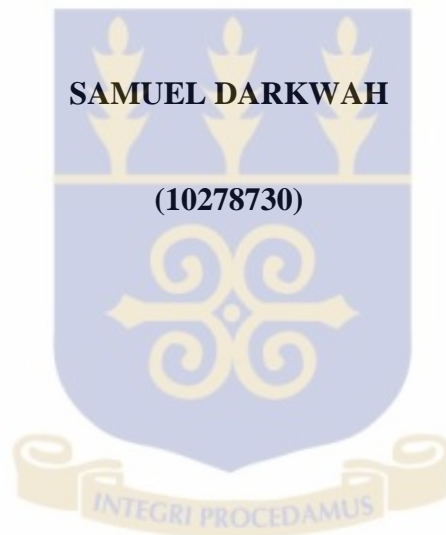


**UNIVERSITY OF GHANA**

**COLLEGE OF HEALTH SCIENCES**

**A STUDY OF POST STROKE URINARY TRACT INFECTION AT THE KORLE-BU  
TEACHING HOSPITAL**

**BY**



**A THESIS SUBMITTED TO THE UNIVERSITY OF GHANA, IN PARTIAL  
FULFILLMENT OF THE REQUIREMENT FOR THE AWARD OF MPhil IN  
MICROBIOLOGY**

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## DECLARATION

I declare that this dissertation is the result of my own research work carried out in the Department of Medical Microbiology, School of Biomedical and Allied Health Sciences, University of Ghana, under the supervision of Prof. Eric Sampane-Donkor and Dr. Albert Akpalu.

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## ABSTRACT

### BACKGROUND

Infections are known to be a major complication of stroke patients. The relationship between stroke and bacteriuria has rarely been studied in sub-Saharan Africa, though this information could be relevant in the management of stroke in the sub-region.

### AIM

The aim of the study was to investigate the epidemiology of post stroke bacteriuria at the Korle-Bu Teaching Hospital including the prevalence, incidence, risk factors and causative organisms.

### METHODS

This was a longitudinal study involving 55 stroke out-patients and 16 in-patients recruited at the Korle-Bu Teaching Hospital. Stroke out-patients were followed up at the Physiotherapy Clinic of the hospital weekly for three months and urine specimens were collected on each occasion for analysis. Urine specimens were collected from the stroke in-patients daily during admission until discharged from the hospital ward. Demographic and clinical information were also collected from all the study subjects.

### RESULTS

Stroke in-patients had a higher prevalence of bacteriuria (18.8%) than stroke out-patients (10.9%) with a relative risk of 1.72 ( $p=0.411$ ). Similarly, stroke in-patients had a higher incidence of bacteriuria (6.3%) than stroke out-patients (1.8%) with a relative risk of 3.5 ( $p=0.125$ ). Three risk factors of bacteriuria and UTI were identified among the stroke patients and included stroke severity ( $p<0.001$ ), diabetes ( $p<0.001$ ) and pyuria ( $p=0.09$ ). Nine bacteria organisms were identified from the urine cultures of the stroke patients but the most common was *Escherichia coli* (33.3%). All the *Escherichia coli* isolates were susceptible to

chloramphenicol and amikacin, with the highest resistance observed with cotrimoxazole, ampicillin, norfloxacin and cefuroxime.

## CONCLUSION

The incidence of bacteriuria observed at Korle-Bu Teaching Hospital was low among both stroke out-patients and in-patients, though the prevalence was quite high. *Escherichia coli* is the main cause of bacteriuria among the stroke patients at this hospital and the infection could be managed with chloramphenicol and amikacin. The study identified several risk factors of post stroke bacteriuria such as stroke severity and diabetes which is useful in the prevention and management of bacteriuria.



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## CHAPTER ONE

### INTRODUCTION

#### 1.1 Background:

Stroke, a cerebrovascular disease globally remains an important public health concern, with direct effect on society and economy (Poisson *et al.*, 2010). Stroke results from the blocking and/or interruption of blood flow to the brain due to a rupture or blockage of a blood vessel. By definition, “stroke is a non-traumatic, focal vascular-induced injury of the central nervous system and typically results in permanent damage in the form of cerebral infarction, intracerebral haemorrhage and/or subarachnoid haemorrhage” (Cheung, 2014). This medical condition can be described in many forms, but grouped into two major types, Ischaemic and Haemorrhagic stroke depending on the two main causative events earlier stated. Stroke is a global health concern and leading cause of long-term permanent disability (Feigin *et al.*, 2003; Sousa *et al.*, 2009), responsible for about six million deaths each year, thus exceeds that of AIDS, malaria and tuberculosis (TB) combined. The disease is the third leading cause of death in developed countries (Poisson *et al.*, 2010; Johnsen *et al.*, 2012). Stroke has a number of risk factors, modifiable (which includes hypertension, diabetes, dyslipidaemia, cardiac conditions, smoking, physical inactivity, among others), and non- modifiable (age, gender, ethnicity, prior attack and family history of stroke).

Stroke patients have an increased risk to a wide range of infection and complications (Rocco *et al.*, 2007). Many mechanisms account for the increased risk of complications and infections among stroke patients. These mechanisms include direct factors such as brain damage leading to brain induced and systemic immune- depressed states, or symptoms caused by stroke such as immobility and dysphagia. Other factors not directly related to the stroke per se may also lead to infections and this may include old age and comorbidities such

as diabetes and cancers (Johnsen *et al.*, 2012). Stroke related treatments also accounts for some percentage of post stroke complications. These may include invasive management procedures, use of mechanical ventilators and other indwelling medical devices in hospitalized stroke patients (Maki *et al.*, 2001).

Bacteria associated pneumonia and urinary tract infection (UTI) are the two most common post stroke infections among acute stroke patients with peak percentages of about 22% and 27% respectively (Langhorne *et al.*, 2000; Harms *et al.*, 2010). Even though infections such as urinary tract infections commonly accounts for morbidity in the general medical population, stroke patients stand a greater risk of this infection, leading to consequences that are more apparent. The use of catheters in the management of hospitalized patients accounts for most nosocomial urinary tract infections (Catheter associated UTI), and is known to be the leading cause of secondary blood stream infection acquired in the hospital (Maki *et al.*, 2001). Most commonly isolated pathogens of urinary tract infections include *Escherichia coli*, *Proteus mirabilis*, *Klebsiella* species and *Staphylococcus* species (Harms *et al.*, 2010). The aetiology of bacteriuria in stroke patients in a community-based study in Ghana revealed coagulase negative *Staphylococcus* species as the predominant bacteria isolated from stroke patients, with females associated with a relatively high risk of bacteriuria (Donkor *et al.*, 2014).

## 1.2 Problem statement:

Globally, stroke is the second leading cause of death with an annual mortality of 5.5 million. There is an increasing burden of stroke in Ghana and the disease ranks among the top three causes of morbidity in the country (Bosu, 2007). This may be attributed to the increased incidence of hypertension, which is an important modifiable risk factor of the disease (Pole *et al.*, 1979; Bosu, 2010). Urinary tract infection is an important complication among stroke in-patients and is associated with poor stroke outcomes. A systematic review reported the prevalence of stroke related urinary tract infection to be 10% in the hospital environment, but this review did not include data from developing countries (Westendorp *et al.*, 2011). Similarly, a cohort study on urinary tract infection after stroke reported an in-hospital incidence of about 16% in patients following an acute stroke (Stott *et al.*, 2009). The increasing resistance of the causative organisms to antibiotics further heightens the burden of urinary tract infections among stroke patients. Prophylactic antibiotics may render some benefit against urinary tract infections in stroke patients caused by bacteria, however, the use of such drugs after stroke is still unclear, and questions concerning the risk of selecting resistant strains, defining the suitable antibiotic regimen, and determining which stroke patients may benefit from prophylaxis still remain unresolved (Van de Beek *et al.*, 2009). Antibiotic resistance associated with post stroke urinary tract infections is more likely to be a problem in developing countries like Ghana where antibiotic treatment options are limited. Therefore, stroke related urinary tract infections in the developing world constitute a major problem and the importance of a study to address this burden cannot be over emphasized (Westendorp *et al.*, 2012).

### 1.3 Justification:

Currently, no data is available concerning aetiology of nosocomial post stroke bacteriuria and urinary tract infections, its prevalence, incidence and associated risk factors in Ghana. This may be a major hindrance to the effective control and management of stroke related urinary tract infections. There is the need for effective and improved management of stroke patients to prevent adverse outcome of the condition. This may possibly reduce extra healthcare cost resulting from post stroke urinary tract infections. With the increasing trend of stroke hospitalization in Ghana, the proposed study is crucial, as it will provide information for better management of stroke related urinary tract infections.

