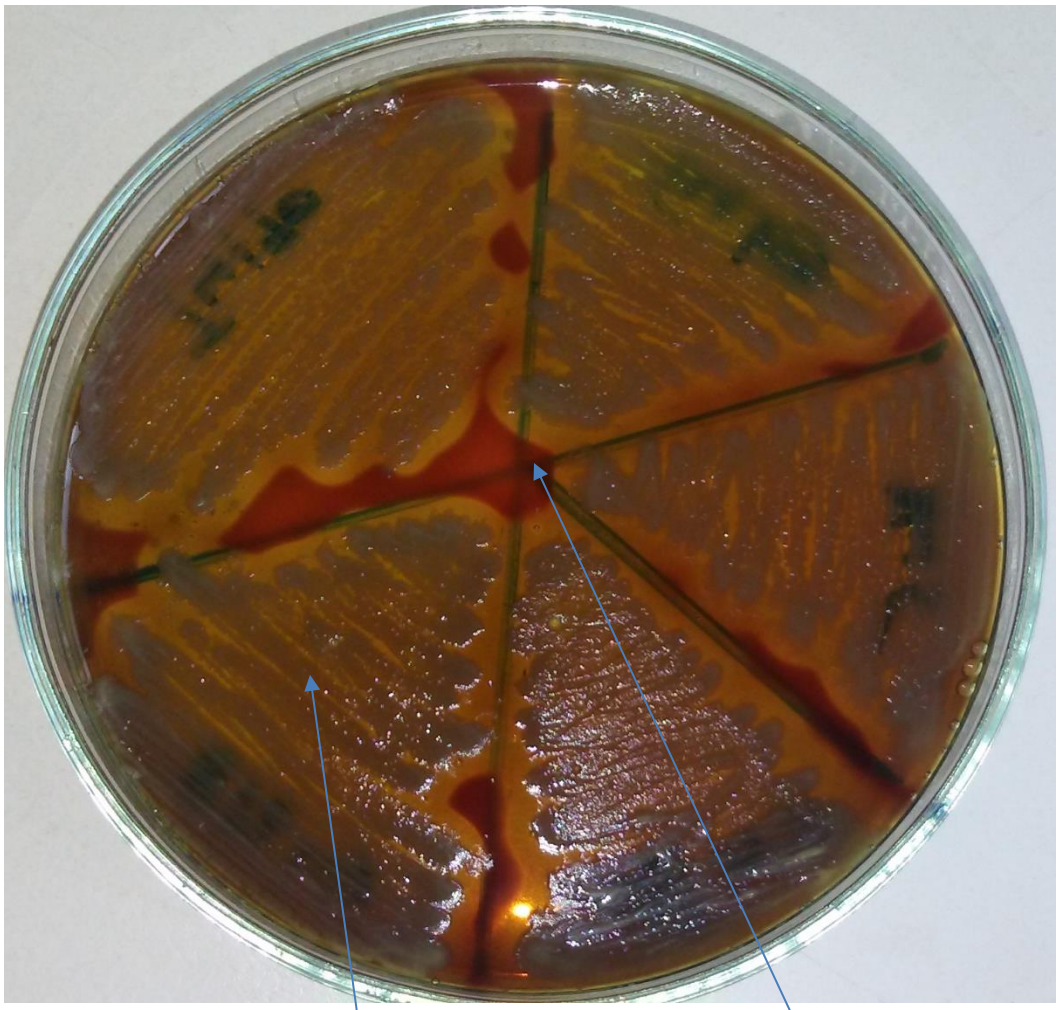

Plate 3. 9: Haemolysis Test

3.10.4 Confirmation of *S. aureus* by Mannitol Salt Fermentation Test

Pure colonies (after 24hrs of incubation) of catalase and coagulase positive strains of Gram positive cocci were streaked on mannitol salt agar using an inoculation loop and incubated at 37 ±2 ^{0}C for 18 to 24hrs. Colonies with yellow colour were classified as *Staphylococcus aureus,* Colonies with pink colouration were classified as coagulase negative *Staphylococcus* (CoNS) while those which showed no growth were categorized as *Streptococci* species (Plate 3.10).

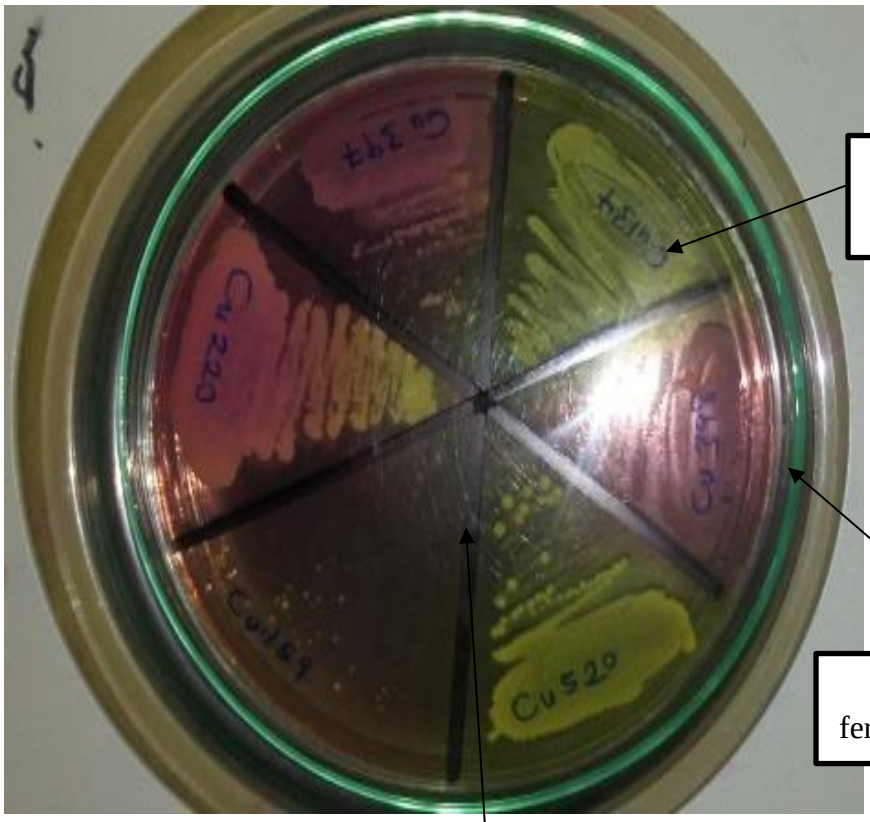

Plate 3. 10: Mannitol Fermentation Test

3.11 Identification of Gram Negative

3.11.1 Triple Sugar Iron (TSI) Test

Gram negative pure colonies (after 24hrs of incubation) were picked with straight loop and inoculated on TSI by stabbing the butt and streaking the slant. It was incubated at 37 ±2 ^{0}C for 18 to 24hrs. The organisms were identified by observing the butt and slant for acid and alkaline reactions, hydrogen sulfide and gas production (Plate 3.11).

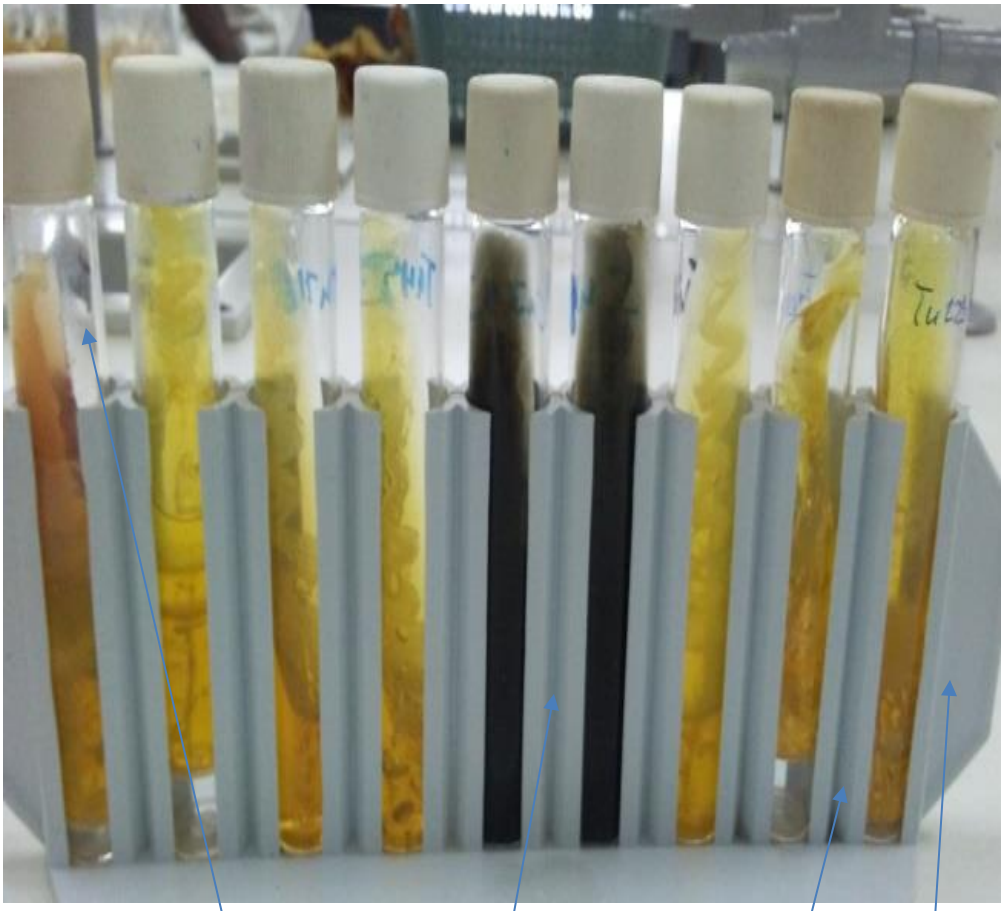

Plate3. 11: TSI Results

3.11.2 Indole Test

This test is aimed at identifying the *Enterobacteracae* that split amino acid tryptophan to form the compound indole.

A loop of the 24hrs pure colonies was inoculated into tryptone soya broth in the test tube and incubated at 37 ±2 ^{0}C for 18 to 24hrs. With a dropper, 3 drops of the indole reagent was added to incubated samples in the test tube. Indole positive was indicated by a red ring whiles the indole negative showed colourless to green colour (Plate 3.12)

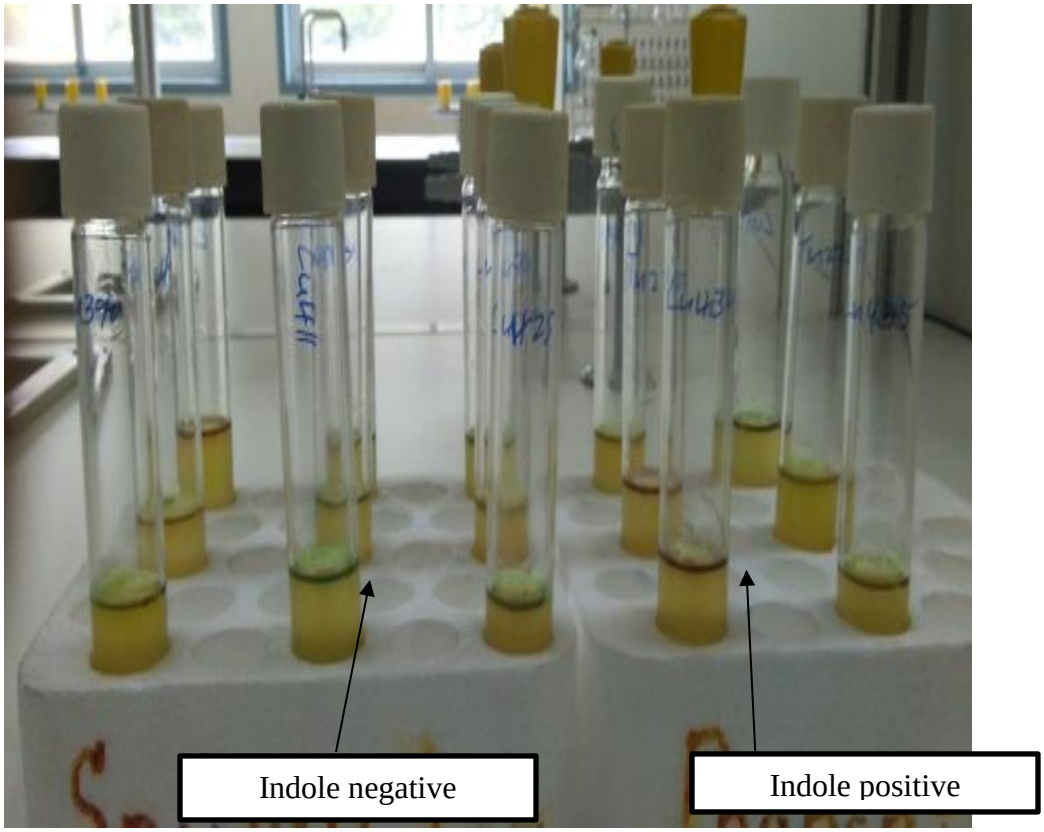

Plate 3. 12: Indole Results

3.11.3 Oxidase Test

It relies on the existence of certain enzyme (oxidases) in bacteria that will catalyze electron transport in the bacteria and its detection by a redox dye-tetramethyl-p-phenylene-diamine. Gram negative pure colony (after 24hrs of incubation) was smeared on the oxidase paper strip using a plastic loop. Oxidase positive was represented by blue colouration in 3 seconds (Plate 3.13).

