MEKELLE UNIVERSITY
COLLEGE OF HEALTH SCIENCES
DEPARTMENT OF MEDICAL MICROBIOLOGY AND IMMUNOLOGY

PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING BACTERIAL SPECIES FROM CATHETERIZED PATIENTS AT AYDER COMPREHENSIVE SPECIALIZED HOSPITAL AND MEKELLE GENERAL HOSPITALS,NORTHEN ETHIOPIA .

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Advisor's Approval Sheet

This is to certify that the Research thesis entitled "prevalence and antimicrobial susceptibility pattern of extended spectrum beta-lactamase producing bacterial species from catheterized patients at Ayder Comprehensive Specialized Hospital and Mekelle General Hospitals,Northen Ethiopia ." is submitted in partial fulfillment of the requirements for the degree of MSc,with specialization in "Medical Microbiology" to the Graduate Program of the College of Health Sciences of Mekelle University and has been carried out by G/giorgis Assefa ID No: CHS/PR169645/12)under my supervision. Therefore, I recommend that the student has fulfilled the requirements and hence hereby can submit the Research thesis to the Department of Microbiology and Immunology.

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LIST OF ABBREVIATIONS

UTI ----------Urinary tract infection

ESBL ----------ExtendedSpectrum beta –lactamase

CAUTI---------- Catheter-associated urinary tract infection

CoNS ----------Coagulates-negative staph

NIs ---------- Nosocomial infections

GNB ----------Gram-negative bacteria

MRSA----------Methicillin resistant *S. aureus*

BLPB ----------Beta-lactamase-producing bacteria

IUTC ---------- Indwelling urinary tract catheterization

PCR----------Polymerase chain reaction

WHO----------World health organization

ICU ----------Intensive care units

EPIC----------Infection Intensive in Care Study

SC---------- Self catheterization

ISC---------- Lower urinary tract

IC---------- Intermittent catheterization

LUT ----------Lower urinary tract

ISC---------- Self-catheterization

BCFC---------- Bacterial colonization on Foley's (urethral) catheters

SPP----------Species

AmpC----------Ampicillin class C

ABSTRACT

Background: Extended spectrum beta –lactamase (ESBL) producing bacteria are a public health problem globally, more than700000 deaths occur every year by multi-drug resistance. Patients catheter associated urinary tract infection and among the most affected by ESBL producing bacteria which results in increases the cost of medical care, extend hospital stay and mortality which needs to undergo regular surveillance and intervention.

Objectives: To determine the prevalence of extended spectrum beta –lactamase producing bacteria and their antimicrobial susceptibility pattern among catheterized patients at Ayder compressive specialist Hospital and Mekelle General Hospital.

Methods:A hospital based cross-sectional study was conducted on 310catheterized patients from October1/2023 to February30, 2024.Urine specimen (5-10mL) from patients catheterized with indwelling urinary catheters were collected in to a sterile labeled container. Urine specimens were delivered to the laboratory immediately and processed within 2hours.Each urine sample was inoculated onto MacConnkey agar and incubated at 37°C for 24 hours. Extend spectrum beta lactamace producing bacteria detection were done using biochemical and culture characteristics method and antimicrobial susceptibility tests to isolated bacterial pathogens was done using the disc diffusion technique. The data was entered and analyzed using Epidata version 3 and SPSS version 20, Chi-square was used to assess association between variables and then logistic regression was used to measure strengths of association, *p*-values less than 0.05 was considered statistically significant.

RESULT: The results show that 37/310(11.9%) of the participants had bacteria. Of these,Escherichia Coli 32/37 (86.5%), K.pnuemoniae 3/37(8.1%) and mixed (E.coli and K.pnuemoniae) 2/37(5.4%). ESBL was seen in 13/37(35.1%) of the bacterial isolated and was all seen on Escherichia *coli*, 13/13 (100%) isolates. Altogether 100% (n=37) isolates were sensitive to meropnem, 83.8% (n=31) to nitrofurantoin, and 59.5% (n=22) to gentamicin. 64.8% (n=24) isolates were resistant to antibiotic ampicillin while 29.7% (n=11) were found as multi-drug resistant (MDR).

Conclusion: Most ESBL-producing bacteria were E.coli, The prevalence of ESBL producing bacteria were on patients who admitted at medical ward. Microbiological-based therapy for patients with UTIs is essential at my study site due to high rates of ESBL production with concomitant high rates of drug resistance to several antibiotics.