### 1.4 Aim:

The aim of the study was to investigate the epidemiology of post stroke urinary tract infections among stroke patients at the Korle-Bu Teaching Hospital (KBTH).

### 1.5 Objectives:

The objectives of the study were to:

- determine the prevalence and incidence of post stroke urinary tract infections among stroke in-patients and out-patients at the KBTH.
- determine the aetiological agents causing the post stroke bacteriuria and urinary tract infection.
- determine antibiotic susceptibility patterns of the aetiological agents.
- determine risk factors associated with the post stroke urinary tract infections.

## CHAPTER TWO

### LITERATURE REVIEW

#### 2.1 Public health burden of stroke:

Stroke is a disease that accounts for about six million deaths in a year, a toll exceeding that of AIDS, malaria and tuberculosis all together (Johnsen *et al.*, 2012). Globally, stroke remains a public health problem ranked as the third leading cause of death in many developed countries and counted among the top five causes of hospital deaths among adults in Africa with varying incidence rates between and within different populations (Nwosu 2001). A study by Murray *et al.* (1997) revealed stroke as the worldwide, third most common cause of death following coronary heart disease and cancers (Murray *et al.*, 1997). Furthermore, a current study by Westendorp *et al.* (2011) revealed that the disease is the leading cause of disability in high-income countries and the second cause of global deaths (Westendorp *et al.*, 2011). Initially, stroke was a disease attributed to the developed world nonetheless; its burden in developed countries has significantly reduced with the help of evidence-based control measures and intervention strategies targeted at modifiable risk factors such as diabetes, hypertension, smoking and lack of physical activity (Nwosu 2001).

Currently, developing countries face increasing burden of stroke with studies attributing about two-thirds of stroke mortality cases to Sub-Saharan Africa (Bravata *et al.*, 2005, Lopez *et al.*, 2006). This increasing burden in the Sub-Saharan regions may be attributed to increase in risk factors of vascular disease due to urbanization and modifications in way of living (Owolabi *et al.*, 2007).

## 2.2 Complications of stroke:

Patients suffering from acute stroke are at risk for various clinical complications, owing to the impaired state of their immune system (Kamel *et al.*, 2012). Irrespective of optimal clinical management, stroke patients may develop infections soon after an acute stroke and the risk acquiring such infections are to a large extent, determined by the severity of stroke (Chamorro *et al.*, 2007). A study in New York (United States of America) showed that stroke patients are faced with several medical and neurological complications such as musculoskeletal pain, urinary retention, hypotension and falls during in-patient rehabilitation. Among these, urinary infection was most common (Dromerick *et al.*, 1994).

Infections are the most important complication after ischaemic stroke and as high as 90% to 95% of patients, within three months of a stroke attack develop at least one complication (Davenport *et al.*, 1996). Post stroke infections are plausibly favoured by stroke/brain induced immune suppression (Emsley *et al.*, 2008). Such complications and infections are associated with adverse outcomes and extend the length of hospital stay (Weimar *et al.*, 2002), thus increasing health care cost and usually impairing neurological outcomes of stroke (Poisson *et al.*, 2010). Bae *et al.*, (2005) in a stroke study concluded that complications among hospitalised patients affect mortality even after the acute stage of the disease and in effect, generally worsens long term and short term prognoses of cerebral vascular accident (Bae *et al.*, 2005).

The severity of stroke is also associated with the risk of nosocomial post-stroke infections (Martino *et al.*, 2005). A study carried out in Germany reported infection prevalence as high as 42% among admitted stroke patients, with pneumonia and urinary tract infections diagnosed in 18% and 29% of these patients respectively. About 11% of patients developed more than one of these infections during their stay in the hospital (Wartenberg *et al.*, 2011).

Supportively, other literature indicate that pneumonia and urinary tract infections are the most common post stroke infections with rates of about 10% and pneumonia is most often associated with death (Langhorne *et al.*, 2000; Westendorp *et al.*, 2011).

The hospital, to a large extent, represents where microorganisms and susceptible patients share a common indoor and outdoor environment. The presence of air borne microorganisms in indoor environment of hospitals such as the specialized stroke wards raises great concerns with respect to the likelihood of nosocomial infections among in-patients (Beggs, 2003; Ekhaise *et al.*, 2008). In developing countries, overcrowding, improper structural designs and ill ventilation setting in health care facilities predisposes patients to risk of infection with harmful microorganisms of which stroke patients are no exception (Fekadu *et al.*, 2015). Human and equipment activity within indoor hospital environments may be an important factor in the accumulation and spread of air borne microorganisms (Wamedo *et al.*, 2012). This may lead to nosocomial infections of which UTI is not an exception.

### **2.3 Stroke in Ghana:**

The mortality and morbidity caused by stroke in Ghana cannot be overlooked, rather, demands urgent efforts in the management and prevention of the disease in the Ghanaian population (Agyemang *et al.*, 2012). Between the mid and later years of the 1990's, mortality from stroke alone (confirmed by autopsy) reported in a study at the Korle-Bu Teaching Hospital was 11% (Wiredu *et al.*, 2001). This study also reports one similar, earlier study with the same proportion rate, suggesting an unchanged proportion of deaths caused by stroke.

Over the years, stroke and other cardiovascular diseases have marked an alarming steady increase in their mortality rates. Such increase is likely to continue considering the increasing prevalence of hypertension, except timely interventions are adopted to curb the increasing

prevalence of hypertension and other risk factors associated with stroke (Agyei-Mensah *et al.*, 2010). Report from a study by Agyemang *et al.*, (2012) in the Ashanti region of Ghana indicates stroke association with such alarming morbidity and mortality in patients at the Komfo Anokye Teaching Hospital (KATH). A great proportion (62.1%) of these stroke deaths occurred within the initial week of hospital admission (Agyemang *et al.*, 2012).

Stroke ranks among the top three leading cause of morbidity in Ghana. By the year 2003, stroke had become the second top cause of death in the Greater Accra region of Ghana with one of its major risk factors, hypertension ranking as the sixth top cause of death (Bosu, 2007).

Studies attribute the threatening mortality of stroke to the high incidence of both undiagnosed stroke and more importantly its major risk factor, hypertension, thus many Ghanaians do not frequently visit the hospitals or report to their doctors unless there is a feeling of unbearable ailment, which may be a reason for many undiagnosed cases of hypertension (Anim *et al.*, 1984; Wiredu *et al.*, 2001).

#### **2.4 Bacteriuria and urinary tract infection:**

Normally, urine is void of microorganisms and considered as a sterile body fluid however, when contaminated with bacteria, results in bacteriuria (Orenstein *et al.*, 1999). Bacteriuria may present with clinical symptoms or without symptoms at all (Orenstein *et al.*, 1999). Hence, it is important to note the significant difference between asymptomatic bacteriuria (ABU) and urinary tract infection (UTI) and their application in this context. While UTI is generally defined in association with genitourinary symptoms and inflammation with a positive urine culture of a known urine pathogen, ABU rather defines the presence of bacteria (in amounts of about  $10^5$  colony forming units per millilitre or more) in urine, without the evidence of clinical signs and symptoms associated with a urinary tract infection (Rowe *et*

*al.*, 2014). In clinical practice however, having identified specific pathogens such as *Staphylococcus saprophyticus* and *Escherichia coli* in a single, midstream urine obtained from symptomatic patients may be considered an indication of infection even if colony counts of less than  $10^5$  (thus  $\geq 10^2 - 10^3$ ) are obtained (Stamm *et al.*, 1982; Schnarr *et al.*, 2008). Likewise such low counts in immune-compromised patients like those with AIDS can be considered for treatment and management of urinary tract infection.

Asymptomatic bacteriuria is commonly seen among elderly patients (especially in those who have been hospitalized), patients with diabetes, catheterized patients and those with urinary system structure abnormalities (Yohanes, 2011).

Urinary tract infection is one of the most commonly diagnosed infections in hospitals (both hospital and community acquired infection) especially among older patients (Rowe *et al.*, 2014) and are characterized by bacteriuria coupled with symptoms such as frequency in urination, dysuria, and pyuria (Nicolle, 2003). In a comparative study of risk factors of urinary infections per age of patients carried out in Tunisia, it was revealed that urinary tract infection is seen more frequently among elderly women with immunosuppression, menopause and urinary incontinence being outstanding risk factors (Rachdi *et al.*, 2014). Comparatively, immunosuppression, mostly as a result of therapy, is the principal risk factor of urinary tract infection in young patients (Rachdi *et al.*, 2014).

Urinary tract infection is common in both males and females however, incidence in women is relatively higher owing to their physiology and anatomic makeup, thus in relation to the relatively shorter urethra length in females (Vasudevan, 2014).