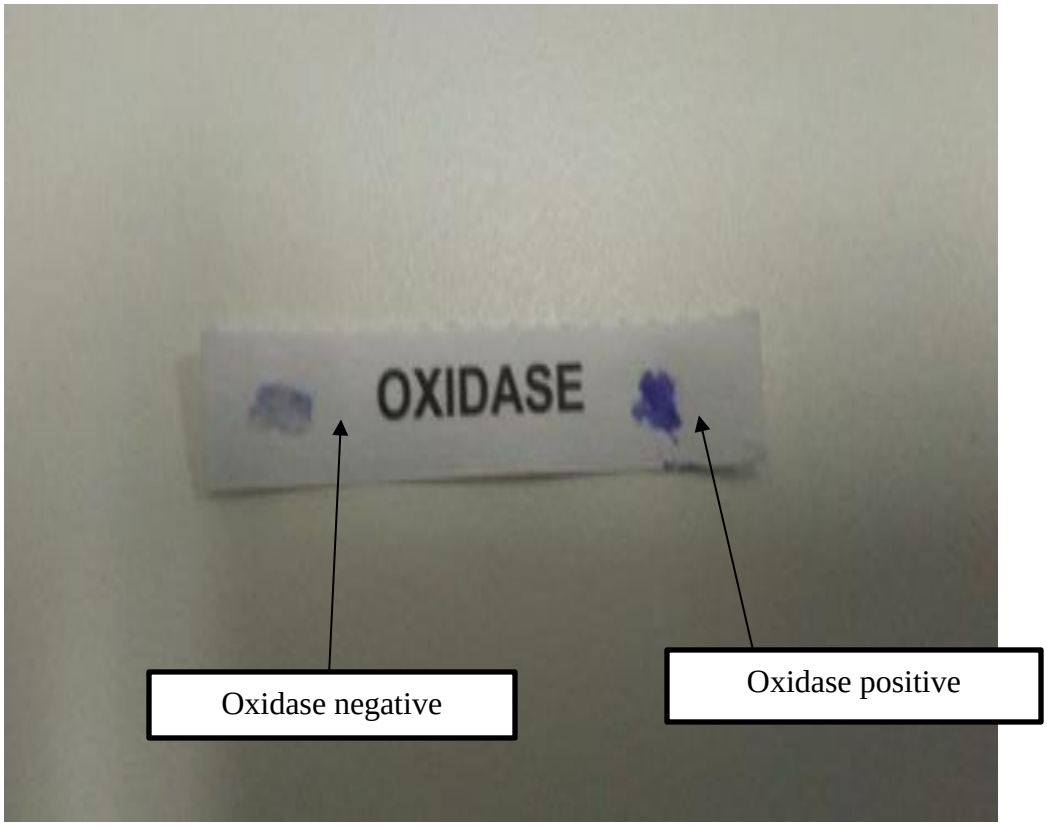

Plate 3. 13: Oxidase Results

3.11.4 Citrate Test

This test is used to identify the organism that utilize sodium as its only source of carbon.

Pure colonies (after 24hrs of incubation) were picked with sterilized straight loop which was used to stab the citrate agar in the test tube. It was incubated at 37 ±2 ^{0}C for 18 to 24 hours. Citrate positive showed blue colouration (Plate 3.14)

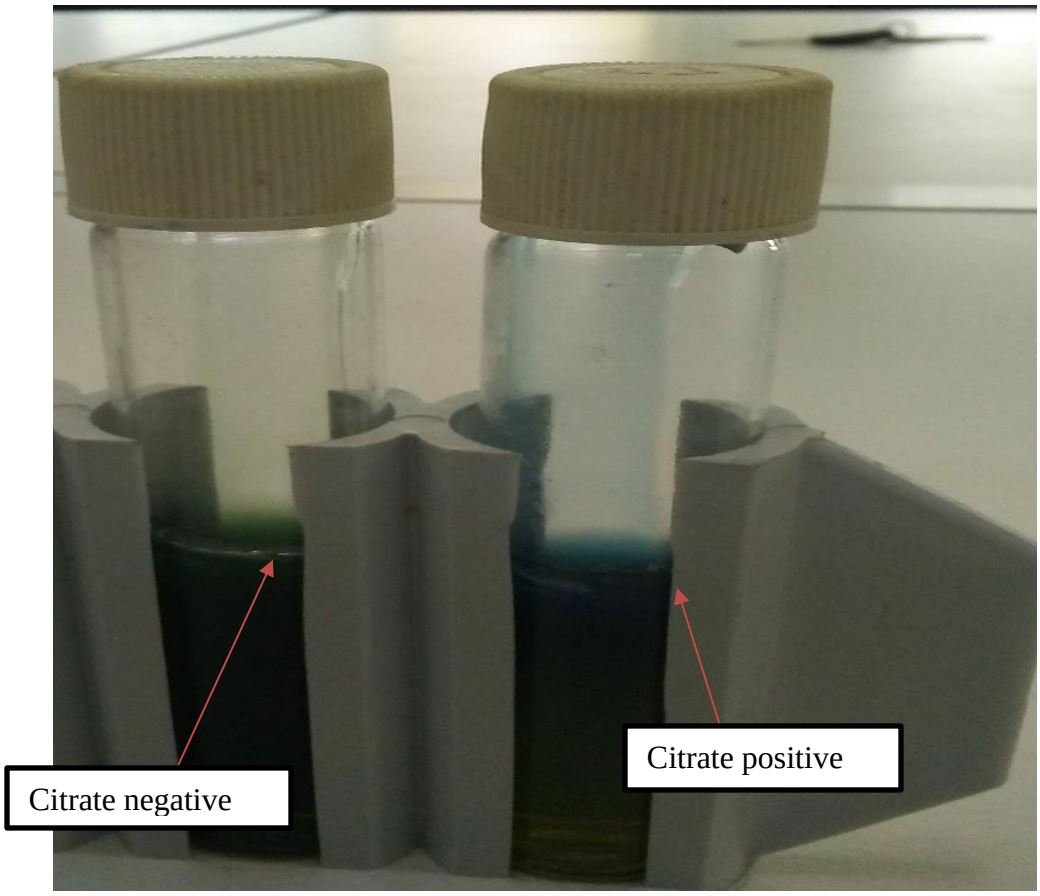

Plate 3. 14: Citrate Results

3.12 Antibiotic Susceptibility Test

The antibiotic susceptibility test of the isolate was done by the disk diffusion technique as described by Clinical and Laboratory Start Institutes (CLSI) (2012). From a pure culture (24hrs colonies), 3 to 5 selected colonies of bacteria were picked with a sterile loop and transferred to a tube containing 2 ml sterile normal saline and mixed gently to make a uniform suspension after which the turbidity of the suspension was compared to a 0.5 McFarland standard.

Two plates were used per an isolate. A sterile cotton swab was dipped in the 0.5 McFarland suspension and used to dispense the bacteria uniformly over the whole surface of Mueller Hinton agar by spreading. The inoculated plates were allowed to dry for 3 to 5 minutes and a set of 14 antibiotics disk, 7 disks for each Mueller Hinton agar plate, placed on the Mueller Hinton agar.

The plates were incubated in aerobic atmosphere at 37 ^{0}C for 18-24hrs (Plate 3.15). Diameters of the zone of inhibition around the disk were measured to the nearest millimeter using a graduated ruler, and the isolates were characterised as susceptible, intermediate, and resistant base on the CLSI interpretive criteria (Appendix 7).

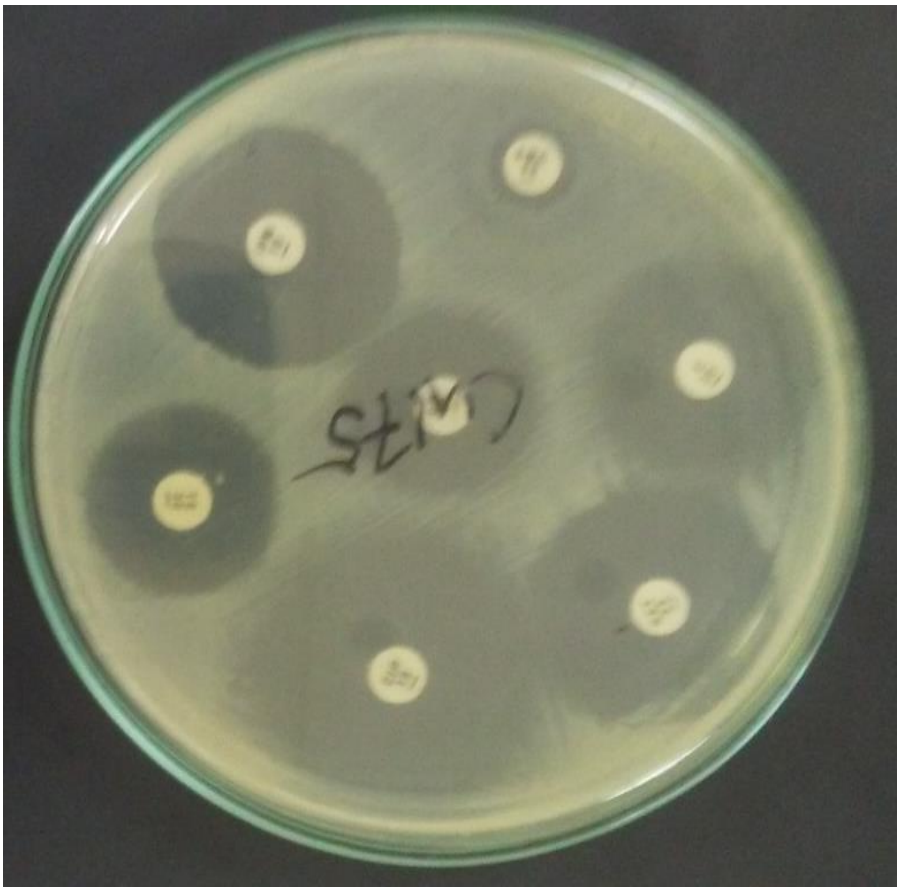

Plate 3. 15: Sample of Antibiotic Susceptibility Test Result

3.13 Data Analysis

Data was checked for completeness, entered into excel, imported and analysed using the SPSS version 20. Chi square test was used to determine significant differences using 95% confidence level and results were presented in percentages and frequencies using graphs and tables.

3.14 Ethical Consideration

Ethics approval was gotten from the Ethical Review Committee of the Tamale Teaching Hospital (TTHERC/25/06/19/14) which covers both the Tamale Teaching Hospital and the Tamale Central Hospital (Appendix 1). A verbal informed consent was sought from the study participants concerning the research because while some of the study participants were unable to read and write, others felt unwilling to write and saw the process as inconvenient.

CHAPTER FOUR

RESULTS

4.1 Prevalence of Urinary Tract Infection

A total, 222 and 514 patients' samples were analysed from the tertiary health care hospital (Tamale Teaching Hospital) and the secondary health care hospital (Tamale Central Hospital), respectively. Out of these, 80 (36.0%) and 110 (21.4%) presented with urinary tract infection (UTI) at the Tamale Teaching Hospital and the Tamale Central Hospital, respectively.

The overall prevalence of UTI was 25.8% (190) out of 736 patients samples analysed (Table 4.1). The prevalence of urinary tract infection (UTI) at the Tamale Central Hospital (TCH) and Tamale Teaching Hospital (TTH) varied significantly ($P \leq 0.05$) (Table 4.1).

Table 4. 1: Prevalence of Urinary Tract Infection at TCH and TTH

	FREQUENCY (%)				
Hospital	**No of Sample**	**Significant Growth (≥1x10^{5}CFU/ml)**	**Insignificant Growth (<1x10^{5}CFU/ml)**	**Negative Growth**	**P Value**
TTH	222	80(36.0)	122 (55.0)	20 (9.0)	
TCH	514	110(21.4)	340(66.1)	64(12.5)	
Total	736	190(25.8)	462(62.8)	84(11.4)	0.001

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital

4.1.1 Prevalence of Urinary Tract Infection (UTI) Among Sexes

At both the Tamale central hospital and the Tamale teaching hospital, the prevalence of UTI was more common with females 153 (80.5%) than males 37 (19. 5%). Whiles no significant difference (P≥ 0.05) was observed among males and females at the Tamale central hospital, there was a significant difference (P≤ 0.05) in infection rate among males and females at Tamale teaching hospital (Table 4.2).

Table 4. 2: Prevalence of Urinary Tract Infection Among Patients at TCH and TTH

	FREQUENCY (%)			
Hospitals	**No of Isolates**	**Male**	**Female**	**P Value**
TTH	80	27(33.8)	53(66.3)	0.005
TCH	110	10(9.1)	100(90.9)	0.902
Total	190	37(19.5)	153(80.5)	0.000

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital

4.1.2 Pathogen Frequency in UTI Infections at TTH and TCH

The frequency of uropathogens was higher in females (80.5%) than males (19.5%). The most isolated organisms in males at the Tamale teaching hospital were *E. coli* (25.9%), *Serratia* spp. (18.5%), CoNS (14.8%) and *Klebsiella* spp. (14.8%) whereas CoNS (35.8%), *S. aureus* (24.5%) and *E. coli* (13.2%) were commonly found in the females (Table 4.3).

At the Tamale central hospital, *E. coli* (30.0%), CoNS (30.0%) and *S. aureus* (20.0%) were frequently recovered from males, whereas CoNS (35.0%), *S. aureus* (23.0%) and *E. coli* (18.0%) were predominant in females (Table 4.3).

Table 4. 3: Frequency of Uropathogens Among Patients at TTH and TCH

	TTH			TCH		
Isolates	**Frequency**	**Male (%)**	**Female (%)**	**Frequency**	**Male (%)**	**Female (%)**
S. aureus	16	3(11.1%)	13(24.5%)	25	2(20.0%)	23(23.0%)
CoNS	23	4(14.8%)	19(35.8%)	38	3(30.0%)	35(35.0%)
Streptococcus	2	0(0.0%)	2(3.8%)	3	0(0.0%)	3(3.0%)
E. coli	14	7(25.9%)	7(13.2%)	21	3(30.0%)	18(18.0%)
***Klebsiella* spp.**	8	4(14.8%)	4(7.5%)	7	0(0.0%)	7(7.0%)
***Enterobacter* spp.**	7	3(11.1%)	4(7.5%)	9	1(10.0%)	8(8.0%)
Serratia	8	5(18.5%)	3(5.7%)	3	0(0.0%)	3(3.0%)
***Pseudomonas* spp.**	0	0(0.0%)	0(0.0%)	1	0(0.0%)	1(1.0%)
Salmonellae	2	1(3.7%)	1(1.9%)	2	1(10.0%)	1(1.0%)
P. vulgaris	0	0(0.0%)	0(0.0%)	1	0(0.0%)	1(1.0%)
Total	80	27(100.0%)	53(100.0%)	110	10(100.0%)	100(100.0%)

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, *CoNS-Coagulase Negative Staphylococcus*

4.1.3 Prevalence of Urinary Tract Infection Among Different Age Groups at TTH and TCH

Within the Tamale teaching hospital, the highest prevalence of urinary tract infection was recorded between the age group of 20-29 years (35%), 30-39years (22.5%) and ≥60 years (22.5%) (Table 4.4). At the Tamale central hospital, highest prevalence of urinary tract infection was observed within the age group of 20-29 years (54.5%) followed by 30-39 years (27.3%) (Table 4.4). There was a statistical difference (P≤ 0.05) in isolation rate among the different age groups at the Tamale central hospital and the Tamale teaching hospital (Table 4.4).