Key words: ESBL; catheterization; Nosocomial infection; antimicrobial resistance, Tigray,

1.INTRODUCTION

Urinary tract infection (UTI) caused by bacteria is one of the major reasons for visiting health institutions, morbidity, and co morbidities in patients with underlying conditions\ worldwide. Though different pathogens cause UTI, various studies described that the causative agents of UTI are predominantly associated with Gram-negative bacteria such as *E. coli*, *Pseudomonas* species, *Klebsiella* spp., *Proteus* spp., and Gram-positive bacteria such as coagulase-negative staph (CoNS) and *S. aureus(*Ameshe, et.al, 2022).A catheter-associated urinary tract infection (CAUTI) is one of the most common infections a person can contract in the hospital, according to the American Association of Critical-Care Nurses. Indwelling catheters are the cause of this infection. An untreated UTI can lead to a more serious kidney infection. In addition, people with catheters may already have conditions that compromise their immune systems. Fighting off a CAUTI can cause further immune system stress. This makes more vulnerable to future infections(Rubi,et.al,2022).

The prevalence of ESBL producer *E. coli* and *Klebsiella* in Latin America showed an increase in 2008 compared to the previous years. Generally, 26% of *E. coli* and 35% of *K. pneumoniae* in Latin American are ESBL producers in 2008. In 2003, 10% of *E. coli* and 14% of *K.pneumoniae* are positive for ESBL production, while in 2004, it is 10% of *E. coli* and 18% of *K. pneumonia* (Rossi et al., 2006). In Iran, undertaken between 2007 and 2008, 45% of the *K.pneumoniae* isolated from urinary tract infections was found to be ESBL producers (Ghafourian et al., 2012). In the same study, it is detected that, 59.2% of *K. pneumoniae* of the clinical isolates from respiratory tract infections tested positive for ESBL production (Ghafourianet al., 2011).

In Kenya GNB infections prevalence is 40.8%, majorly caused by ESBL—producers (67.3%) predominated by *Klebsiella pneumoniae* (45.5%). mainly CTX-M-type (59%, 17/29) in *K. pneumoniae* (76.9%, 20/26). GNB harbouring TEM-type (83%, 10/12) and SHV-type (100%, 7/7) genes showed ESBLs phenotypes and inhibitor resistance (Mutua *et al 2023).*ESBL-producing Gram-negatives is determined 50.1%. Among different species, ESBL production rates are 65.7% (n = 263) for Klebsiella spp. 62.2% (n = 33) for Enterobacter spp., 48.4 %(n = 90) for Salmonella spp., 47.0% (n = 383) for E. coli, 46.8% (n = 22) for Citrobacter spp., 43.8% (n = 7) (Tufa ET al.2020).

The controlling of infectious diseases caused by pathogenic bacteria has become challenged in the last years due to the extension of bacterial resistance to several antibiotics. Infections caused by bacteria carrying resistant determinants have been associated with increased rates of mortality, hospital stay, therapeutic failure, and health costs.Antibacterial agents of the *β*-lactam group are frequently prescribed medications for the treatment of infections caused by Gram-negative bacteria (GNB). Members of GNB can hydrolyze many *β*-lactam antibiotics through the production of one or both of extended-spectrum *β*-lactamases (ESBLs) and AmpC *β*-lactamases. The production of ESBLs and AmpC *β*-lactamases mediated by both chromosomal and plasmid genes can transfer horizontally between GNB members. Bacterial strains carrying such enzymes are capable of being resistant to a wide variety of antibiotics, including *β*-lactam drugs. AmpC *β*-lactamases are clinically significant cephalosporinases encoded on chromosomes of Gram-negative rods which mediate resistance to cefoxitin, cephalothin, cefazolin, most of the penicillins, and *β*-lactamase inhibitor(Ibrahim, et. al, 2019).

*Enterobacteriaceae*are common causes of hospital and community acquired infections. The key challenge intheir treatment has been their tendency to develop resistance to commonly used beta-lactam agents. Yet, these drugs are the main stay of treatment especially in low income countries (Ampaire,et.al, 2017).

Limited therapeutic options for extended spectrum beta-lactamase (ESBL)-producing bacteria result in poor prognosis, high carrier rate, infectivity and an increased capacity to cause hospital acquired infections. Manystudies report *Klebsiella pneumonia* and *Escherichia coli* as the most common ESBL producing bacterial species. However, other bacterial species in the families of Enterobacteriaceae and Pseudomonadaceae are also known to produce such enzymes.

Escherichia coli is the most common causative agent of catheter-associated urinary tract infections (>20%). ESBL-producing strains of E. coli, while representing a small percentage (<10%), are particularly concerning because they confer resistance to a myriad of antibiotics including penicillins and third generation cephalosporins, and because their prevalence has been increasing in community and hospital settings during recent years(Raphael, Glymour and Chambers 2021). Extended-spectrum beta-lactamases (ESBLs) are enzymes that confer increased resistance to commonly used antibiotics. The prevalence rates of ESBL producing bacteria are increasing, and the associated increase in morbidity and mortality is becoming a public health concern. ESBL producers are emerging as an important cause of UTI and empirical

therapy should therefore be carefully selected for patients with UTI. Ertapenem or cefepime might be recommended for initial empirical therapy patients suspected of having complicated UTI(Lim, et.al,2015).