## 2.5 Aetiology of urinary tract infections:

A wide range of microorganisms are implicated in urinary tract infections ranging from viruses (Paduch, 2007) to mycological agents such as yeasts. Among these, bacteria cause most of urinary tract infections, making UTI the most common bacterial infection (Vasudevan, 2014). Generally, *Escherichia coli*, *Proteus mirabilis*, *Klebsiella* species and *Staphylococcus* species are the most common pathogens isolated (Harms *et al.*, 2010). A community based, cross-sectional study in Ghana observed similar bacterial aetiology associated with stroke related bacteriuria in both stroke patients and healthy individuals (Donkor *et al.*, 2014).

Most commonly, positive cultures from urine presents bacilli bacteria as the predominant cause of urinary tract infections with *Escherichia coli* being the lead of such pathogens. *Escherichia coli*, for so long a time has stood as the single most common pathogen implicated in bacteriuria of women (Evans *et al.*, 1978; Bengtsson *et al.*, 1998). In a Russian study, urinary isolates from over 500 in-patients' sampled revealed *Escherichia coli* as the most common isolated pathogen and accounts for about 86% of all isolates obtained (Stratchounski *et al.*, 2006). *Escherichia coli* when found in the urinary tract of patients most often, inevitably results in urinary tract infection (Adukauskiene *et al.*, 2006). Coagulase negative *Staphylococci*, *Enterococci* and Gram negative bacilli such as *Klebsiella pneumoniae* are similarly uro-pathogens common in men with bacteriuria (Mims *et al.*, 1990).

## 2.6 Stroke and urinary tract infections:

Studies have shown that key factors such as the severity of stroke and the location of lesion are associated with the risk of post stroke infections however, effective treatment and management of post stroke infections can improve the outcome of the condition (Grabska *et al.*, 2011). A study on infections and stroke outcome in ischaemic stroke patients carried out

in Poland also observed a relatively high frequency of nosocomial pneumonia and urinary tract infections among subjects who had infections within seven days before their admissions as compared to those that had no records of pre-infection (Grabska *et al.*, 2011). This suggests that the risk of acquiring nosocomial post stroke infections may be closely associated with pre-stroke infections. Their study concluded that in-hospital post stroke infections are associated with poor ischemic stroke outcomes. A study in Turkey also showed a urinary tract infection percentage of 27.3% (Ersoz *et al.*, 2007). Interestingly, stroke patients' level of education proved a significant factor associated with significant bacteriuria in about 39% of 110 stroke patients studied. Donkor *et al.*, (2014) in a case control study on stroke patients attending a physiotherapy clinic in Ghana observed significantly higher percentage bacteriuria of about 24% among stroke patients relative to matched, healthy control group (about 7%). The study also revealed no difference in the aetiology of bacteriuria among healthy individuals and stroke patients, with *Staphylococcus* as the predominant isolate implicated in both groups (Donkor *et al.*, 2014).

Some clinical presentations of acute stroke often warrant the use of catheter placement either permanently or for a short while. This is usually to manage urinary dysfunction and urine retention which occurs in approximately 29-58% of stroke patients. The use of catheters in the management of hospitalized patients accounts for most nosocomial urinary tract infections (Catheter associated UTI), known to be the leading cause of secondary blood stream infection acquired in the hospital (Maki *et al.*, 2001). Older age and gender (females) have also been identified as risk factors for post stroke urinary tract infections (Ovbiagele *et al.*, 2006; Westendorp *et al.*, 2011).

## 2.7 Treatment of urinary tract infections:

It is quite unclear in literature concerning the necessity and significance of treating people with asymptomatic bacteriuria (Olowe *et al.*, 2013). Although bacteriuria is common among the impaired elderly such as most stroke patients, treatment with antibiotics or other antimicrobial agents is not recommended if signs and symptoms of a urinary infection are absent. Such therapy may result in complicated side effects and emergence of resistant strains of microorganisms (Yohanes, 2011). Treatment of asymptomatic bacteriuria with antibiotics has however been known to improve uro-genital conditions presenting with no clinical signs and symptoms.

First line antibiotics for the treatment of uncomplicated urinary tract infections include sulfamethoxazole and trimethoprim drugs, nitrofurantoin and ampicillin. Due to increasing resistance of bacteria to antibiotics, however, susceptibility to these first line drugs continually fail especially with the *Escherichia coli* and other members of the family *Enterobacteriaceae* (Gupta *et al.*, 2001; Brown *et al.*, 2002). Fluoroquinolones such as ciprofloxacin and levofloxacin were introduced into the management regimen for urinary tract infections due to the increase burden of resistance to first line empirical treatment options. Nonetheless, fluoroquinolones more recently have had their share of decreasing susceptibility patterns with *Escherichia coli* and other *Enterobacteriaceae* isolates implicated in urinary infections (Sahm *et al.*, 2001).

With respect to resistance of urinary isolates to antibiotics, *Enterobacteriaceae* especially *Escherichia coli* that are mostly implicated in UTI, are known to have high resistance rates to ampicillin and sulphamethoxazole/ trimethoprim drugs and more recently, fluoroquinolones such as ciprofloxacin, norfloxacin and nalidixic acid (Akram *et al.*, 2007; Borsari *et al.*, 2008).

## **CHAPTER THREE**

### **MATERIALS AND METHODS**

#### **3.1 Study site**

The study was conducted at the Korle-Bu Teaching hospital (KBTH), in Accra. The hospital is currently the third largest hospital in Africa and the leading national referral centre in Ghana with a bed capacity of about 2000 and seventeen clinical and diagnostic departments, which includes the department of medicine where the study subjects were recruited. The hospital has an average daily attendance of 1,500 patients and about 250 patient admissions (KBTH, 2012). There has recently been an establishment of a stroke unit, which admits and takes care of acute stroke cases at the medical block. This unit has a maximum bed capacity of fifteen. Korle-Bu Teaching Hospital has a Physiotherapy Department which operates under the administration of sub-Budget Management Centre (sub-BMC), providing physical therapeutic and rehabilitative services to both out-patients and in-patients. The department has a clinic and gymnasium that receives and render medical services to out-patients, including stroke patients in need of physiotherapy.

#### **3.2 Study design and subject recruitments**

This was a cohort study carried out from May, 2015 to July, 2015. A total of 71 stroke patients were recruited from the Korle-Bu Teaching Hospital for the study (based on 90% confidence limit, an error margin of 10% and an estimated stroke prevalence of 10%) (Donkor, 2014). Both in-patients (admitted for not less than 48 hours in the stroke ward) and out-patients from the physiotherapy clinic diagnosed of stroke were enrolled. The recruitment of stroke patients in the stroke ward was based on definite clinical and/ or radiological diagnosis of stroke. Patients with ambiguous diagnosis (clinically unconfirmed) of stroke

were excluded from the study. Similarly, stroke patients reporting to the physiotherapy clinic at the Korle-Bu Teaching Hospital were recruited based on definite clinical and/or radiological diagnosis provided in their clinic records. Both stroke in-patients and out-patients, who had been on antibiotics two weeks before the selection of the study subjects were excluded from the study. Eligible study participants were then verbally informed of the study and a consent form provided for formal approval by the study participant. In-patients who were not in a conscious position to provide consent were consented for by their caregivers. Information on demographics and clinical history of the study participants were extracted from their clinical records with the approval of the medical staff. The two groups of study subjects (stroke in-patients and out-patients) were followed up for the development of bacteriuria and urinary tract infection. Urine sampling and culture from in-patient subjects of the study at the stroke ward was attempted each day until the patient was discharged from the stroke ward. With the out-patients at the physiotherapy clinic, samples were collected at each of the patients' visit to the clinic every week or two, depending on the patients' management plan for physiotherapy sessions.

### **3.3 Laboratory investigations**

#### **3.3.1 Analysis of urine samples (isolation and enumeration):**

Laboratory investigations for the study were carried out at the Medical Microbiology Department of the School of Biomedical and Allied Health Sciences, University of Ghana. Midstream, clean-catch urine samples of about 15mls (aseptically collected, labelled and transferred to the laboratory on ice packs) were immediately plated on agar plates of Blood and Cysteine Lactose Electrolyte Deficient (CLED) media and incubated at 37<sup>0</sup>C for 18-24 hours (Aspevall *et al.*, 2001). The procedure for culturing the urine samples was as follows: each pair of CLED agar plate and blood agar plate was divided into four and each quadrant allocated to a sample. The quadrants were labelled with the subjects' identification number.

A sterile 20 µl inoculating loop was dipped into the well mixed urine sample and immediately streaked onto the agar plates, with intermittent flaming of the loop after each streaking to prevent contamination. The agar plates were then placed in an aerobic incubator set at 37<sup>0</sup>C for a period of 24 hours.