The mean age (years) of patients suffering from urinary tract infection at the Tamale teaching hospital was 40.01±2.2.58, whilst that of patients at the Tamale central hospital was 30.11±1.04. The overall mean age (years) of patients suffering from urinary tract infection was 34.28±1.29 (Appendix 8) (Table 5).

Table 4. 4: Distribution of Urinary Tract Infection Among Different Age Groups

	TTH		TCH		P
Ages(years)	**Frequency**	**Percent (%)**	**Frequency**	**Percent (%)**	**Value**
1-9	5	6.3	1	0.9	
10-19	2	2.5	7	6.4	
20-29	28	35	60	54.5	
30-39	18	22.5	30	27.3	
40-49	6	7.5	6	5.5	
50-59	3	3.8	3	2.7	
≥60	18	22.5	3	2.7	
Total	80	100	110	100	0.000

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital

4.1.4 Frequency of Uropathogens Among the Different Age Groups

Coagulase negative *Staphylococcus* was the predominant uropathogens found among the age group of 20-29 years (46.4%), whereas *S. aureus* was commonly associated with age groups of 1-9 years (60.0%) and 30-39 years (38.9%), at the Tamale teaching hospital (Table 4.5). Also, the predominant uropathogens from the age group ≥ 60 years were *E. coli* (27.8%) and CoNS (22.2%). However, *Serratia* spp. (33.3%) were recovered from the age group 40-49 years (Table 4.5). At the Tamale central hospital, patients between

the age of 1 - 9 years, 50-59 years and above 60 years were associated with *E. coli* (Table 4.5). However, most of the organisms were isolated from patients between 20-29 years and 30-39 years at the Tamale central hospital, with CoNS (36.7%) and *S. aureus* (30.0%) predominating (Table 4.5).

Table 4. 5: Distribution of Uropathogens Among the Different Age Groups

ΓH		Gram Positives				Gram Negatives					
ge	Isol.	*S. aureus*	*CoNS*	*Strept.* spp	*E. coli*	*Kleb. spp*	*Entero.* spp	*Serratia* spp	*Pseud.* spp	*Salm.*	*p vulgaris*
9	5	60.0%	20.0%	0.0%	0.0%	20.0%	0.0%	0.0%	0.00%	0.0%	0.00%
-19	2	50.0%	0.0%	50.0%	0.0%	0.0%	0.0%	0.0%	0.00%	0.0%	0.00%
-29	28	14.3%	46.4%	0.0%	14.3%	3.6%	10.7%	10.7%	0.00%	0.0%	0.00%
-39	18	38.9%	22.2%	5.6%	11.1%	5.6%	5.6%	5.6%	0.00%	5.6%	0.00%
-49	6	0.0%	16.7%	0.0%	16.7%	16.7%	0.0%	33.3%	0.00%	16.7%	0.00%
-59	3	0.0%	0.0%	0.0%	66.7%	33.3%	0.0%	0.0%	0.00%	0.0%	0.00%
0	18	5.6%	22.2%	0.0%	27.8%	16.7%	16.7%	11.1%	0.00%	0.0%	0.00%
CH											
9	1	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
-19	7	28.6%	42.9%	0.0%	14.3%	0.0%	14.3%	0.0%	0.0%	0.0%	0.0%
-29	60	25.0%	36.7%	1.7%	13.3%	10.0%	8.3%	3.3%	0.0%	0.0%	1.7%
-39	30	30.0%	26.7%	6.7%	26.7%	0.0%	6.7%	0.0%	0.0%	3.3%	0.0%
-49	6	0.0%	33.3%	0.0%	0.0%	16.7%	16.7%	16.7%	16.7%	0.0%	0.0%
50-59	3	0.0%	66.7%	0.0%	33.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
≥60	3	0.0%	33.3%	0.0%	33.3%	0.0%	0.0%	0.0%	0.0%	33.3%	0.0%

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, *Strept.=Streptococcus spp, Kleb.=Klebsiella* spp, *Entero.=Enterobacter* spp, *Pseud.=Pseudomonas* spp, *CoNS=Coagulase Negative Staphylococcus, Sal.=Salmonellae*

4.1.5 Distribution of Urinary Tract Infection at the Various Departments of the Hospitals

Within the Tamale teaching hospital, the highest prevalence of urinary tract infection was recorded at the Antenatal Care department (54%). Also, within the Tamale central hospital, highest prevalence of urinary tract infection was recorded in the Antenatal Care department (70.9%) (Table 4.6).

Table 4. 6: Urinary Tract Infection at the Various Departments of the Hospitals

	TTH		TCH		
Ward	**Frequency**	**Percent (%)**	**Frequency**	**Percent (%)**	**P Value**
Antenatal care	38	54	78	70.9	
Emergency ward	2	3.2	0	0.0	
Gynecology	2	1.6	0	0.0	
Out-Patient Dep.	12	7.9	17	15.5	
Female ward	2	11.8	3	2.7	
Prenatal	1	5.9	0	0.0	
Male ward	0	0.0	1	0.9	
Maternity ward	1	1.6	1	0.9	
Urology	22	31.7	0	0.0	
ART	0	0.0	7	6.4	
Fistula	0	0.0	3	2.7	
Total	80	100	110	100	0.000

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, ART=Anti-Retroviral Treatment.

4.1.6 Diagnosis Associated with UTI Infections at TTH and TCH

At both hospitals, the highest prevalence of UTI was associated with Cyesis (Table 4.7). There was a statistical difference (P≤ 0.05) among the various diagnosis and between the two hospitals (Table 4.7).

Table 4. 7: Prevalence of Urinary Tract Infection Associated with Various Diagnosis.

Clinical Diagnosis	TTH		TCH		P Value
	Frequency	Percent (%)	Frequency	Percent (%)	
Appendicitis	1	1.3	0	0.0	
Cyesis	34	42.5	80	72.7	
Diabetes Mellitus	1	1.3	0	0.0	
Deep Vein Thrombosis	1	1.3	0	0.0	
Benign Prostrate Hyperplasia	9	11.3	0	0.0	
Epididymitis	1	1.3	0	0.0	
UTI	17	21.3	20	18.2	
Urine Retention	4	5	0	0.0	
Hepatitis B	1	1.3	0	0.0	
Hyperparathyroidism	2	2.5	0	0.0	
Malaria/Anaemia	1	1.3	0	0.0	
Scrotal Crop	1	1.3	0	0.0	
Urethral Stricture	3	3.8	0	0.0	
Sepsis	1	1.3	0	0.0	
Urethroplasty	2	2.5	0	0.0	
HIV AIDS	0	0.0	7	6.4	
Visco-vaginal fistula	1	1.3	3	2.7	
Total	80	100	110	100	0.000

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital.

4.2 Incidence of Sterile Pyuria Among Patients at TCH

A total of 53 patients' samples from the Tamale central hospital were analysed for sterile pyuria, out of which a prevalence of 36 (67.9%) was observed. Females recorded higher prevalence of sterile pyuria (94.2%) than males (5.8%) (Figure 4.1). There was no significant difference (P =0.164) of sterile pyuria between sexes.

The mean age of the patients associated with sterile pyuria was 27.8±1.68 (Appendix 8) (Table 5). Sterile pyuria associated with females was high among the age group of 20-29 years (70.6%). However, with the males, it was high among the age group of <20 years (50.0%) and >40 years (50.0%) (Figure 4.2).

Sterile pyuria was observed mostly in samples from the Antenatal Care department (91.7%). Male ward recorded the least (2.8%) prevalence of sterile pyuria (Figure 4.3). Also, sterile pyuria was mostly associated with Cyesis (91.7%). Severe abdominal pains with frequent urination had the least (2.8%) prevalence of sterile pyuria (Figure 4.4).