After the culture process, ten (10) millilitres of the remaining urine samples were aseptically transferred into 15 ml transparent falcon tubes. The urine colour and appearance were observed and recorded. Urine dipsticks were immersed into the urine to measure biochemical parameters such as glucose, proteins, bilirubin, pH, and specific gravity of the urine. The dipsticks also gave an indication of the presence of leucocytes, red cells and nitrite. Urine in the falcon tubes were then centrifuged at 2500 rpm for three minutes and the sediments were used to prepare a wet mount which were observed microscopically for evidence of bacteria, parasites, yeast cells, casts, crystals, and blood cells. After incubation, bacterial colonies on the agar plates were counted and count of 10<sup>5</sup> or more colony-forming units per millilitre (cfu/ml) were considered as significant bacteriuria (Nicolle *et al.*, 2005). Plates with significant bacteriuria were eligible for further identification and susceptibility testing. Agar plates that showed no visible growth of bacteria colonies were allowed an extra day of incubation after which they were discarded if no growth was recorded again. Contaminated plates were also discarded and a new sample taken for repeat of the culture process. Similarly, heavy mixed growth cultures were not considered for bacteria identification and also repeated with a new sample.

Pure cultures were obtained from positive cultures by picking single, isolated colonies of the counted bacteria with a sterile loop and streaking onto a new CLED agar plate, flaming intermittently to prevent contamination and produce isolated colonies in the pure culture.

Isolated bacteria were identified with the characteristics of their colonial morphology on both the CLED and Blood Agar plates, followed by Gram's staining (using crystal violet and neutral red as primary and counter stains respectively with acetone to decolorize and Gram's iodine as mordant), appropriate biochemical tests, and microscopy. Biochemical tests for Gram negative isolates included triple sugar iron (TSI) fermentation tests, citrate and urea utilization test and the indole test. A slide wet preparation of the isolates was used to monitor motility to help in identification. Gram positive isolates were identified by Catalase reaction using hydrogen peroxide which helped distinguish non catalase producing organisms such as streptococcal and enterococci isolates from *Staphylococcus* species producing catalase that breakdown hydrogen peroxide into water and oxygen (seen as bubbles). This was followed by a tube coagulase test using coagulase plasma to distinguish coagulase producing *Staphylococcus* species as *Staphylococcus aureus* from non- coagulase producing species. The coagulase test was done as follows: the suspected *Staphylococcus aureus* isolates were grown overnight in fresh peptone water and 0.2 ml of the overnight broth culture added to 0.5 ml of coagulase plasma. The solution was well mixed and incubated at 37°C and observed after two hours, four hours and overnight for evidence of clots in the plasma (Sperber *et al.*, 1975).

### 3.3.2 Antibiotic Susceptibility testing:

The Kirby Bauer disc diffusion method based on the Clinical Laboratory Standards Institute (CLSI) guidelines of antimicrobial susceptibility testing was used to determine the pattern of resistance of isolates obtained from the cultures (Bauer *et al.*, 1966; CLSI, 2012). Thus, an inoculum was prepared with sterile distilled water to turbidity comparable to the appearance of 0.5 McFarland standard solution of barium sulphate. The standardized inoculum was then swabbed onto the whole surface of Muller Hinton agar plate and appropriate antibiotic multi-disc (Gram negative isolate and Gram positive isolate discs for Gram negative and Gram

positive isolates respectively) aseptically placed on the agar with pre flamed forceps. The swabbed agar plates were then incubated at 37<sup>0</sup>C for 24 hours and the zones of inhibition read afterwards with a rule and a calliper. Zone sizes were compared to the CLSI guideline references to determine resistance and *in-vitro* susceptibility (Beyene *et al.*, 2011).

### 3.3.3 Investigation of risk factors:

A questionnaire was used to obtain demographic data from study participants. This included information on patients' age, occupation, place of residence, level of education, marital status, and state of monetary income. Information on history of the participants' medication usage was also obtained by the questionnaire. Other complementary data such as clinical history of comorbidities, length of hospital stay and other medical complications were obtained from participants' hospital records as well as verbal enquiries. Stroke severity for both in- patients and out- patients was measured using the modified Rankin's scale (mRs), described by other relevant publications (Bonita *et al.*, 1988). Per the mRs scale, stroke severity was measured with scores of zero (mRs 0) to six (mRs 6). Stroke patients with no symptoms at all were scored zero whereas those with no significant disability despite the presence of symptoms were scored one (mRs 1). Moderately disabled stroke patients who were able to walk without assistance and those who needed aid in walking and other bodily needs were scored three (mRs 3) and four (mRs 4) respectively. Severely disabled participants who were bedridden, incontinent and needed constant nursing care and attention were scored five (mRs 5). A score of six denotes a dead patient. Stroke patients with a mRs score of one to three were classified as mild stroke patients whereas those with mRs 4 and mRs 5 were considered as having severe stroke (Bonita *et al.*, 1988).

#### 3.3.4 Environmental assessment of the ward:

Sampling procedure for this investigation was by simple sedimentation technique for air borne microorganisms (Augustowska *et al.*, 2006). Three sterile, petri dishes comprising two Nutrient agar and Blood agar was opened and placed at different parts of the ward for 60 minutes. Sampling was done in the early hours of the morning and early hours of the evening. The culture plates were sent to the laboratory for incubation at 37<sup>0</sup>C for 48 hours after which appropriate count and identification was done for bacteria that grew. Additionally, sterile swab sticks were used to sample edge of beds of patients, treatment pans and bed trays.

The swab sticks were seeded onto Blood agar and MacConkey agar and incubated for 24 hours at 37<sup>0</sup>C. Bacteria grown were identified by standard biochemical procedures.

#### 3.4 **Data analysis**

All data collected were entered into Microsoft Excel and further analysed using STATA version twelve. Descriptive analysis including computation of arithmetic means, frequencies and percentages were done with the study variables. Uni-variable associations were performed between bacteriuria and all other study variables and significance of independent variables were assessed by p-values, risk ratios and confidence intervals.

#### 3.5 **Ethical clearance**

Ethical approval for this study was obtained from the Ethics and Protocol Review Committee of the College of Health Sciences, University of Ghana. Urine samples as well as demographic information were obtained from study participants following their consent to partake in the study.

## CHAPTER FOUR

### RESULTS

#### 4.1 Demographic and clinical features of the study participants

A total of seventy-one (71) stroke patients comprising 55 outpatients and 16 in-patients were recruited in the study and their demographic features from the study participants are summarized in Table 4.1. The gender distribution, marital status, and highest education of out-patients and in-patients were similar. Overall, majority of the study participants were males (67.6%), married (70.4%) and the most common education attained was tertiary (39.4%). The overall mean age of the stroke patients was  $57.9 \pm 12.01$  years; mean age of out-patients and in patients were  $58.7 \pm 8.1$  and  $55.3 \pm 13.9$  respectively.

In terms of stroke type, ischemic stroke constituted 35 (49.3%) of total stroke cases and 12 (16.9%) cases were haemorrhagic stroke; 23 (32.4%) subjects did not have their stroke type classified on records. Twenty nine (40.8%) patients had the left side of their body affected by stroke while 30 (42.3%) had their right part affected; 2.8% (2) of study participants had both sides of their body affected. In terms of stroke severity, mRs 2 (33.8%) and mRs 3 (32.4%) were the most common levels of stroke severity among the stroke patients. Hypertension (81.7%) was the most prevalent risk factor among the stroke patients, followed by diabetes (23.9%). As shown in Table 4.2, the trend of stroke type, side of the body affected, stroke severity and risk factors were similar among the stroke out-patients and in-patients.

The mean time for hospital stay in the in- patients group was nine (9) days and 91.5% of the stroke cases were acute first time attacks with only 5.6% being recurrent stroke attacks.

**Table 4.1 Demographic features of the study participants**

Feature	Outpatients		Inpatients		Overall	
	n	%	n	%	n	%
<b>Age (mean= 57.9 ± 12.0)</b>						
<b>Gender</b>						
Male	36	65.5	12	75.0	48	67.6
Female	19	34.5	4	25.0	23	32.4
<b>Marital status</b>						
Single	3	5.5	2	12.5	5	7.0
Married	37	67.3	13	81.3	50	70.4
Separated/ Divorced	3	5.5	0	0.0	3	4.2
Widowed	8	14.5	1	6.3	9	12.7
<b>Education</b>						
Primary	13	23.6	2	12.5	15	21.1
Secondary	9	16.4	4	25.0	13	18.3
Tertiary	20	36.4	8	50.0	28	39.4
None	4	7.3	2	12.5	6	8.5

*Mean age of stroke patients were 57.9 ± 12.01 years (overall); 58.7 ± 8.1 years (out-patients) and 55.3 ± 13.9 years (in-patients). “n” – number of study subjects*

**Table 4.2 Clinical features of study participants**

Feature	Outpatients		Inpatients		Overall	
	n	%	n	%	n	%
<b>Stroke subtype</b>						
Ischaemic	25	45.5	10	62.5	35	49.3
Haemorrhagic	6	10.9	6	37.5	12	16.9
Not available	23	41.8	0	0.0	23	32.4
<b>Side of body affected</b>						
Right	25	45.5	5	31.3	30	42.3
Left	23	41.8	6	37.5	29	40.8
Left and right	2	3.6	0	0.0	2	2.8
<b>Stroke severity (mRs)</b>						
mRs 0	1	1.8	1	6.3	2	2.8
mRs 1	6	10.9	1	6.3	7	9.9
mRs 2	21	38.2	3	18.8	24	33.8
mRs 3	19	34.5	4	25	23	32.4
mRs 4	4	7.3	5	31.3	9	12.7
mRs 5	1	1.8	2	12.5	3	4.2
mRs 6	0	0.0	0	0.0	0	0.0
<b>Stroke risk factors</b>						
Hypertension	46	83.6	12	75.0	58	81.7
Diabetes	16	29.1	1	6.3	17	23.9
Family history	1	1.8	1	6.3	2	2.8
Dyslipidaemia	4	7.3	1	6.3	5	7.0
Atrial fibrillation	1	1.8	1	6.3	2	2.8
Others	1	1.8	2	12.5	3	4.2

*“n” – number of study subjects.*

*“mRs”- modified Rankin’s scale*

#### 4.2 Bacteriuria and associated risk factors

The overall prevalence and incidence of bacteriuria were 12.7% (9/71) and 2.8% (2/71) respectively (Table 4.3). Stroke in-patients had a higher prevalence of bacteriuria (18.8%) than stroke out-patients (10.9%) with a relative risk of 1.72 ( $p=0.411$ ). Similarly, stroke in-patients had a higher incidence of bacteriuria (6.3%) than stroke out-patients (1.8%) with a relative risk of 3.5 ( $p=0.125$ ). Among the stroke out-patients, one (1.8%) of the bacteriuria cases was symptomatic while among the stroke in-patients, none (0.0%) of the bacteriuria cases were symptomatic. The prevalence of bacteriuria among male and female stroke patients were 12.5% and 13% respectively ( $p>0.05$ ). The most common symptom/sign of UTI among the stroke patients was pyuria (12.7%), followed by haematuria (9.9%) (Figure 4.1). As shown in Table 4.5, three risk factors of bacteriuria and UTI were identified among the stroke patients and included stroke severity ( $p<0.001$ ), diabetes ( $p<0.001$ ) and pyuria ( $p=0.09$ ).

One case of asymptomatic bacteriuria progressed into a urinary tract infection, with the patient presenting symptoms of UTI after the second week of follow up. This was found in a 60 years old, male out-patient with a medical history of prostate cancer. Accompanying signs and symptoms identified with the single case of UTI included dysuria and pyuria.

#### 4.3 Causative organisms of bacteriuria and their antibiotic susceptibility patterns

Nine bacteria organisms were identified from the urine cultures including *Escherichia coli*, *Enterococcus* species, *Staphylococcus* species, *Klebsiella pneumoniae*, *Moraxella catarrhalis* and *Morganella morganii* (Table 4.4). *E. coli* was the most common bacteria isolated (33.3%) followed by *Staphylococcus* (22.2%).

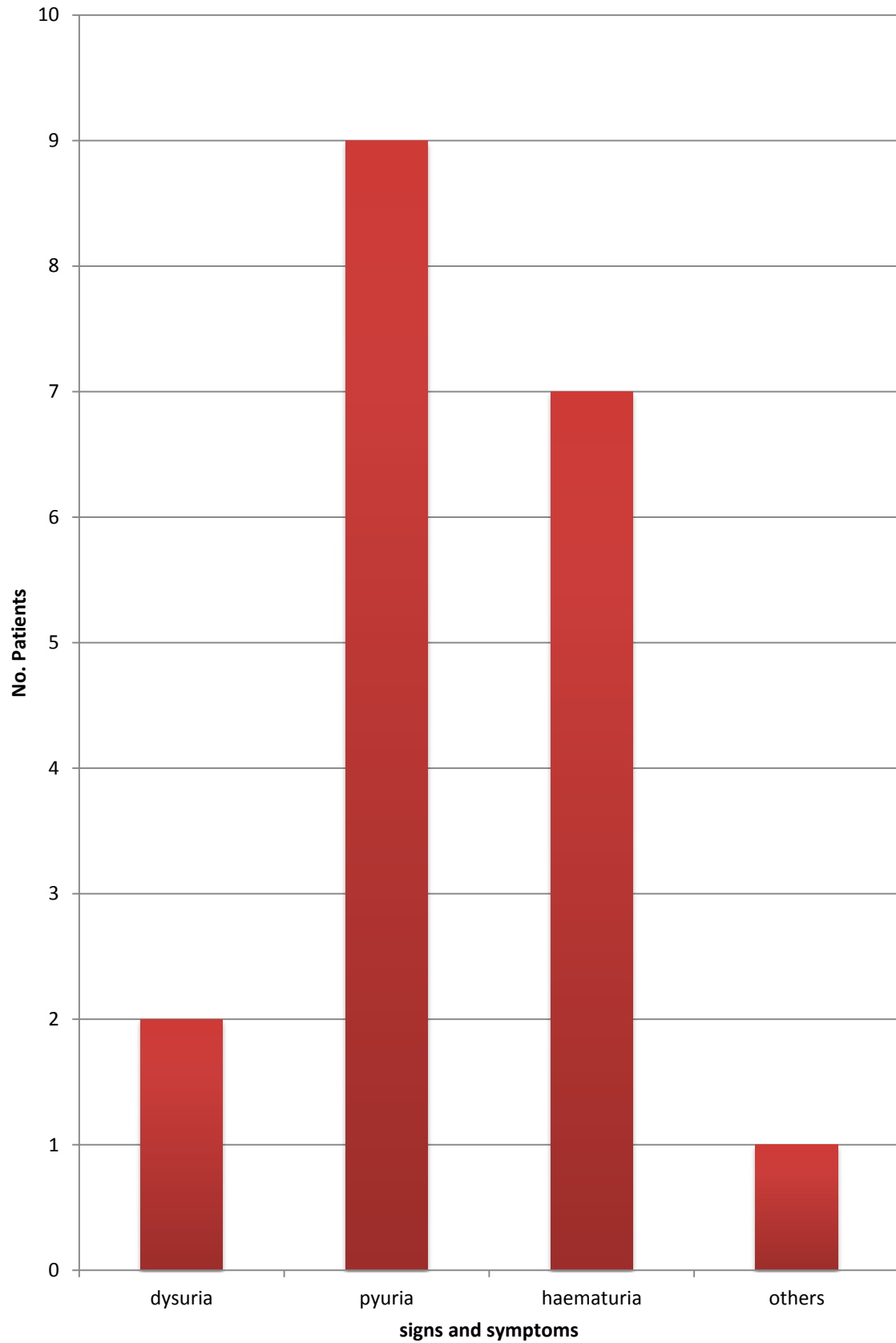
All *Escherichia coli* were susceptible to chloramphenicol and amikacin, with the highest resistance observed with cotrimoxazole, ampicillin, norfloxacin and cefuroxime. *Staphylococci* isolates were also susceptible to amikacin, nitrofurantoin and gentamycin. Penicillin recorded the highest resistance with all *Staphylococci* isolates.

Tables summarising the antibiotic susceptibility patterns of the isolates obtained from the study are shown in Appendix IV.

**Table 4.3 Prevalence and incidence of bacteriuria among stroke out-patients and in-patients**

	Prevalence		Incidence	
	n	%	n	%
<b>Outpatients</b>	6	10.9	1	1.8
<b>Inpatients</b>	3	18.8	1	6.3
<b>Overall</b>	9	12.7	2	2.8

*“n”- number of study participants.*



**Figure 4.1 Urinary tract infection symptoms among the study participants.**

**Table 4.4 Bacteria isolated from urine samples of stroke patients**

<b>BACTERIA ISOLATES</b>	<b>FREQUENCY (n)</b>	<b>%</b>
<i>Staphylococcus</i> sp.	2	22.2
<i>E. coli</i>	3	33.3
<i>M. catarrhalis</i>	1	11.1
<i>M. morgani</i>	1	11.1
<i>K. pneumoniae</i>	1	11.1
<i>Enterococcus</i> sp.	1	11.1
<b>TOTAL</b>	<b>9</b>	<b>100.0</b>

“n”- number of study participants.