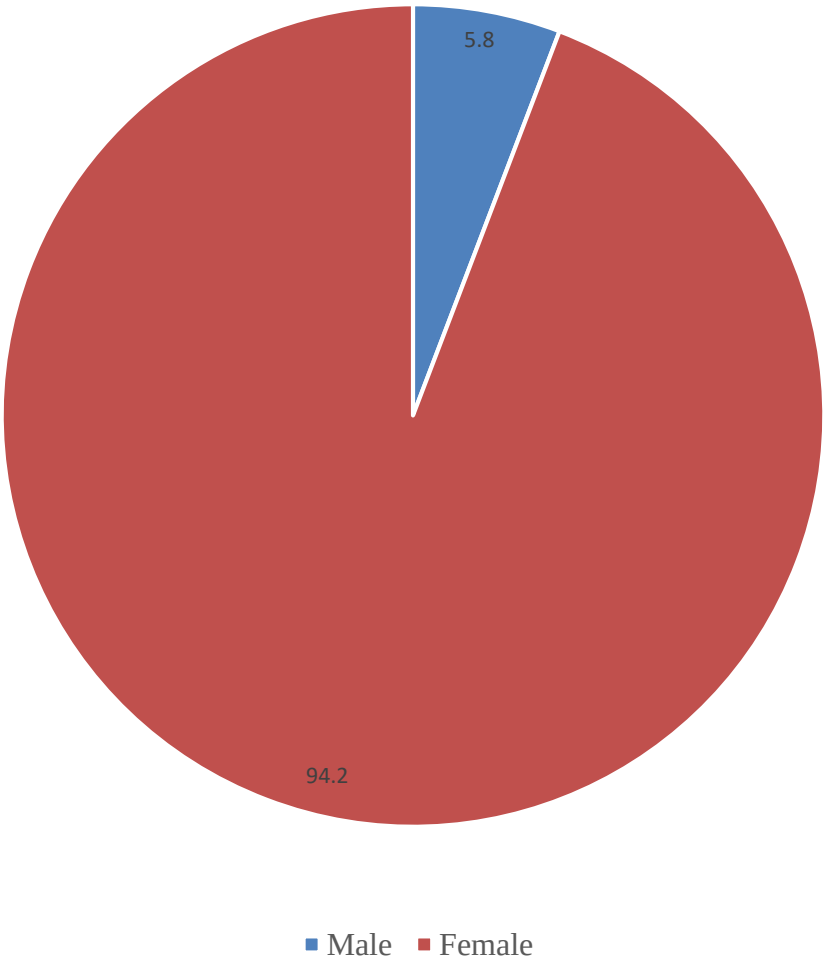

Figure 4. 1: Incidence of Sterile Pyuria Among Different Sexes

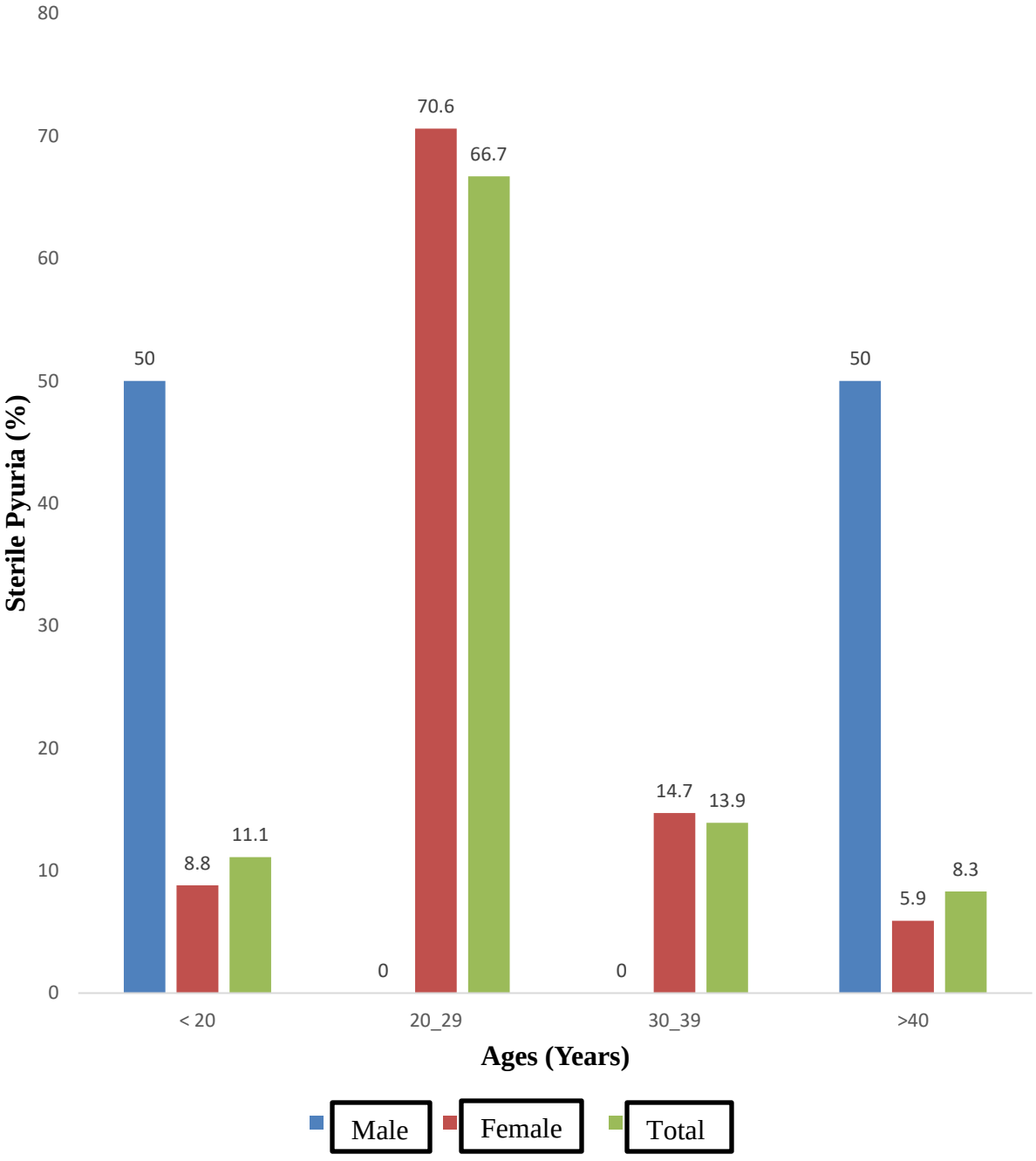

Figure 4. 2: Frequency of Sterile Pyuria Among the Different Age Groups

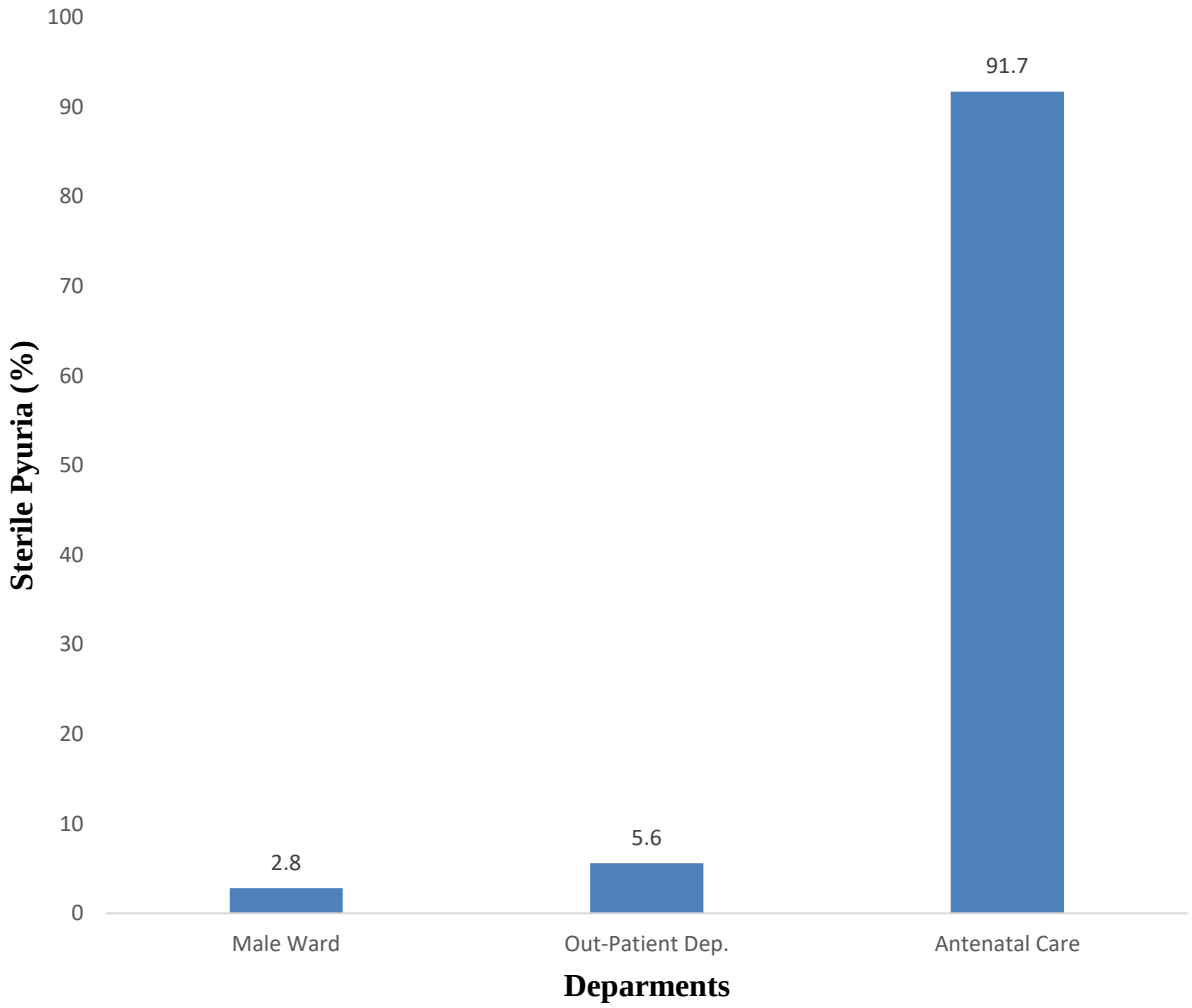

Figure 4. 3: Incidence of Sterile Pyuria in the Various Departments

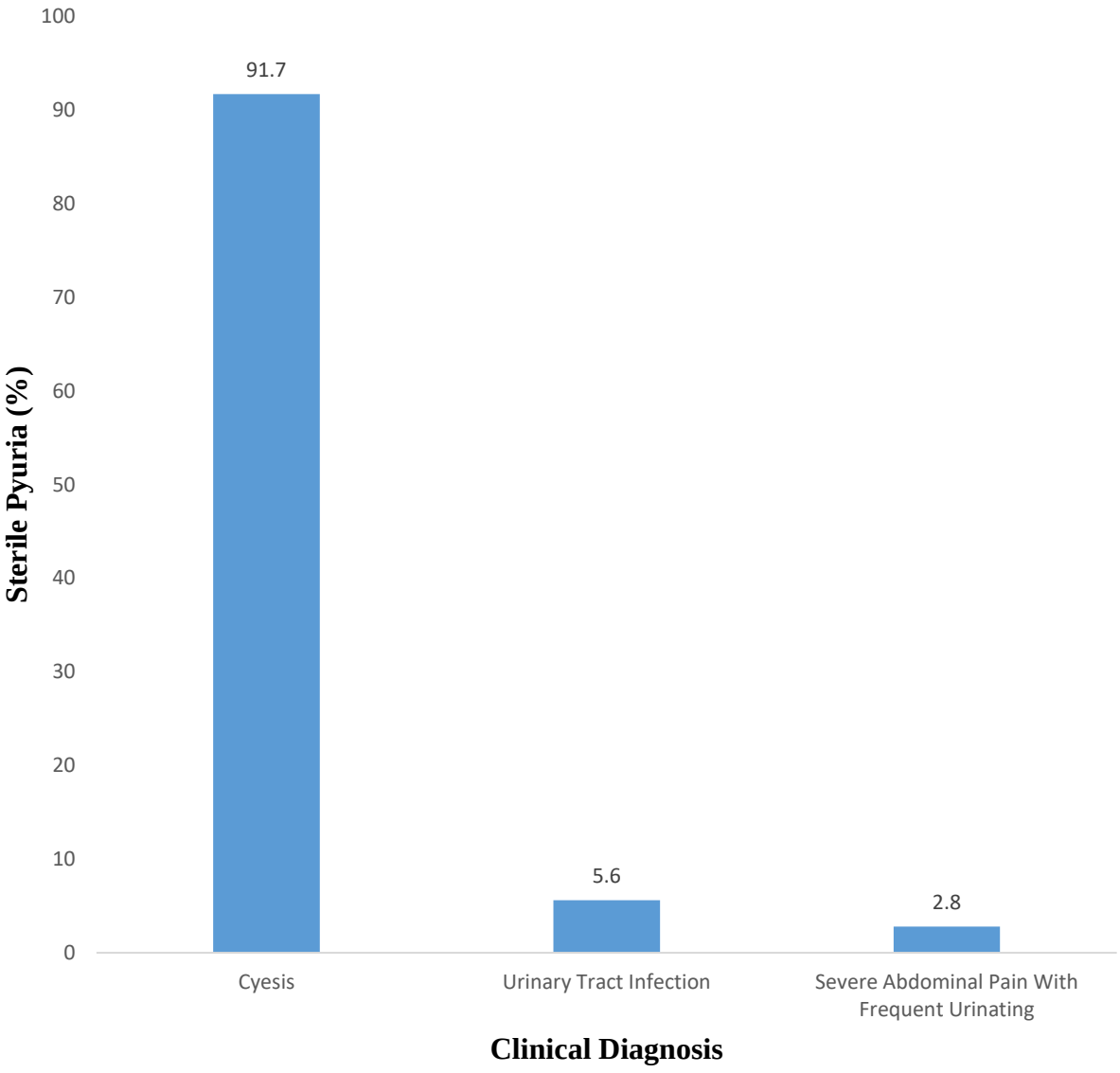

Figure 4. 4: Diagnosis Associated with Sterile Pyuria

4.3 Prevalence of Asymptomatic Bacteriuria (ASB)

Out of 433 and 157 patients' samples analysed for asymptomatic bacteriuria at the Tamale central hospital and Tamale teaching hospital, respectively the prevalence of asymptomatic bacteriuria at the Tamale central hospital was 20.8% (90), whilst the prevalence of asymptomatic bacteriuria at the Tamale teaching hospital was 40.1% (63) with the overall prevalence of asymptomatic bacteriuria being 153 (25.9%) out of 590 patient samples analysed (Table 4.8). The prevalence of asymptomatic bacteriuria at the Tamale teaching hospital was 19.3% higher than the prevalence observed at Tamale central hospital.

There was a statistical difference ($P \leq 0.05$) in prevalence of asymptomatic bacteriuria at the Tamale central and the Tamale teaching hospitals (Table 4.8). The prevalence of asymptomatic bacteriuria was greater in females (81.7%) than males (18.3%) at both hospitals (Table 4.9).

The most isolated organisms in the males at the Tamale teaching hospital were *E. coli* (20.8%), *Serratia* spp. (20.8%), CoNS and *Klebsiella* spp. (16.7%) while the common pathogen found in the females were CoNS (35.9%), *S. aureus* (30.8%) and *E. coli* (10.3%) (Table 4.10). In the case of the Tamale central hospital, *E. coli* (50.0%), *S. aureus* (25.0%) and *Enterobacter* spp. (25.0%) were the most isolated organisms from males whereas CoNS (33.7%), *S. aureus* (26.7%) and *E. coli* (16.3%) were recovered from females (Table 4.10).

The mean age of patients presenting with asymptomatic bacteriuria at the Tamale teaching hospital was 38.37±2.76, whilst the mean age of patients at the Tamale central

hospital was 28.37±2.76 with the overall mean age of patients being 32.48±1.29 (Appendix 8)(Table 5). These were significantly different (P≤0.05) from each other (Table 4.11).

At the Tamale teaching hospital, the highest prevalence of asymptomatic bacteriuria was recorded among the age group of 20-29 years (41.3%) and 30-39 years (22.2%) (Table 4.11). Also, at the Tamale central hospital, the highest prevalence was observed within the age group 20-29 years (61.1%) (Table 4.11).

Whilst the predominant uropathogen associated with asymptomatic bacteriuria (ASB) from the age group of 20-29 years at the Tamale teaching hospital and the Tamale central hospital were CoNS (46.2%) and CoNS (38.2%) respectively. The predominant uropathogen associated with asymptomatic bacteriuria (ABS) isolated from the age group 30-39 years at the Tamale teaching hospital and the Tamale central hospital were *S. aureus* (42.9%) and *S. aureus* (30.8%), respectively (Table 4.12).

There was highest prevalence of asymptomatic bacteriuria in the Antenatal Care department at both the Tamale teaching hospital (54%) and the Tamale central hospital (86.7%) (Table 4.13).

Table 4. 8: Prevalence of Asymptomatic Bacteriuria

	FREQUENCY (%)				
Hospitals	**No of Sample**	**Significant Growth (≥1x10^{5}CFU/ml)**	**Insignificant Growth (<1x10^{5}CFU/ml)**	**Negative**	**P Value**
TTH	157	63(40.1)	90(57.3)	4(2.5)	
TCH	433	90(20.8)	294(67.9)	49(11.3)	
Total	590	153(25.9)	384(65.1)	53(9.0)	0.000

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital

Table 4. 9: Asymptomatic Bacteriuria Among Patients

	FREQUENCY (%)			
Hospitals	**No of Isolates**	**Male**	**Female**	**P Value**
TTH	63	24(38.1)	39(61.9)	0.000
TCH	90	4(4.4)	86(95.6)	0.730
Total	153	28(18.3)	125(81.7)	0.000

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital

Table 4. 10: Frequency of Uropathogens Associated with Asymptomatic Bacteriuria

Isolates	TTH			TCH		
	Frequency	Male (%)	Female (%)	Frequency	Male (%)	Female (%)
S. aureus	14	2(8.3%)	12(30.8%)	24	1(25.0%)	23(26.7%)
CoNS	18	4(16.7%)	14(35.9%)	29	0(0.0%)	29(33.7%)
Streptococcus	2	0(0.0%)	2(5.1%)	3	0(0.0%)	3(3.5%)
E. coli	9	5(20.8%)	4(10.3%)	16	2(50.0%)	14(16.3%)
***Klebsiella* spp.**	6	4(16.7%)	2(5.1%)	5	0(0.0%)	5(5.8%)
***Enterobacter* spp.**	6	3(12.5)	3(7.7%)	8	1(25.0%)	7(8.1%)
Serratia	7	5(20.8%)	2(5.1%)	2	0(0.0%)	2(2.3%)
***Pseudomonas* spp.**	0	0(0.0%)	0(0.0%)	1	0(0.0%)	1(1.2%)
Salmonellae	1	1(4.2%)	0(0.0%)	1	0(0.0%)	1(1.2%)
P. vulgaris	0	0(0.0%)	(0.0%)	1	0(0.0%)	1(1.2%)
Total	63	24(100.0%)	39(100.0%)	90	4(100.0%)	86(100.0%)