**Table 4.5 Risk associations to bacteriuria**

	ABU		RR (90%CI)	p-val	UTI		RR (90%CI)	p-val
	Yes	No			Yes	No		
<b>GENDER</b>								
Male	6	42	1.0(0.7- 0.5)	1.0	1	47	1.5(1.3- 1.7)	1.0
Female	3	20	1.0(0.4- 2.4)		0	23	*	
<b>STROKE TYPE</b>								
Ischaemic	6	30	1.0(0.7- 1.4)	1.0	0	36	*	1.0
haemorrhagic	2	10	1.0(0.3- 3.0)		0	12		
<b>SITE AFFECTED</b>								
Left	3	26	0.9(0.4- 1.8)	1.0	0	29	*	
Right	4	26	1.0(0.6- 2.1)		1	29		
<b>FIRST TIME</b>								
Yes	9	56	1.1(1.0- 1.1)	1.0	1	64	*	1.0
No	0	4	0 ( * )		0	4		
<b>SEVERITY</b>								
Mild	3	53	0.4(0.2- 0.8)	0.0	1	49	*	1.0
Severe	6	6	6.6(3.1- 13.8)		0	12		
<b>LENGTH OF HOSPITAL STAY</b>								
Short (within a week)	2	5	1.7 (0.7- 4.2)	0.6	0	7	*	1.0
Long (over a week)	1	8	0.5 (0.1- 2.1)		1	8		
<b>DYSURIA</b>								
Yes	1	1	6.8 (0.7- 64.4)	0.2	1	1	*	1.0
No	8	60	0.9 (0.7- 1.1)		0	68		

TABLE 4.5 Continued.

## Risk associations to bacteriuria and UTI

<b>PYURIA</b>								
Yes	6	3	13.6 (5.0-37.0)	0.0	1	8	*	1.0
No	3	58	0.4 (0.2- 0.8)		0	61		
<b>HAEMATURIA</b>								
Yes	1	6	1.1 (0.2- 6.0)	1.0	0	7	*	1.0
No	8	55	1.0 (0.8- 1.2)		0	63		
<b>STROKE DURATION</b>								
In a year	6	37	1.2 (0.8- 1.7)	0.7	0	43	*	1.0
Over a year	2	20	0.7 (0.2- 2.0)		1	21		
<b>DIABETES</b>								
Yes	0	18	0 ( * )	0.1	0	18	*	1.0
No	9	41	1.4 (1.2- 1.7)		1	49		
<b>HYPERTENSION</b>								
Yes	8	50	1.0 (0.8- 1.3)	1.0	1	57	*	1.0
No	1	8	0.8 (0.2- 4.1)		0	9		
<b>MARITAL STATUS</b>								
married	6	44	1.1 (0.7- 1.6)	1.0	1	49	*	1.0
unmarried	3	26	*		0	50		
<b>AGE</b>								
50 years and below	2	14	1.0 (0.3- 2.8)	1.0	0	16	*	1.0
Above 50 years	7	45	1.0 (0.7- 1.3)		1	51		

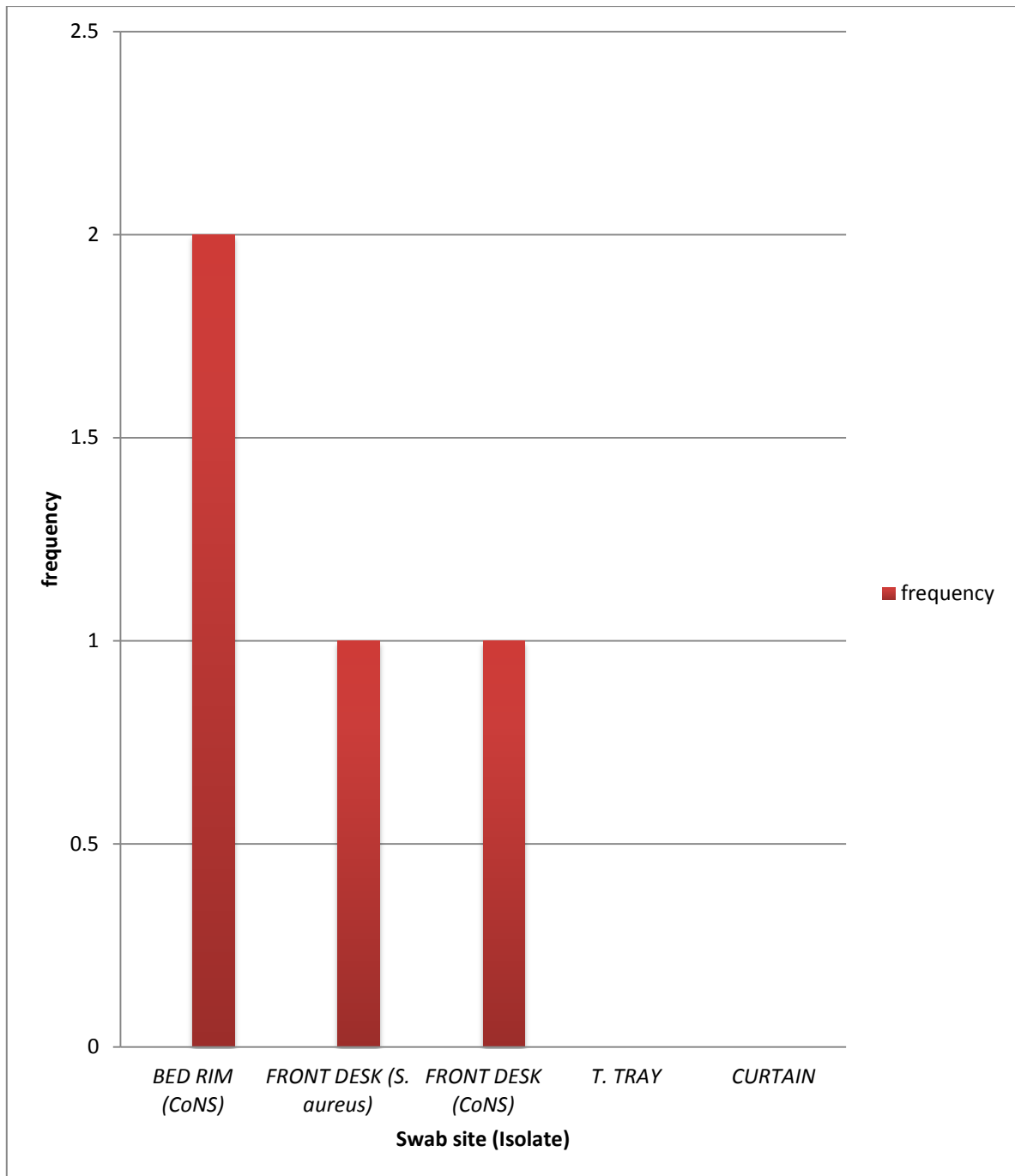
*ABU- Asymptomatic bacteriuria, UTI- Urinary tract infection, RR- Relative risk.*

*(\*) denotes non applicable entries.*

*Highlighted portions demarcate values of statistically significant interest.*

#### 4.4 Microbial assessment of stroke ward

Environmental isolates identified from the ward included *Staphylococcus aureus* and coagulase negative *Staphylococcus* species (Figure 4.2). These were obtained from swab cultures of bed rims and the surface of the front desk in the stroke ward. The average total aerobic bacteria count obtained from the ward was 312.5 cfu/ hour.



*CoNS*- Coagulase negative Staphylococcus

**Figure 4.2 Bacteria isolated from the stroke ward of KBTH**

## CHAPTER 5

### DISCUSSION AND CONCLUSIONS

#### 5.1 DISCUSSION:

The aim of this study was to investigate the epidemiology of post stroke urinary tract infections among stroke patients at the Korle-Bu Teaching Hospital. This was to be specifically addressed by determining the incidence of post stroke urinary tract infections among stroke patients at the hospital, identifying the aetiological agents causing the post stroke urinary tract infection, determining the antibiotic susceptibility patterns of the aetiological agents and identifying the risk factors associated with the post stroke urinary tract infection at the Korle-Bu Teaching Hospital.

The incidence of bacteriuria was low among both the out-patients (1.8%) and in-patients (6.3%), though the prevalence was a bit higher; 10.9% for out-patients and 18.8% for in-patients. The relatively higher prevalence of bacteriuria observed among in-patients concurs with a previous study in Nigeria where bacteriuria prevalence among in-patients and out-patients were 12.3% and 9.3% respectively, though these were not stroke patients (Jombo *et al.*, 2006). Prevalence and incidence of bacteriuria reported in this study is lower than what is reported in most literature. For example, Stott *et al.* (2009) observed approximately 16% incidence in their study of stroke in-patients in Scotland (Stott *et al.*, 2009). Likewise, other studies in developed countries have reported incidence of post stroke urinary tract infection of 6-27% (Harms *et al.*, 2010). These studies, however, included participants with urinary catheters and other medical implants. In this study however, none of the study participants were catheterized. Per internal infection control policies aimed at reducing and possibly eliminating the use of indwelling urinary catheters in the management of stroke patients in

the newly established stroke unit where sample population were recruited, none of the study participant recruited was catheterized. Catheterization is a known predictor of nosocomial post stroke urinary tract infections and consequently associated with high frequencies of bacteriuria and urinary tract infections (Maki *et al.*, 2001).

Additionally, incidence of UTI may be increased in years' long duration longitudinal studies with greater population size as compared to a few months of follow up in this study.

Studies have shown that stroke patients who have had infections within seven (7) days prior to the development of the stroke recorded a high frequency of post stroke bacteriuria (Grabska *et al.*, 2011). It was observed that participants recruited in this study did not include those with prior infections and were not on antibiotics owing to the exclusion criteria of the study. This may be accounting for the generally, lower prevalence and incidence obtained from the study.

A 13% prevalence of bacteriuria in women obtained in this study is consistent with reports from Yohanes (2011) who reported 13.6% prevalence in women. Conversely, literature from developed countries reveals bacteriuria prevalence of 2.8%- 8.6% in post-menopausal women aged above 50 years (Nicolle, 2003). Comparison of prevalence obtained for such women in this study to the literature shows that elderly women with stroke have relatively higher percentages of asymptomatic bacteriuria compared to elderly women of the general population as reported by Nicolle (2003). Considering the mean age of participants (57.9 years), most female participants were post-menopausal women; hence factors that may have accounted for this relatively high prevalence in women compared to men (12.5%) may be due to post-menopausal reduction in oestrogen and increase in the pH of the female genital tract due to the absence of lactobacilli allowing for colonization of uro-pathogens (Childs *et al.*, 1996).

Studies have reported general bacteriuria prevalence of between 3% and 19% among aged men (Nicolle, 2003). Prevalence obtained for post stroke bacteriuria among male patients in this study was 12.5%, which corresponds to general prevalence among aged men (Nicolle, 2003). The reduction of prostatic fluid bacterial activity in older men possibly accounts for the relatively higher prevalence of bacteriuria seen in this population as compared to young males (Childs *et al.*, 1996). Percentage of post stroke bacteriuria in males from this study does not differ much from that of older males as reported in literature.

*Escherichia coli* and coagulase negative *Staphylococcus* species observed from the study were the predominant bacteria implicated in post stroke bacteriuria. *Escherichia coli* was the predominant isolate implicated in urinary tract infection from the study. Similar pattern of aetiology have been reported by Schnarr *et al.* (2008) and Stratchounski *et al.* (2006) reporting predominant isolates of *Staphylococcus saprophyticus* and *Escherichia coli* respectively. Members of the *Enterobacteriaceae* (especially *E. coli*) and *Staphylococci* species are known to be the most common uro-pathogens generally (Harms *et al.*, 2010). Aetiology of post stroke bacteriuria and urinary tract infection may not be different from aetiology generally seen in other populations (Donkor *et al.*, 2014).

Nalidixic acid and ampicillin, used in first line empirical treatment of urinary tract infection recorded the highest resistance. *Escherichia coli* isolates resistance to fluoroquinolones was high especially with norfloxacin. Most *Staphylococcus* species are known to be highly resistant to penicillin and ampicillin with rates as high as 97% (Zou *et al.*, 2012) and exhibit outstanding versatile characteristics to antibiotics, hence most strains overcoming commonly used antibiotics (Grassi, 1988).

*Enterobacteriaceae* resistance to fluoroquinolones as well as *Escherichia coli* resistance to ampicillin and cotrimoxazole (observed in the study) is recognized as a common in-vitro resistance phenomenon (Akram *et al.*, 2007; Borsari *et al.*, 2008).

Stroke severity was found to be strongly associated with post stroke asymptomatic bacteriuria. The higher the mRs score, that is, the more severe a patient's stroke is, the greater the risk of bacteriuria. With a relative risk of 6.6 (CI: 3.1- 13.8,  $p=0.00$ ) obtained in the study, severe stroke cases are at a greater risk of bacteriuria and plausibly subsequent UTI. This is comparable to most studies in this light (Chamorro *et al.*, 2007; Grabska *et al.*, 2011). Post stroke infections are plausibly favoured by stroke/brain induced immune suppression (Emsley *et al.*, 2008) as a result of brain tissue damage. Observations are that severe stroke patients are likely to receive more invasive management such as insertion of intravenous lines for medications and nasogastric (NG) tubes for feeding, making them more susceptible to comorbidities. These explain the association of severe stroke cases to bacteriuria and subsequently UTI.

Pyuria was observed to have strong association to post stroke bacteriuria. Stroke patients with pyuria are about fourteen times (relative risk: 13.6,  $p=0.00$ ) likely to have bacteria in the urine. Increased white blood cells in urine may be an indication of urinary tract inflammation that could be an evidence of an infection, breach of mucosal lining and response to structural abnormalities. Inflammation and mucosal breach predisposes the human host to colonization with uro-pathogens (Childs *et al.*, 1996; Yohanes, 2011). Diabetes from the study was significantly associated with post stroke bacteriuria in study participants. Diabetics and some kidney disease patients may present with glycosuria which supports the proliferation of uro-pathogens implicated in bacteriuria. Diabetes Mellitus may also increase the risk of patients

developing bacteriuria via the impairment of the immune system as a result of hyperglycaemia and diabetes associated microangiopathy (Childs *et al.*, 1996).

*Staphylococci* obtained from the ward environment are ubiquitous bacteria adaptable to the hospital environment and shown to resist strong desiccation and harsh osmotic stress. *Staphylococci* species are normal flora of human skin (Marples *et al.*, 1990) and hence contact of hands to bed rims and desks by human activities in the ward introduces these pathogens onto such surfaces. Relatively acceptable aerobic bacteria count was observed from the indoor air of the stroke ward where in-patient participants were recruited. A count of 312cfu/hr observed falls within the acceptable range of 250cfu/hr- 450cfu/hr (Chalachew *et al.*, 2011). This could be attributed to the restricted human activity and foot traffic observed in the stroke ward, minimizing the introduction of aerobic contaminants into the ward. There is fairly good circulating indoor air in the Stroke Ward of the KBTH.

## 5.2 CONCLUSIONS:

The incidence of bacteriuria was low among both the out-patients (1.8%) and in-patients (6.3%), though the prevalence was rather high; 10.9% for out-patients and 18.8% for in-patients.

*Escherichia coli* was the predominant uro-pathogen implicated in post stroke bacteriuria among stroke patients at the KBTH. Majority of isolates implicated in post stroke bacteriuria at the Korle-Bu teaching hospital are likely to be resistant to fluoroquinolones. Amikacin could be an effective antibiotic for treating asymptomatic bacteriuria and UTI infections at the study site. The use of first line empirical antibiotic choice such as ampicillin, nitrofurantoin, nalidixic acid and cotrimoxazole may not be ideal for the management of stroke related UTI and bacteriuria at the KBTH considering rate of in-vitro resistance of uro-pathogens to these agents.

Risk factors identified to be associated with post stroke bacteriuria in the study are diabetes, pyuria and severity of stroke. Severe stroke attacks may pose a risk to bacteriuria and possibly urinary tract infection over time.

Indoor air environment at the stroke ward of the KBTH proves to be within limits of acceptable contamination with *Staphylococcus* species predominating surfaces of objects in the ward. All *Staphylococcus* isolates in the stroke ward of the KBTH were observed to be resistant to ampicillin and cotrimoxazole.

### **5.3 LIMITATIONS:**

The main limitation of this study was the short period of follow up of both in-patients and out-patients. Additionally, antibiotic susceptibility testing was carried out on a limited number of isolates.

### **5.4 RECOMMENDATIONS:**

- There is the need for further investigations into the resistance patterns of urinary isolates implicated in post stroke bacteriuria and UTI. Molecular methods to investigate genotypic evidence of resistance will be necessary to confirm patterns of drug resistance.
- Studies that will employ much larger sampling and longer participant follow-up over will be of benefit to this field.
- There is need for a nation-wide study to include data from other health and rehabilitation institutions on post stroke urinary tract infection to ascertain the national burden of the problem.
- It is necessary to monitor and manage bacteriuria among patients with severe stroke and diabetes.