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital

Table 4. 11: Prevalence of Asymptomatic Bacteriuria

	Tamale TeachingHospital N = 157	Tamale Central Hospital N = 433	
Ages	**Frequency (%)**	**Frequency (%)**	**P Value**
1-9	3(4.8)	1(1.1)	0.000
10-19	2(3.2)	4(4.4)	
20-29	26(41.3)	55(61.1)	
30-39	14(22.2)	26(28.9)	
40-49	3(4.8)	2(2.2)	
50-59	2(3.2)	1(1.1)	
≥60	13(20.6)	1(1.1)	
Total	63(40.1)	90 (20.8)	

Table 4. 12: Uropathogens Associated with Asymptomatic Bacteriuria Among the Different Age Groups

TTH		Gram Positives				Gram Negatives					
Age	Isol.	*S. aureus*	*CoNS*	*Strept.* spp.	*E. coli*	*Kleb.* spp.	*Entero.* spp.	*Serratia* spp.	*Pseud.* spp.	*Salm.*	*p vulgaris*
1-9	3	66.7%	0.0%	0.0%	0.0%	33.3%	0.0%	0.0%	0.0%	0.0%	0.0%
10-19	2	50.0%	0.0%	50.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
-29	26	15.4%	46.2%	0.0%	15.4%	3.8%	7.7%	11.5%	0.0%	0.0%	0.0%
-39	14	42.9%	28.6%	7.1%	7.1%	7.1%	7.1%	0.0%	0.0%	0.0%	0.0%
-49	3	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	66.7%	0.0%	33.3%	0.0%
-59	2	0.0%	0.0%	0.0%	50.0%	50.0%	0.0%	0.0%	0.0%	0.0%	0.0%
0	13	7.7%	15.4%	0.0%	23.1%	15.4%	23.1%	15.4%	0.0%	0.0%	0.0%
CH											
9	1	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
-19	4	50.0%	25.0%	0.0%	0.0%	0.0%	25.0%	0.0%	0.0%	0.0%	0.0%
-29	55	25.5%	38.2%	1.8%	12.7%	9.1%	7.3%	3.6%	0.0%	0.0%	1.8%
-39	26	30.8%	26.9%	7.7%	19.2%	0.0%	11.5%	0.0%	0.0%	3.8%	0.0%
-49	2	0.0%	0.0%	0.0%	50.0%	0.0%	0.0%	0.0%	50.0%	0.0%	0.0%
-59	1	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
0	1	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, *Strept. -Streptococcus* spp., *Kleb. -klebsiella* spp., *Entero. -Enterobacter* spp., *pseud.-pseudomonas* spp., *CoNS-coagulase negative Staphylococcus*

Table 4. 13: Distribution of Asymptomatic Bacteriuria in the Various Departments of the Hospitals

	TTH		TCH		
WARD	**Frequency**	**Frequency%**	**Frequency**	**Frequency%**	**P Value**
Antenatal Care	34	54	78	86.7	
Emergency	2	3.2	0	0.0	
Gynecology	1	1.6	0	0.0	
Maternity ward	1	1.6	0	0.0	
Out-Patient Dep.	5	7.9	2	2.2	
Urology ward	20	31.7	0	0.0	
ART	0	0.0	7	7.8	
Fistula surgical	0	0.0	3	3.3	
Total	63	100.0	90	100.0	0.000
P Value	0.094		0.000		

TTH=Tamale Teaching Hospital, TCH=Tamale Central Hospital, ART=Anti-Retroviral Treatment.

4.4 Susceptibility Profile of Uropathogens Recovered from TTH and TCH

Generally, Uropathogens from the Tamale teaching hospital showed high resistance to the antibiotics tested than the uropathogens from the Tamale central hospital (Table 4.14). Gram negatives presented more resistance to the antibiotics than the Gram positives recovered from both hospitals, with resistance rate of 48.1-62.1% and 33.0-37.9%, respectively (Table 4.15).

Ampicillin recorded the highest resistance on the uropathogens at both hospitals with resistance percentages of 90.2% and 92.3% for Gram positives and Gram negative, respectively at the Tamale teaching hospital (Table 4.15). Ciprofloxacin and Gentamicin were the most effective against the Gram positives at the Tamale teaching hospital, with resistance percentages of 9.8% (Table 4.15). In the same Tamale teaching hospital, the effective antibiotic against the Gram negative bacteria was Imipenem which showed resistance of 25.6%.

However, at the Tamale central hospital, the percentage resistance of ampicillin was 84.8% and 86.4% for Gram positive bacteria and Gram negative bacteria, respectively (Table 4.15). Amikacin and Gentamicin were the most effective against the Gram positive bacteria at the Tamale central hospital, with resistance of 9.1% and 10.6%, respectively (Table 4.15). In the same Tamale central hospital, the most potent antibiotic against the Gram negative bacteria were Imipenem and Gentamycin which showed resistance of 9.1% and 13.6%, respectively (Table 4.15).

Table 4. 14: Susceptibility Profile of Uropathogens Isolated from TTH and TCH

	TTH		TCH	
	Gram Positive (n=41)	Gram Negative (n=39)	Gram Positive (n=66)	Gram Negative (n=44)
Antibiotic	**S I R**	**S I R**	**S I R**	**S I R**
Ciprofloxacin	36 1 4	20 1 18	42 14 10	32 1 11
Tr. Sulphamethoxazole	22 1 18	8 0 31	38 3 25	11 3 30
Gentamicin	35 2 4	20 1 18	54 5 7	36 2 6
Amikacin	32 2 7	25 1 13	57 3 6	30 0 14
Ampicillin	4 0 37	2 1 36	9 1 56	4 2 38
ACA	19 0 22	6 12 21	37 6 23	20 11 13
Chloramphenicol	21 0 20	7 2 30	41 2 23	18 0 26
Nitrofurantoin	21 5 15	8 1 30	33 11 22	5 6 33
Ceftriaxone	8 18 15	4 9 26	19 30 17	17 9 18
Erythromycin	15 11 15	2 4 33	21 15 30	7 5 32
Tetracycline	24 3 14	7 5 27	41 7 18	7 1 36
Norfloxacin	34 0 7	16 1 22	43 1 22	30 0 14
Cefoxitin	20 4 17	NT	44 10 12	NT
Clindamycin	17 4 20	NT	31 4 31	NT
Vancomycin	23 0 18	NT	40 1 25	NT
Imipenem	NT	27 2 10	NT	40 0 4

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, NT= Not Tested, S= sensitive, I= intermediate, R= resistant, ACA= Amoxicillin Clavulanic Acid, Tr=Trimethoprim

Table 4. 15: Resistance Pattern Among the Uropathogens

	TTH		TCH		
	Gram Positive	Gram Negative	Gram Positive	Gram Negative	P
Antibiotic	(n=41)	(n=39)	(n=66)	(n=44)	Value
Ciprofloxacin	9.8	51.3	15.2	25	0.000
Tr. Sulphamethoxazole	43.9	79.5	37.9	68.2	0.000
Gentamycin	9.8	46.2	10.6	13.6	0.000
Amikacin	17.1	33.3	9.1	31.8	0.000
Ampicillin	90.2	92.3	84.8	86.4	0.000
ACA	53.7	53.8	34.8	29.5	0.000
Chloramphenicol	48.8	76.9	34.8	59.1	0.000
Nitrofurantoin	36.6	76.9	33.3	75	0.000
Ceftriaxone	36.6	66.7	25.8	40.9	0.000
Erythromycin	36.6	84.6	45.5	72.7	0.000
Tetracycline	34.1	69.2	27.3	81.8	0.000
Norfloxacin	17.1	56.4	33.3	31.8	0.000
Cefoxitin	41.5	NT	18.2	NT	0.000
Clindamycin	48.8	NT	47	NT	0.000
Vancomycin	43.9	NT	37.9	NT	0.000
Imipenem	NT	25.6	NT	9.1	0.000
Overall	37.9	62.1	33.0	48.1	0.000
P Value	0.000	0.000	0.000	0.000	

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, NT= Not Teste, ACA= Amoxicillin Clavulanic Acid, Tr=Trimethoprim

4.5 Multidrug Resistance Among the Uropathogens

High multidrug resistance was observed among isolates from Tamale central hospital (90.9%) and the Tamale teaching hospital (88.8%) (Table 4.16). Multidrug resistance among the Gram negatives was 97.4% and 100.0% at the Tamale teaching hospital and the Tamale central hospital, respectively (Table 4.16). While Gram negative bacteria recovered from the Tamale teaching hospital were 16.9% higher in multidrug resistance than the Gram positive bacteria from the Tamale teaching hospital, the Gram negative bacteria from the Tamale central hospital were 15.2% higher in multidrug resistance than the Gram positive bacteria from the Tamale central hospital. However, the Tamale central hospital only recorded 2.1% higher multidrug resistance than the Tamale teaching hospital.

High (100.0%) multidrug resistance was observed in the uropathogens from the Tamale central hospital with the exception of CoNS (76.3%) and *Streptococcus* (66.7%) (Table 4.16). However, the CoNS, *Streptococcus* and *Serratia* spp from the Tamale central hospital recorded 6.7%, 16.7% and 12.5% respectively higher multidrug resistance than the CoNS, *Streptococcus* and *Serratia* from the Tamale teaching hospital (Table 4.16).

Multidrug resistance was recorded in isolates from males (78.4%) than females (74.5%) in this research (Table 4.17). At the Tamale teaching hospital, higher multidrug resistance was identified in males (85.2%) than females (73.6%) (Table 4.17) however, at the Tamale central hospital, higher multidrug resistance was observed in females (75.0%) than males (60.0%) (Table 4.17). Though, these variations observed were not significant (P = 0.263).

Except for the age groups of 20-29 years (75.0%) and ≥60 years (83.3%), multidrug resistance was high (100.0%) across all other age groups at the Tamale teaching hospital (Table 4.18). However, within the Tamale central hospital, highest multidrug resistance was observed within the age groups of 1-9 years (100.0%) and 40-49 years (100.0%) (Table 4.18).

All the bacteria (uropathogens) isolated from the patients at the various departments of both hospitals showed >80% multidrug resistance (Table 4.19).

Except for isolates associated with cyesis (91.2%), urine retention (25.0%), urethral stricture (66.7%) and visco-vaginal fistula (0.0%), all isolates associated with the various diagnosis showed 100% multidrug resistance at the Tamale teaching hospital (Table 4.20).

At Tamale central hospital, uropathogens from patients diagnosed with cyesis showed multidrug resistance of 93.8%. But isolates associated with HIV AIDS and visco-vaginal fistula showed 100% multidrug resistance at the Tamale central hospital (Table 4.20).

Table 4. 16: Multidrug Resistance Among Uropathogens

	TTH		TCH		
Isolates	**No of Isolates**	**MDR (%)**	**No of Isolates**	**MDR (%)**	**P Value**
Gram Positive	41	33(80.5)	66	56(84.8)	
Gram Negative	39	38(97.4)	44	44(100.0)	
Total	80	71(88.8)	110	100(90.9)	0.624
S. aureus	16	16(100.0)	25	25(100.0)	
CoNS	23	16(69.6)	38	29(76.3)	
Streptococcus	2	1(50.0)	3	2(66.7)	
E. coli	14	14(100.0)	21	21(100.0)	
***Klebsiella* spp.**	8	8(100.0)	7	7(100.0)	
***Enterobacter* spp.**	7	7(100.0)	9	9(100.0)	
***Serratia* spp.**	8	7(87.5)	3	3(100.0)	
***Pseudomonas* spp.**	0	0(0.0)	1	1(100.0)	
Salmonellae	2	2(100.0)	2	2(100.0)	
P. vulgaris	0	0(0.0)	1	1(100.0)	
Total	80	71(88.8)	110	100(90.9)	0.624

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, MDR= Multidrug Resistance, *CoNS-Coagulase Negative Staphylococcus*

Table 4. 17: Multidrug Resistance Distribution by Sexes of Patients

	Male		Female	
Hospitals	**No of Isolates**	**MDR (%)**	**No of Isolates**	**MDR (%)**
TTH	27	23(85.2)	53	39(73.6)
TCH	10	6(60.0)	100	75(75.0)
Total	37	29(78.4)	153	114(74.5)

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, MDR=Multidrug Resistance

Table 4. 18: Multidrug Resistance Distribution by Age Groups

	TTH		TCH	
Ages	**No of Isolates**	**MDR (%)**	**No of Isolates**	**MDR (%)**
1-9	5	5(100.0)	1	1(100.0)
10-19	2	2(100.0)	7	5(71.4)
20-29	28	21(75.0)	60	59(98.3)
30-39	18	18(100.0)	30	28(93.3)
40-49	6	6(100.0)	6	6(100.0)
50-59	3	3(100.0)	3	2(66.7)
≥60	18	15(83.3)	3	2(66.7)

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, MDR=Multidrug Resistance

Table 4. 19: Multidrug Resistance of Uropathogens Among Different Wards

	TTH		TCH	
WARD	**No of Isolates**	**MDR (%)**	**No of Isolates**	**MDR (%)**
Antenatal care	38	33(86.8)	78	75(96.2)
Emergency ward	2	2(100.0)	0	0(0.0)
Gynecology	2	2(100.0)	0	0(0.0)
Out-Patient Dep.	12	10(83.3)	17	13(76.5)
Female ward	2	1(50.0)	3	2(66.7)
Prenatal	1	1(100.0)	0	0(0.0)
Male ward	0	0(0.0)	1	1(100.0)
Maternity ward	1	0(0.0)	1	1(100.0)
Urology	22	20(90.9)	0	0(0.0)
ART	0	0(0.0)	7	7(100.0)
Fistula	0	0(0.0)	3	3(100.0)

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, MDR=Multidrug Resistance, ART=Anti-Retroviral Treatment.

Table 4. 20: Multidrug Resistance of Uropathogens Associated with Different Diagnosis

	TTH		TCH	
Clinical Diagnosis	**No of Isolates**	**MDR (%)**	**No of Isolates**	**MDR (%)**
Appendicitis	1	1(100.0)	0	0(0.0)
Cyesis	34	31(91.2)	80	75(93.8)
Diabetes Mellitus	1	1(100.0)	0	0(0.0)
Deep Vein Thrombosis	1	1(100.0)	0	0(0.0)
Begnin Prostrate Hyperplasia	9	9(100.0)	0	0(0.0)
Epididymitis	1	1(100.0)	0	0(0.0)
UTI	17	15(88.2)	20	16(80.0)
Urine Retention	4	1(25.0)	0	0(0.0)
Hepatitis B	1	1(100.0)	0	0(0.0)
Hyperparathyroidism	2	2(100.0)	0	0(0.0)
Malaria/Anaemia	1	1(100.0)	0	0(0.0)
Scrotal Crop	1	1(100.0)	0	0(0.0)
Urethral Stricture	3	2(66.7)	0	0(0.0)
Sepsis	1	1(100.0)	0	0(0.0)
Urethroplasty	2	2(100.0)	0	0(0.0)
HIV AIDS	0	0(0.0)	7	7(100.0)
Viscos vaginal fistula	1	0(0.0)	3	3(100.0)

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital, MDR=Multidrug Resistance

CHAPTER FIVE

DISCUSSION

5.1 Prevalence of Urinary Tract Infection

This research revealed that the prevalence of urinary tract infection (UTI) at the Tamale central hospital and the Tamale teaching hospital was 21.4% and 36.0%, respectively with the overall prevalence of 25.8%. These results are higher than the prevalence (18.5%) reported by Labi *et al.* (2019) in both the northern and the southern sector of the country. However, it is similar to the findings by Agyepong *et al*. (2018) and Gyansa-Lutterodt *et al*. (2014) who reported 31.6% and 34.5% at the Ghana police hospital and the Komfo Anokye teaching hospital, respectively both in the southern sector of Ghana. The differences in prevalence can be attributed to different ways of practices and human activities relating to personal hygiene as well as socioeconomic conditions. According to Badran *et al*. (2015), cross infections from partners, socioeconomic conditions and human activities relating to personal hygiene remain some of the contributory factors for the development of UTI. The socioeconomic situations (level of education, presence of co-wives) of the people in the northern part of Ghana are different from the southern sector, these could be the reasons why prevalence was different from the prevalence reported in the southern sector.

Females recorded higher prevalence of urinary tract infection than males at both the Tamale teaching hospital and the Tamale central hospital. A similar trend of result was found by Gyansa-Lutterodt *et al*. (2014) at the Ghana police hospital in Accra, Ogbukagu *et al.* (2016) in Nigeria and Salwa & Maher (2014) in Yemen which showed that females can be 34.8%, 4% and 32.8% respectively, more infected than males. This can be

attributed to variation in length of urethra among the sexes. Unlike men who have longer urethra, women have shorter urethra and the nearness of the anal opening to the vagina sometimes lead to the incidence of symptomatic infection (Levinson, 2010; Minardi *et al*., 2011). According to Minardi *et al*. (2011), "fecal-perineal urethral contamination is the most probable explanation for urinary tract infections caused by enteric bacteria in women".

The frequency of uropathogens was higher in females than males at both the Tamale teaching hospital and the Tamale central hospital. The most isolated organism in males at both the Tamale teaching hospital and the Tamale central hospital was *E. coli*. This is related to findings by Gyansa-Lutterodt *et al*. (2014) at the Ghana police hospital in the southern sector. It also agrees with other research in Nigeria (Ogbukagu *et al*., 2016), in Yemen (Salwa & Maher, 2014) and in Brazil (Luiz *et al*., 2012) who also found *E. coli* as dominant uropathogens in males. The higher frequency of *E. coli* isolated may be attributed to the contamination of the urinary tract from the rectal area and various enhanced virulence factors (adhesive nature) specific for colonization and invasion of the urinary epithelium (Kabew *et al.*, 2013; Kucheria *et al*., 2005).

However, predominant organisms found in females at both the Tamale teaching hospital and the Tamale central hospital were CoNS and *S. aureus* which is comparable to results in Nigeria by Ibadin *et al*. (2012). This is attributed to *Staphylococcus* spp. being a normal flora of the urogenital area at puberty, which may invade the urinary tract during sexual activity especially in females (Michael & Adenike, 2016). Studies have also found *Staphylococcus* spp. as an increasing cause of UTI which could be assigned to increased instrumentation (Foxman, 2003; Muder *et al*., 2006). According to Pereira *et*

al., (2013) *Staphylococcus* spp. is an opportunistic pathogen carried asymptomatically on the human body that can find their way into the body at any given opportunity.

Within the Tamale teaching hospital and the Tamale central hospital, the highest prevalence of urinary tract infection was recorded among the age group between 20-29 years and 30-39 years. This can be compared to a similar research by Ogbukagu *et al.* (2016) in Nigeria who reported that, in both sexes, the highest incidence of UTI can be found among the age group of 26 to 38 years but in contrast with Iregbu *et al*. (2013) in the same country who reported that, the highest rate of urinary tract infections are found in the age group below 1 year and above 57 years. This is as a result of these age groups (1 year and above 57 years) not being sexually active as it has been reported by other researchers that urinary tract infections are more common in sexually active individuals (Mccormick *et al*., 2008) because of the frequent sexual activities. Sexual intercourse can injure the uroepithelium of the distal urethra (Mccormick *et al*., 2008) resulting in increased bacterial colonisation. According to Nicolle (2008) about 75% to 90% bladder infections are caused by sexual activity in young sexually active women.

The significant difference ($P \leq 0.05$) of urinary tract infections among different age groups of people within and between the Tamale teaching hospital and the Tamale central hospital is contrary to Getu (2015) who reported that UTI can be found among any age group of people but does not vary statistically ($P>0.05$) with diverse age groups.

This research also revealed highest prevalence of urinary tract infection in the Antenatal Care department, and patients associated with cyesis at both the Tamale teaching hospital and the Tamale central hospital. According to Otajevwo (2013), the prevalence of UTI

in out- patients can be as high as 41.7% to 58.3%. Also, patients from Antenatal Care department and patients associated with cyesis are mostly pregnant women. Donkor *et al*. (2019) found that pregnancy is the main factor of UTI. During pregnancy development, urinary tract infection is associated with immobility of urine in the ureters, which restricts draining of the bladder, with a rise in post void residual urine volume, and a rise in urinary pH (Krcmery *et al*., 2001). These changes can allow uropathogens to penetrate, multiply and rise proximally causing UTI in women. Most pregnant women (about 70%) suffer glycosuria and this, in mixture with physiological amino acid urea at pregnancy and a drop in urine osmolality, favour bacterial spread (Mccormick *et al.*, 2008).

5.2 Incidence of Sterile Pyuria Among Patients at TCH

A prevalence of 67.9% sterile pyuria was observed at the Tamale central hospital. Though this result is higher than the result found in India (28.8%) (Awasthi *et al*., 2012), it is however comparable with the result found in the United States (74%) (Shipman *et al*., 2018).

Females recorded higher prevalence of sterile pyuria than males which agrees with the study of Hooker *et al*. (2014) who found that sterile pyuria is common with women as compared with men due to pelvic infections which are always associated with women. Alwall & Lohi (1973) also reported that sterile pyuria is a common disorder, for which the rate for women and men are 13.9% and 2.6%, respectively, though sometimes sterile pyuria can be as high as 46% in males suffering from Genitourinary tuberculosis (GU-TB) (Garcia-Tello *et al*., 2010).

Sterile pyuria associated with females was high among the age group of 20-29 years. This may be ascribed to pelvic infection as these age groups being women are at their reproductive ages. According to Awasthi *et al.* (2012) sterile pyuria can be found among pregnant women between 21 and 35 years. This is as a result of pelvic infection being common during pregnancy (Hooker *et al*., 2014).

High prevalence of sterile pyuria was also observed in the Antenatal Care department and patients associated with cyesis. This can be attributed to participants in this ward always being women at their reproductive ages and most of them being pregnant since the factors (pelvic infection) associated with sterile pyuria are mostly associated with pregnancy (Hooker *et al*., 2014).

5.3 Prevalence of Asymptomatic Bacteriuria

This research revealed that the rate of asymptomatic bacteriuria at the Tamale central hospital was 20.8% whereas the rate of asymptomatic bacteriuria at the Tamale teaching hospital was (40.1%) with the overall rate of asymptomatic bacteriuria of 25.9%. These results are higher than the 5-8% reported in the southern sector of Ghana (Labi *et al*., 2015; Turpin *et al*., 2007), in India (8.47%) (Awasthi *et al*., 2012) but lower than the prevalence (56.5%) reported in Cape Coast in the southern sector of Ghana (Boye *et al*., 2014). The differences of asymptomatic bacteriuria (ASB) can be ascribed to sexual behavior and socioeconomic status of the people. According to Mittal & Wing (2005) socioeconomic conditions, sexual behavior are some of the factors that cause ASB. In northern Ghana, most of the populist are low income earners with different socioeconomic status (level of education, presence of co-wives) from the southern sector

and that could have been the reasons for the differences in the prevalence of ASB (Kanmiki et al., 2014).

The most isolated organisms associated with asymptomatic bacteriuria within the males at the Tamale teaching hospital and the Tamale central hospital were *E. coli*. This is comparable to the findings by Boye *et al*. (2014) in Cape Coast in the southern sector of Ghana. It also agrees with another research in Brazil (Luiz *et al.*, 2012).

However, the most isolated organisms associated with asymptomatic bacteriuria within females at the Tamale teaching hospital and the Tamale central hospital were CoNS and *S. aureus*. A similar result was found in Nigeria by Ibadin *et al*. (2012).

The prevalence of asymptomatic bacteriuria was higher in females than males at both the Tamale teaching hospital and the Tamale central hospital. The differences of ASB in sex can also be due to the structural disparity of their Urinary Tracts. Unlike men who have longer urethra, women have shorter urethra and the closeness of it to the anus and vaginal introitus sometimes lead to the incidence of asymptomatic infection (Hooton *et al*., 1999; Levinson, 2010; Minardi *et al*., 2011). According to Minardi *et al*. (2011), infections caused by enteric bacteria are caused by fecal perineal urethral contamination.

5.4 Susceptibility Profile of Uropathogens Recovered from TTH and TCH

Generally, the isolates presented high resistance to the antibiotics tested at both the Tamale teaching hospital and the Tamale central hospital. Ampicillin recorded the highest resistance on the pathogens recovered at both hospitals with resistance of over 90% for Gram positives and Gram negative isolates. These findings is consistent with results in the northern region of Ghana (>90%) (Darkom, 2014), in the northern, middle

and southern sector of Ghana (>70) (Opintan *et al.*, 2015) and in Nigeria (>90%) (Iregbu *et al*., 2013). It also agrees with Agyepong *et al*. (2018) who reported that the resistance pattern of ampicillin and trimethoprim/sulfamethoxazole can be as high as 94.4% and 84.5%, respectively. This may be ascribed to self-medication and misuse of antibiotics as inappropriate exposure to antibiotics drives development of resistance (Iregbu *et al*., 2013; Opintan *et al*., 2015; Prestinaci *et al*., 2016). However, whilst ciprofloxacin, amikacin and gentamicin were the most effective against the Gram positive bacteria at both hospitals, the most effective antibiotic for the Gram negative bacteria was Imipenem. This may be as a result of these antibiotic not being always prescribed for the treatment of UTI in Ghana. A research in Nigeria and North Eastern Karnataka proved that Imipenem could be a better option for dealing with Gram negative bacteria (Iregbu *et al*., 2013; Morehead & Scarbrough, 2018).

5.5 Multidrug Resistance Among the Uropathogens

High multidrug resistance was observed in all the uropathogens from the Tamale central hospital and at the Tamale teaching hospital. The high multidrug resistance observed confirms the findings of Getu (2015) who reported that multidrug resistance can be as high as 96% with uropathogens in Addis Ababa, Ethiopia. Also, according to Agyepong *et al*. (2018), about 89.5% of bacterial isolates are multidrug resistance in Ghana, varying from 53.8% to 100% for *Enterobacter* spp. and *Acinetobacter* spp., respectively. Misuse of antibiotics and self-medication of cheaper antibiotics, and their frequent use in both humans and animals (Opintan *et al*., 2015; Provincial Infection Control (PIC), 2011) as well as prolonged use of antibiotics and its usage for food and animal production

(Prestinaci *et al*., 2016) are some of the factors that induce bacteria to render antibiotics useless or inactive (PIC, 2011) causing antibiotic and multidrug resistance.

Generally, high multidrug resistance was recorded in males than females in this research. However, at the Tamale teaching hospital, higher multidrug resistance was present in males than females. This is comparable to a result reported by Baral *et al.* (2012) but inconsistent with the findings of Mbanga & Dube (2010) who stated no difference in antibiotic resistance between males and females, though the results of this research seem higher, which could be attributed to misuse of antibiotics as reported by Garcia-Vello *et al*., (2020) in the Tamale teaching hospital in the Northern Region of Ghana.

Except for patients between 20-29 years (75.0%) and ≥60 years (83.3%) multidrug resistance was high among isolates across all the age groups at the Tamale teaching hospital and the Tamale central hospital. According to Mbanga & Dube (2010) and Mehta *et al*. (2012), antibiotic resistance increases with age. Another research conducted in Korea indicated that age can lead to antibiotic resistance among Gram negative isolates that are associated with UTI (Yun *et al*., 2017). This means multidrug resistance can occur across all the age groups due to the misuse of antibiotics.

Except for the bacterial isolates from the Antenatal care, out-patients' department, female ward, maternity ward and urology department, all the bacteria isolated from the patients of the various wards at the Tamale teaching hospital and the Tamale central hospital showed 100% multidrug resistance. Similar results was found by Baral *et al.* (2012).

Almost all the bacteria isolated from the people associated the various diagnosis at the Tamale teaching hospital and the Tamale central hospital showed 100% multidrug

resistance. This is attributed to misuse of antibiotics and self-medication of cheaper antibiotics (Opintan *et al*., 2015). Evidence of misuse of antibiotic had been reported in the Tamale teaching hospital in the Northern Region of Ghana. (Garcia-Vello *et al*., 2020). In Ghana, a wide range of antibiotics are available on the market and acquiring drugs over the counter is a very common practice, facilitating self-medication which is thought to be highly prevalent in the Ghanaian community (Feglo & Adu-Sarkodie, 2016; Van den Boom *et al*., 2010). High prevalence (70%) of self-medication was reported in Accra which was attributed to inexpensive compared to medical care in the hospital, delays in medical care in hospitals (Donkor *et al*., 2012).