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## **APPENDIX I**

### **CONSENT FORM**

#### **A STUDY OF POST STROKE URINARY TRACT INFECTIONS AT THE KORLE BU TEACHING HOSPITAL**

I am seeking your consent to enrol you in a study in which urine specimen shall be collected from you to investigate bacteriuria. This activity is part of a study on stroke related urinary tract infections at the Korle-Bu Teaching Hospital, Accra. Stroke patients are at an increased risk of infections and complications of which urinary tract infection is the second most important post stroke infection following pneumonia. In hospitalized patients however, the acquisition of post stroke infections may be nosocomial and may be due to patient management practices. The study aims at investigating the burden of urinary tract infection to stroke patients in the Korle-Bu Teaching Hospital to help improve management of the condition.

### **WILLINGNESS TO PARTICIPATE**

You are to understand that:

1. Your decision to partake in this research is entirely voluntary and your refusal to participate in the study will not prevent you from being attended to at the health facility.
2. After accepting to participate in the study, you have the option of changing your mind and withdraw from the study at any a time without any objection. This will not prevent you from being attended to at the health facility.
3. In the course of the study, you may be made to answer questions about your personal life style and health. I may also review your medical records.

## **CONFIDENTIALITY**

The information I shall obtain from you will be kept in the investigator's confidence. In the event of scientific reporting of the findings of the study your name will not be mentioned and identity kept secret.

## **RISK TO PARTICIPANT**

The possible risks involved in the study may be the fact that you may not be comfortable answering questions about yourself, in that you may fear that information and findings from the study will be shared with other. You are assured of complete confidentiality. Please understand that the urine sampling process will not be harmful. In the case of any problem, the doctors at the Medicine Department would attend to you.

## **BENEFITS TO PATIENTS**

The study would also help to identify the antibiotics suitable for treating bacteriuria identified to improve patient management and recovery. The study would help us to identify risk factors of hospital acquired urinary tract infections among stroke patients, which would help us to prevent the infection and improve patient recovery.

### **Section A: to be completed by researcher.**

I have fully explained to.....the nature and purpose of the above described study procedure and the risk that are involved in its performance.

I have asked the participant if he/she has any questions and I have answered all of his/her questions.

NAME OF RESEARCHER: ..... Contact: 0233919146

SIGNATURE:

Date.....

**Section B: to be completed by the study participant**

I have fully been informed of the above-described study with its possible benefits and risk I may face. I have been made to understand that, the study is entirely voluntary and that I can decide to participate or withdraw from it at any time without any consequences to the subsequent treatment and care my I receive at the health facility. I have been given the opportunity to ask questions that I have in relation to the research. All my questions have been answered to my satisfaction.

Name..... Signature..... Date.....

**Section C: to be completed by a witness to the consenting process**

**Name of witness.....**

**Signature/ thumbprint..... Date.....**

**APPENDIX II****STUDY QUESTIONNAIRE****A STUDY OF POST STROKE URINARY TRACT INFECTIONS AT THE KORLE  
BU TEACHING HOSPITAL**

Date: .....

Name: .....

ID: .....

**GENDER: MALE/ FEMALE****AGE: .....**

(YEARS)

**OCCUPATION: .....****PLACE OF RESIDENCE: .....***Please tick the box option that apply***MARITAL STATUS:** MARRIED SINGLE DIVORCED WIDOW/WIDOWER SEPARATED**HIGHEST EDUCATION COMPLETED:** PRIMARY SECONDARY TERTIARY NONE**MONTHLY INCOME (GHC):** 100-500 600-1000 1000-2000 2000-3000 >3000**1. Have you ever had a stroke attack before this current one? :** YES NO

If 'Yes', please continue with questions 2 to 4. If 'No', please skip to question 5

**2. When did you first develop stroke? .....****3. How many stroke attacks have you had in the past? .....**

4. When was your last stroke attack before the current one? .....

5. Have you had any infection prior to the current stroke?  YES  NO

6. If YES, please specify.....

7. Have you had a urinary tract infection prior to the stroke?

8. If YES, how was it treated?  Antibiotics  Herbal  Spiritual  Untreated

9. Do you smoke?  YES  NO

10. Do you drink alcohol?  YES  NO

*To be filled by investigator*

**STROKE TYPE:** .....

**AFFECTED PART:** .....

**SEVERITY (with Modified Rankin Scale (mRS))**  MILD  SEVERE

**PATIENT CATHETERIZED:**  YES  NO

**KNOWN COMOBIDITIES**

*Please tick all that apply:*

hypertension  Diabetes  dyslipidaemia  Atrial fibrillation  C.A.D.

M.I.  C.H.F.  Others :  
 1.  
 2.  
 3.  
 4.  
 5.

*C.A.D.- coronary artery disease, M.I.- myocardial infarction, C.H.F.- congestive heart failure*

Does the patient have any symptoms of UTI  YES  NO

Please specify the specific signs and symptoms:

1. 2. 3. 4. 5.
----------------------------

**MEDICATIONS:**

Is the patient on any medication  YES  NO

If yes, list the drug(s) and purpose of usage

- 1. ....
- 2. ....
- 3. ....
- 4. ....

**APPENDIX III****LETTER OF ETHICAL APPROVAL**

UNIVERSITY OF GHANA  
COLLEGE OF HEALTH SCIENCES  
ETHICAL AND PROTOCOL REVIEW COMMITTEE

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**MS-AA/C.2/Vol.18<sup>A</sup>**

10<sup>th</sup> April, 2015

My Ref. No.....

**Mr. Samuel Darkwah, M.Phil**  
**Department of Microbiology**  
**SBAHS**  
**Korle-Bu**

**ETHICAL CLEARANCE**

Protocol Identification Number: **MS-Et/M.6 – P 3.3/2014-2015**

The Ethical and Protocol Review Committee of the College of Health Sciences on 25<sup>th</sup> March, 2015 unanimously approved your research proposal.

TITLE OF PROTOCOL: **"A Study of Post Stroke Urinary Tract Infections at the Korle-Bu Teaching Hospital"**

PRINCIPAL INVESTIGATOR: **Mr. Samuel Darkwah**

This approval requires that you submit six-monthly review reports of the protocol to the Committee and a final full review to the Ethical and Protocol Review Committee at the completion of the study. The Committee may observe, or cause to be observed, procedures and records of the study during and after implementation.


Please note that any significant modification of this project must be submitted to the Committee for review and approval before its implementation.

You are required to report all serious adverse events related to this study to the Ethical and Protocol Review Committee within seven (7) days verbally and fourteen (14) days in writing.

As part of the review process, it is the Committee's duty to review the ethical aspects of any manuscript that may be produced from this study. You will therefore be required to furnish the Committee with any manuscript for publication.

**This ethical clearance is valid till October, 2015.**

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

Signed:   
PROFESSOR ANDREW A. ADJEI  
CHAIRMAN, ETHICAL AND PROTOCOL REVIEW COMMITTEE

cc: Provost, CHS  
Head of Department  
Research Office

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## APPENDIX IV

## Antibiotic susceptibility of Gram negative isolates

Antibiotics	Gram negative isolates				
	<i>E. coli</i>	<i>E. coli</i>	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>M. morganii</i>
Ceftriaxone	R	R	S	R	S
Ciprofloxacin	S	R	R	R	R
Augmentin	R	R	R	R	R
Ceftadizime	I	R	S	R	S
Nalidixic acid	I	R	R	R	R
Norfloxacin	R	R	R	R	R
Levofloxacin	S	R	R	R	R
Piperacillin	S	R	S	R	R
Gentamycin	S	R	S	R	R
Amikacin	S	S	S	S	S
Nitrofuratoin	S	I	R	R	R
Tetracycline	R	R	R	S	R
Cefuroxime	R	R	R	R	R
Chloramphenicol	S	S	S	S	R
Cotrimoxazole	R	R	R	R	R
Ampicillin	R	R	R	R	R
Cefotaxime	R	R	S	R	R
Meropenem	R	R	R	R	R

R- represent resistance, S- represent susceptible and I-represent intermediate susceptibility

**Antibiotic susceptibility pattern of Gram positive isolates and *Moraxella* sp.**

Antibiotics	Gram positive isolates		
	<i>Staphylococci sp</i>	<i>Staphylococci sp</i>	<i>M. catarrhalis</i>
Ciprofloxacin	R	I	S
Augmentin	R	S	S
Erythromycin	R	R	S
Ceftadizime	R	I	I
Nalidixic acid	R	R	R
Norfloxacin	R	I	R
Levofloxacin	R	I	S
Piperacillin	R	R	S
Gentamycin	I	S	S
Amikacin	S	S	S
Nitrofuratoin	S	S	S
Tetracycline	R	R	S
Cefuroxime	R	S	S
Cotrimoxazole	R	R	S
Ampicillin	R	R	S
Meropenem	R	R	S

*R- represents resistance, S- represents susceptible and I-represent intermediate susceptibility*