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

Urinary tract infection (UTI) at both the Tamale teaching hospital and the Tamale central hospital was 36.0% and 21.4% respectively, which is much higher than reported rates from Kumasi and Accra, both in the Southern sector of the country. The prevalence of UTI is higher among females as compared to males. Coagulase negative *Staphylococcus* (CoNS), *E. coli, S. aureus, Serratia* spp. *Klebsiella* spp. and *Enterobacter* spp. are the common organisms isolated from UTI patients. The high prevalence of urinary tract infection is recorded between 20-29 years.

In this research, the prevalence of sterile pyuria is 67.9%, which is much higher than prevalence reported by other researchers in Africa and is frequently found in females than males.

Asymptomatic bacteriuria at both the Tamale teaching hospital and the Tamale central hospital is 40.1% and 20.8%, respectively with a higher prevalence in females than males. It is significantly high ($P \leq 0.05$) among the age group of 20-29 years.

Generally, Uropathogens isolated at both the Tamale teaching hospital and the Tamale central show significantly high ($P \leq 0.05$) resistance to almost all the antibiotics tested. Ampicillin recorded the least effective against uropathogens in this study. However, Ciprofloxacin, Imipenem, Amikacin and Gentamicin are the only moderately effective antibiotics against uropathogens. High (100%) multidrug resistance is observed with *S.*

aureus, *E. coli*, *Enterobacter* spp. and *Klebsiella* spp.. Multidrug resistance is generally seen in male isolates than females.

6.2 Recommendations

- There should be public education on the consequences of misuse of antibiotics.
- Due to the high resistance rate observed, susceptibility test to confirm the efficacy of antibiotics at these hospitals is necessary.
- Asymptomatic bacteria and sterile pyuria are conditions which must be critically considered in the management of UTI infections in these hospitals due to the high rates recorded among patients in this study.
- Future work should be geared towards ascertaining the prevalence rates of UTI and ASB in the various trimester of pregnant women.

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APENDICES

Appendix 1: Ethical clearance

TAMALE TEACHING HOSPITAL ETHICAL REVIEW COMMITTEE

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

My Ref. NO:
TTHERC/25/06/19/14

Your Ref. No:

Tamale Teaching Hospital
P O Box 16
Tamale
03720-22545/22483

25th June 2019

Dr. Akosua Bonsu Kakari
Department of Clinical Microbiology
School of Medicine and Health Sciences
University for Development

Dear Dr Akosua,

ETHICS APPROVAL –ID NO: TTHERC/25/06/19/14

The Tamale Teaching Hospital Ethical Review Committee (TTHERC) reviewed and approved your study protocol titled: **"Prevalence of Urinary Tract Infections among Patients Reporting at the Tamale Teaching Hospital"** during the committee's full board meeting on 19th of June, 2018.

Please note that this approval is for a period of 12 months, beginning **1st January 2019 to 31st December 2019.** Any modification to your approved research protocol requires TTHERC approval.

You are required to report all serious adverse events related to the ERC within seven days verbally and fourteen days in writing and to submit a final report to the TTHERC at the end of the research project.

Please always quote the protocol identification number in all future correspondence in relation to this approved protocol.

Sincerely,

Dr Solomon K. Gumanga.
TTH ERC Ag. Chairperson

THE CHAIR
TAMALE TEACHING HOSPITAL
ETHICAL REVIEW COMMITTEE
NORTHERN REGION-GHANA

Cc. Head Research and Development, Tamale Teaching Hospital, Northern Region-Ghana

Appendix 2: Participant Information Leaflet

Title of Research: Urinary Tract Infections

Name and affiliation of researcher: This study is being conducted by Dr. Akosua Bonsu Karikari of University for Development Studies, Tamale.

Background: Urinary tract infection (UTI) is a common clinical presentation in most hospitals worldwide. Effective management of UTI infections is often hindered by inadequate facilities for isolation and antimicrobial susceptibility testing. Studies conducted in southern Ghana revealed striking resistance among isolates to commonly prescribed antibiotics but data in northern part of the country is virtually non-existent.

Purpose of research:

The purpose of this research is to find out the pattern of microbial isolates and their susceptibility profiles.

Procedure of the research: Urine samples will be obtained from participants, processed in the laboratory to isolate the target organism and carry out susceptibility test to obtain the resistance profiles.

Risk: Procedure is non-invasive

Confidentiality:

All information collected in this study will be given code numbers. No name will be recorded. Data collected cannot be linked to you in anyway. No name or identifier will be used in any publication or reports from this study.

Voluntariness: Taking part in this study should be out of your own free will. You are not under obligation to. Research is entirely voluntary.

Alternatives to participation: If you choose not to participate, this will not affect your treatment in this hospital in any way.

Contacts: If you have any question concerning this study, please do not hesitate to contact Dr. Akosua Bonsu Karikari on 026 5464738).

Appendix 3: Consent Form

Statement of person obtaining informed consent:

I have fully explained this research to _____ and have given sufficient information about the study, including that on procedures, risks and benefits, to enable the prospective participant make an informed decision to or not to participate.

DATE: _____ NAME: _____

Statement of person giving consent:

I have read the information on this study/research or have had it translated into a language I understand. I have also talked it over with the interviewer to my satisfaction.

I understand that my participation is voluntary (not compulsory).

I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it.

I understand that I may freely stop being part of this study at any time without having to explain myself.

I have received a copy of this information leaflet and consent form to keep for myself.

NAME: _____

DATE: _____ SIGNATURE/THUMB PRINT: _____

Statement of person witnessing consent (Process for Non-Literate Participants):

I _____ (Name of Witness) certify that information given to

_____ (Name of Participant), in the local language, is a true reflection of what l have read from the study Participant Information Leaflet, attached.

WITNESS' SIGNATURE (maintain if participant is non-literate): _____

MOTHER'S SIGNATURE (maintain if participant is under 18 years): _____

MOTHER'S NAME: _____

FATHER'S SIGNATURE (maintain if participant is under 18 years): _____

FATHER'S NAME: _____

Appendix 4: Media Preparation

Preparation Cysteine Lysine Electrolyte Deficient (CLED)

CLED was prepared according to the manufacturer's protocol. A total of 36.2 grams of the CLED was weighed using an electronic balance. It was then suspended in 1000ml of distilled water in a conical flask. It was brought to boil with constant agitation to dissolve completely using a heating mantle with a magnetic stirrer. It was autoclaved at a temperature of 121 ^{0}C and a pressure of 1bar for 15 minutes. It was allowed to cool to about 37 ^{0}C and poured into petri dishes to solidify before use.

Preparation of Nutrient Agar

Nutrient agar was prepared according to the manufacturer's protocol. A total of 28 grams of the Nutrient agar was weighed using an electronic balance. It was then suspended in 1000ml of distilled water in a conical flask. It was brought to boil with constant agitation to dissolve completely using a heating mantle with a magnetic stirrer. It was autoclaved at a temperature of 121 ^{0}C and a pressure of 1bar for 15 minutes. It was allowed to cool to about 37 ^{0}C and poured into petri dishes to solidify before use.

Preparation of Simon Citrate Agar

Simon Citrate agar was prepared according to the manufacturer's protocol. A total of 23 grams of the Simon citrate agar was weighed using the electronic balance. It was then suspended in 1000ml of distilled water in a conical flask. It was brought to boil with constant agitation to dissolve completely using a heating mantle with a magnetic stirrer. It was autoclaved at a temperature of 121 ^{0}C and a pressure of 1bar for 15 minutes. It was allowed to cool to about 37 ^{0}C and poured into petri dishes to solidify before use.

Preparation of Blood Agar

Blood agar was prepared according to the manufacturer's protocol. A total of 39 grams of the blood agar was weighed using an electronic balance. It was then suspended in 1000ml of distilled water in a conical flask. It was brought to boil with constant agitation to dissolve completely using a heating mantle with a magnetic stirrer. It was autoclaved at a temperature of 121 ^{0}C and a pressure of 1bar for 15 minutes. It was allowed to cool to about 50 ^{0}C and 10% of sterile sheep blood was added, mixed well using a magnetic stirrer and poured into petri dishes to solidify before use.

Triple Sugar Iron (TSI) Preparation

TSI was prepared according to the manufacturer's protocol. A total of 65 grams of the TSI was weighed using an electronic balance. It was then suspended in 1000ml of distilled water in a conical flask. It was brought to boil with constant agitation to dissolve completely using a heating mantle with a magnetic stirrer. It was dispensed in test tubes and autoclaved at a temperature of 121 ^{0}C and a pressure of 1bar for 15 minutes. The test tubes with the TSI were tilted and allowed to cool and solidify before use.

Tryptone Soya Broth Preparation

Tryptone soya broth preparation was prepared according to the manufacturer's protocol. A total of 30 grams of the Tryptone soya broth was weighed using an electronic balance. It was then suspended in 1000ml of distilled water in a conical flask. It was mixed well to dissolve completely using a magnetic stirrer. It was dispensed in test tubes and autoclaved at a temperature of 121 ^{0}C and a pressure of 1bar for 15 minutes. It was allowed to cool before use.

Preparation of Storage Medium

Tryptone soya broth was prepared according to the manufacturer's protocol. A total 30 grams of the Tryptone soya broth was weighed using an electronic balance. It was then suspended in 1000ml of distilled water in a conical flask. And 20% of glycerol was added. It was mixed well to dissolve completely using a magnetic stirrer. It was dispensed in cryovial and autoclaved at a temperature of 121 ^{0}C and a pressure of 1bar for 15 minutes using an autoclave. It was allowed to cool before use.

Preparation of Mueller Hinton Agar

Preparation of Mueller Hinton agar was according to the manufacturer's protocol. A total of 38 grams of Mueller Hinton agar was weighed using an electronic balance. It was then suspended in 1000ml of distilled water in a conical flask. It was brought to boil with constant agitation using a heating mantle with a magnet stirrer to dissolve completely. It was autoclaved at a temperature of 121 ^{0}C and a pressure of 1bar for 15 minutes. It was allowed to cool to about 37 ^{0}C and poured into petri dishes to solidify before use.

Appendix 5: Biochemical Tests

Source: Microbe Online (2019)

Coagulase Test

Coagulase test is used to distinguish *Staphylococcus aureus* which is coagulase positive from Coagulase Negative Staphylococcus (CoNS). Coagulase is an enzyme produced by *S. aureus* that converts soluble fibrinogen in plasma to insoluble fibrin. *Staphylococcus aureus* is detected when plasma coagulates when isolate is introduced.

Catalase Test

Catalase test reveals the presence of the enzyme catalase, an enzyme that catalyses the release of oxygen from hydrogen peroxide (H_2O_2). This is used to differentiate organisms that produce an enzyme catalase, such as *staphylococci*, from non-catalase producing bacteria such as *streptococci*. Usually for the routine culture 3% H_2O_2 is used whereas 15% H_2O_2 is used for detection of catalase in anaerobes. The enzyme catalase facilitates the breakdown of hydrogen peroxide into oxygen and water. The presence of the enzyme in a bacterial isolate is evident when a small inoculum is introduced into hydrogen peroxide, and the rapid release of oxygen bubbles occurs. The lack of catalase is evident by a lack of or weak bubble production.

Mannitol Fermentation Test

The aim of mannitol agar test is to see if the microbe can ferment mannitol as a carbon source. If mannitol is fermented to produce acid as the end products, the pH of the medium will drop. A pH indicator in the medium changes colour to designate acid production. Most commonly used indicator is phenol red. The pH indicator phenol red is

red at neutral pH but turns yellow at pH less than 6.8. It also changes to magenta or hot pink at pH greater than 8.4.

Triple Sugar Iron Agar Test

It is used to define whether gram negative bacilli ferment glucose and lactose or sucrose and produce hydrogen sulfide (H_2S). It comprises ten parts of lactose, ten parts of sucrose, 1 part of glucose and peptone. Acidification of medium and H_2S production are detected by phenol red and ferrous sulphate respectively. First, fermentative organism utilize glucose and turning the whole medium acidic in 8 to 12 hours showing yellow colouration. It remains acidic even after 18 to 24 hours of incubation period because of the presence of organic acids resulting from the fermentation of glucose under anaerobic conditions in the butt of the tube. The slant reverts to alkaline state that is shown by red colour as the fermentation products become oxidised to carbon dioxide (CO_2) and water (H_2O). Also, peptone in aerobic condition the slant undergoes oxidation releasing alkaline amines (Phenol red in alkaline pH turns red while in acidic pH turns yellow). The slant becomes red and butt remains yellow within 18 to 24 hrs if the organism ferments glucose but does not ferment lactose and/or sucrose. The fermentation product formed on the slant is more than neutralize the alkaline amines if the organism in addition to glucose ferments lactose and/or sucrose, rendering the slant acidic (yellow) provided the reaction is read within 18 to 24 hours. If the organism is a non-fermenter, instead of sugars, peptone is utilised as an alternate source of energy under aerobic condition on the slant which makes it alkaline indicated by the red color while there is no change in the color of the butt. Reactions in TSI should not be read after 24 hours of incubation, because aerobic oxidation of fermentation products from lactose and/or sucrose will

occur and the slant will eventually revert to alkaline state. The formation of CO_2 and H_2 is indicated by the presence of bubbles or cracks in the medium or by the separation of the agar from sides or bottom of the tube. The production of H_2S requires an acidic condition and is indicated by blackening of the butt of the medium in the tube.

Indole Test

This test is used to determine the ability of an organism to split amino acid tryptophan into the compound indole. Tryptophan is hydrolysed by tryptophanase to form three end products, one of which is indole. Indole production is observed by Kovac's reagent which comprises 4 (p)-dimethyl amino benzaldehyde, this compound reacts with indole to produce a red coloured compound. It is a normally used biochemical test which aids to differentiate *Enterobacteriaceae* and other genera.

Oxidase Test

The oxidase test is used to identify bacteria that produce the enzyme, cytochrome c oxidase, an enzyme of the bacterial electron transport chain. In its existent, the cytochrome c oxidase oxidizes the reagent, tetramethyl-p-phenylenediamine to indophenols purple colour end product. When the enzyme is not present, the reagent remains reduced and is colourless.

Citrate Test

Citrate test is used to demine the ability of the organism to utilize sodium as its only source of carbon. When an organic acid like citrate is used as a carbon and energy source, alkaline carbonates and bicarbonates are released, also ammonium hydroxide are formed when the ammonium salt in the medium is used as the sole source of nitrogen. Utilization of exogeneous citrate requires citrate transport proteins (permeases). Upon the uptake by

the cells, citrate is cut by the citrate lyase to oxaloacetate and acetate. The oxaloacetate is then broken down to pyruvate and carbon dioxide. Further metabolic breakdown depends upon the pH of the medium.

Under alkaline conditions, pyruvate is metabolized to acetate and formate. pyruvate = acetate + formate. At pH 7.0 and below, lactate and acetoin are also produced.

pyruvate =acetate+lactate+CO_2

pyruvate=acetoin+CO_2

The carbon dioxide that is released will subsequently react with water and the sodium ion in the medium to produce sodium carbonate, an alkaline compound that will raise the pH. In addition, ammonium hydroxide is produced when the ammonium salts in the medium are used as the sole nitrogen source. Growth usually results in the bromothymol blue indicator, turning from green to blue. The bromothymol blue pH indicator is deep forest green at neutral pH. With an increase in medium pH to above 7.6, bromothymol blue changes to blue.

Appendix 6: Key Identification Characteristics for the most Common Enterobacteriaceae

Table 1: Biochemical Identification Chart

Species	URE	VP	ONPG	LACT	MAN	GLU	SUC	OX	CIT	MOT	IND	LDC	MR	PAD	ORN	ARG	TSI			
																	SLOPE	BUTT	H_2S	GAS
E. coli.	-	-	+	+	+	+	D	-	-	+	+	+	+	-	+/-	-/+	Y	Y	-	+
Shigella spp.	-	-	-	-	d	+	-	-	-	-	D	-	+	-	-	-	R	Y	-	-
Edward. Tarda	-	-	-						-	+	+		+	-	+	-	R	Y	+	+
Sal. paratyphi A	-	-	-	-	+	+	-	-	-	+	-	-					R	Y	-	+
Sal. Typhi	-	-	-	-	+	+	-	-	-	+	-	+					R	Y	+/weak	-
Other Salmonellae	-	-	-	-	+	+	-	-	+	+	-	+	+	-	+	+/-	R	Y	+	d
Cit. freundii	D	-	+	+/late	+	+	D	-	+	+	-	-	+	-	-/+	+/-	R/Y	Y	d	+
Kleb. Pneumoniae	+/slow	+	+	+	+	+	+	-	-	-	-	+	+	-	-	-	Y	Y	-	+
Kleb. Oxytoca	+	+	+						+	-	+	+	-	-	-	-	Y	Y	-	+
Enterobacter. spp.	-	+	+	+	+	+	D	-	+	+	-	d	+	-	+		Y	Y	-	+
S. marcescens	D	+	+	d	+	+	+	-	+	+	-	+	+	-	+	-	R/Y	Y	-	d
P. vulgaris	+	-	-	-	-	+	+	-	d	+	+	-	+	+	-	-	R	Y	+	d
P. mirabilis	+	d	-	-	-	+	D	-	+	+	-	-	+	+	+	-	R	Y	+	+
Providencia spp.	D	-	-	-	d	+	D	-	+	+	+	-	-	+	-	-	R	Y	-	d
Y.enterocolitica	+/slow	-	+	-	+	+	+	-	-	+	D	-	+	-	+	-	R	Y	-	-
V. cholera	-	d	+	-/24hr	+	+	+	+	d	+	+	+					R	Y	-	-

V.parahaemolyticus	-	-	+	-	+	+	-	+	d	+	+	+					R	Y	-	-
M. morgana	+	-	-	-	-	+	-	-	-	+	+	-	+	+	+	-	R	Y	-	d
Hafnia alvei	-	+	+						-	+	-	+	-/+	-	+	-	R	Y	-	+
Pant. agglomerans	-/+	+/-	+						+/-	+	-/+	-	-/+	-/+	-	-	R/Y	Y	-	-/+

Source: Biochemical Identification Chart (Bacteriology Sop 0646 V1.0 –A01)

KIA- Kligler's iron agar, H_2S- Hydrogen sulphide, MR- Methyl red, VP- Voges Proskauer, IND- Indole, CIT- Citrate, PAD- Phenylalanine deaminase, URE- Urease, MOT- Motility, LYS- Lysine, ARG- Arginine, ORN- Orithine, ONPG- O-nitrophenyl-B-D-galactopyranoside(beta-galactosdase), LDC- Lysine decarboxylase, LAC- Lactose, MAN- Mannitol, GLU- Glucose, SUC- Sucrose, OX- Oxidase test, +/- = 50-90% of strains positive, -/+ = 50-90 of strains negative, R=Red- pink(alkaline reaction), Y=Yellow(acid reaction), d = different strains give different results.

Appendix 7: Clinical and Laboratory Standards Institute (CLSI) Standard for Zone Interpretation.

Table 1: susceptibility interpretation chart: (Performance Standards for Antimicrobial Susceptibility Testing. 28th ed)

Zone Diameter Interpretive Standards for Organisms Other Than Haemophilus and Neisseria gonorrhoeae				
Antimicrobial Agent	Disk Content	Resistant	Intermediate	Susceptible
β-LACTAMS PENICILLINS				
Ampicillin				
when testing gram enteric organisms	10µg	≤13	14-16	≥17
when testing staphylococci	10µg	≤28	-	≥29
when testing etercocci	10µg	≤16	-	≥17
when testing Listeria monocytogenes	10µg	≤19	-	≥20
B-LACTAM/B-LACTAMASE INHIBITOR COMBINATIONS				
Amoxicillin/clavulanic acid				
when testing staphylococci	20/10µg	≤19		≥20
when testing other organisms	20/10µg	≤13	14-17	≥18
Ampicillin/sulbactam				
when testing gram-negative enterics and staphylococci	10/10µg	≤11	12-14	≥15
CEPHALOSPORINS AND OTHER CEPHEMES				

Cefoxitin	30µg	≤14	15-17	≥18
Ceftriaxone	30µg	≤13	14-20	≥21

Zone Diameter Interpretive for Organisms Other Than Haemophilus and Neisseria gonorrhea

Antimicrobial agent	Disk Content	Resistant	Intermediate	Susceptible
CARBAPENEMS				
Imipenem	10µg	≤13	14-15	≥16
GLYCOPEPTIDES				
Vancomycin				
when testing enterococci	30µg	≤14	15-16	≥17
when testing other gram-positive organisms	30µg	≤9	10-11	≥12
AMINOGLYCOSIDES				
Amikacin	30µg	≤14	13-14	≥17
MACROLIDES				
Erythromycin	15µg	≤13	14-22	≥23
TETRACYCLINES				
Tetracycline	30µg	≤14	15-18	≥19
QUINOLONES				
Ciprofloxacin	5µg	≤15	16-20	≥21
Norfloxacin	10µg	≤12	13-16	≥17
OTHERS				
Chloramphenicol	30µg	≤12	13-17	≥18
Clindamycin	2µg	≤14	15-20	≥21
Nitrofurantoin	300µg	≤14	15-16	≥17

Trimethoprim/sulfamethoxazole	1.25/23.75µg	≤10	11-15	≥16

Source: CLSI (2018).

Appendix 8: Incidence of Sterile Pyuria Among Patients at TCH

Table 3: Uropathogens Associated with Asymptomatic Bacteriuria Among Different Age Groups

Ages	Frequency (%)	Gram Positives				Gram Negatives					
		S. aureus	*CoNS*	*Strept.* spp	*E. coli*	*Kleb.spp*	*Entero.* spp	*Serratia* spp	*Pseud.* spp	*Salm.*	*p. vulgaris*
Tamale Teaching Hospital											
9	3(4.8)	2	0	0	0	1	0	0	0	0	0
-19	2(3.2)	1	0	1	0	0	0	0	0	0	0
-29	26(41.3)	4	12	0	4	1	3	2	0	0	0
-39	14(22.2)	6	4	1	1	1	1	0	0	0	0
-49	3(4.8)	0	0	0	0	0	0	2	0	1	0
-59	2(3.2)	0	0	0	1	1	0	0	0	0	0
0	13(20.6)	1	2	0	3	2	3	2	0	0	0
tal	63(100.0)	14	18	2	9	6	7	6	0	1	0
Tamale Central Hospital											
9	1(1.1)	0	0	0	1	0	0	0	0	0	0
-19	4(4.4)	2	1	0	0	0	1	0	0	0	0
-29	55(61.1)	14	21	1	7	5	4	2	0	0	1
-39	26(28.9)	8	7	2	5	0	3	0	0	1	0
-49	2(2.2)	0	0	0	1	0	0	0	1	0	0
-59	1(1.1)	0	0	0	1	0	0	0	0	0	0
0	1(1.1)	0	0	0	1	0	0	0	0	0	0
tal	90 (100.0)	24	29	3	16	5	8	2	1	1	1

Strept.=Streptococcus spp, *Kleb.=Klebsiella* spp, *Entero.=Enterobacter* spp, *Pseud.=Pseudomonas* spp, *CoNS=Coagulase Negative Staphylococcus*, *Sal.=Salmonellae*

Table 4: Prevalence of Asymptomatic Bacteriuria Among the Different Age Groups

	TTH		TCH		
Ages	**Frequency**	**Frequency%**	**Frequency**	**Frequency %**	**P Value**
1-9	3	4.8	1	1.1	
10-19	2	3.2	4	4.4	
20-29	26	41.3	55	61.1	
30-39	14	22.2	26	28.9	
40-49	3	4.8	2	2.2	
50-59	2	3.2	1	1.1	
≥60	13	20.6	1	1.1	
Total	63	100	90	100	0.000
P Value	0.000		0.966		

TTH= Tamale Teaching Hospital, TCH= Tamale Central Hospital

Table 5: Mean Age of Patients

	Mean Ages± Standard Error of Means		
Hospital	**UTI**	**ASB**	**SP**
TTH	40.01±2.2.58	38.37±2.76	
TCH	30.11±1.04	28.37±2.76	27.8±1.68
Overall	34.28±1.29	32.48±1.29	27.8±1.68

Appendix 9: Multidrug Resistance Among the Uropathogens

Table 6: Multidrug Resistance Among the Uropathogens

Tamale Teaching Hospital					
Isolates	**No of MDR isolates**	**R2_R4**	**R5_R7**	**R8_R10**	**≥R11**
Gram Positive	33	7(21.2%)	11(33.3%)	11(33.3%)	4(12.1%)
Gram Negative	38	5(13.2%)	8(21.1%)	15(39.5%)	10(26.3%)
Total	71	12(16.9%)	19(26.8%)	26(36.6%)	14(19.7%)
S. aureus	16	3(18.8%)	6(37.5%)	5(31.3%)	2(12.5%)
CoNS	16	4(25.0%)	5(31.3%)	5(31.3%)	2(12.5%)
Streptococcus	1	0(00%)	0(0.0%)	1(100.0%)	0(0.0%)
E. coli	14	1(7.1%)	4(28.6%)	5(35.7%)	4(28.6%)
***Klebsiella* spp.**	8	0(0.0%)	2(25.0%)	4(50.0%)	2(25.0%)
***Enterobacter* spp.**	7	1(14.3%)	1(14.3%)	3(42.9%)	2(28.6%)
***Serratia* spp.**	7	3(42.9%)	1(14.3%)	2(28.6%)	1(14.3%)
Salmonellae	2	0(0.0%)	0(0.0%)	1(50.0%)	1(50.0%)
Total	71	12(16.9%)	19(26.8%)	26(36.6%)	14(19.7%)

R2-R4=Resistant to 2-4 antibiotics, R5-R7=Resistant to 5-7 antibiotics, R8-R10=Resistant to 8-10 antibiotics, ≥R11=Resistant to 11 antibiotics and above

Table 7: Multidrug Resistance Among the Uropathogens

Isolates	Tamale Central Hospital				
	No of MDR isolates	**R2_R4**	**R5_R7**	**R8_R10**	**≥R11**
Gram Positive	56	24(42.9%)	21(37.5%)	9(16.1%)	2(3.6%)
Gram Negative	44	16(36.4%)	18(40.9%)	7(15.9%)	3(6.8%)
Total	100	40(40.0%)	39(39.0%)	16(16.0%)	5(5.0%)
S. aureus	25	8(32.0%)	10(40.0%)	5(20.0%)	2(8.0%)
CoNS	29	15(51.7%)	11(37.9%)	3(10.3%)	0(0.0%)
Streptococcus	2	1(50.0%)	0(0.0%)	1(50.0%)	0(0.0%)
E. coli	21	8(38.1%)	9(42.9%)	4(19.0%)	0(0.0%)
***Klebsiella* pp.**	7	0(0.0%)	5(71.4%)	0(0.0%)	2(28.6%)
***Enterobacter* spp.**	9	6(66.7%)	2(22.2%)	1(11.1%)	0(0.0%)
***Serratia* spp.**	3	2(66.7%)	1(33.3%)	0(0.0%)	0(0.0%)
***Pseudomonas* spp.**	1	0(0.0%)	0(0.0%)	1(100.0%)	0(0.0%)
Salmonellae	2	0(0.0%)	1(50.0%)	0(0.0%)	1(50.0%)
P. vulgaris	1	0(0.0%)	0(0.0%)	1(100.0%)	0(0.0%)
Total	100	40(40.0%)	39(39.0%)	16(16.0%)	5(5.0%)

R2-R4=Resistant to 2-4 antibiotics, R5-R7=Resistant to 5-7 antibiotics, R8-R10=Resistant to 8-10 antibiotics, ≥R11=Resistant to 11 antibiotics and above