2. STATEMENT OF THE PROBLEM

The quality of health care provision at any level of health facilities is affected by many factors among which nosocomial infection is the leading one. Nosocomial infections increase the cost of medical care, extend the duration of hospital stay and increase the morbidity and mortality rate among admitted patients.Urinary tract infection includes symptomatic urinary tract infection, asymptomatic bacteriuria, and other infections of the urinary tract(Garner, et. al,1988)

Reducing the duration of catheterization may be a key intervention in CAUTI prevention(Crouzet, et. al, 2007).Intermittent catheterization (IC) and self-catheterization (ISC) are nowadays considered the methods of choice for the management of neurogenic lower urinary tract (LUT) dysfunction. Nevertheless, many still choose urethral catheterization (ID) or suprapubic catheterization (SC) as a means of management of urinary incontinence due to difficulty in performing IC/ISC or persistent leakage between catheterizations(Igawa, et.al,2008).

Indwelling urinary tract catheterization (IUTC) is a very common intervention frequently required in hospitalized patients. It is estimated that 10-12% of hospital patients and 4% of patients in the community have urinary catheters *in situ* at any given time. Nosocomial urinary tract infections(UTIs) develop in 5% of catheterized patients per day in the US, with associated bacteremia in 4% and as many as 80% are a consequence of urinary catheters Fever, pyelonephritis, urinary tract stones and chronic renal inflammation are some of the other complications of this procedure. IUTC also prolongs hospital stay and increases the cost of healthcare. Unfortunately, inappropriate and excessive catheter use still persists. Researchers have shown that just reminding physicians to remove unnecessary urinary catheters can significantly reduce the duration of urinary catheterization and the catheter associated urinary tract infection (CAUTI) rate in a hospital(Bhatia, et. al, 2010).

It is generally not recommended to treat asymptomatic catheter associated bacteriuria. However, it has been shown to be an important cause of hospital acquired urinary tract infections especially in post-operative patients. Bacterial colonization on Foley's (urethral) catheters (BCFC) can precede the emergence of bacteriuria and has a significantly higher rate of culture positives as compared to urine culture. This is especially true in the initial two to three days of catheterization. Hence, it is important to consider this parameter instead of a urine culture in order to obtain a more precise picture of asymptomatic infections of the urinary tract in catheterized patients. One of the important reasons for inappropriate catheterization could be the

lack of widely accepted guidelines regarding the indications for IUTC placement in medical patients. This makes the distinction between appropriate and inappropriate catheterization obscure(Bhatia, et. al, 2010).

Prevalence of ESBLs since dissemination of these enzymes is not restricted to the healthcare setting but also involves the community, especially among *Escherichia coli*. Since the beginning of the century, the prevalence of infection with ESBL, notably among *E.coli* and *Klebsiella pneumoniae*, has increased dramatically. Infections caused by ESBL producers have been associated with severe adverse clinical outcomes, leading to increased mortality, prolonged hospital stay, and increased costs, mostly because of delayed effective therapy(Razazi, et. al,2012).

In the face of the advance in modern medicine nosocomial infection still poses excessive and unselective consumption of broad spectrum and higher antimicrobial compound, contributing to the problem of bacterial drug resistance occurring in the association with catheterization and susceptibility pattern and risk of increased morbidity and mortality to patients which could able global problem. Therefore, the present study will be undertaken to investigate the bacteriology, drug susceptibility pattern of potential bacterial pathogens and detect the extended spectrum beta-lactamase-producing bacteria of the uropathogens among patients with indwelling urinary catheter at Ayder Teaching referral Hospital and Mekelle hospital.

3. LITERATURE REVIEW

UTI is one of the most common infections occurring in all age groups from neonates to old age. Due to anatomical pre- disposition i.e., close approximation of urethra and vagina and being sexually active during the reproductive age (15-50) UTI is more common in female. The relative frequency of the pathogens acquired by catheterization also varies depending upon age, sex and catheterization. UTI caused by bacteria is one of the major reasons for visiting health institutions, morbidity, and co morbidities in patients with underlying conditions worldwide. (ought different pathogens cause UTI, various studies described that the causative agents of UTI are predominantly associated with Gram-negative bacteria such as *E. coli*, *Pseudomonas* species, *Klebsiella* spp., *Proteus* spp., and Gram-positive bacteria such as coagulase-negative staph(CoNS) and *S. aureus* (Ameshe, et.al, 2022).

.Urinary catheters are mostly used to manage urinary incontinence and retentions, to measure urine output, or to help patients who had surgery or other medical conditions. Up to 25% of hospitalized patients need urinary catheters; however, catheterization is associated with increased risk of infection of the urinary tract. More over about 40% of all nosocomial infections in hospitalized patients are attributed to catheter-associated urinary tract infections the risk of acquiring an infection increases by 5% each day the catheter remains *in situ*. This indicates the critical need of following procedures that able to minimize the risk of infection in practice associated with catheter insertion and maintenance(Rubi, et.al, 2022).Hospital environment is a potential source of nosocomial infections, since it houses both patients with diverse pathogenic microorganism and a large number of susceptible individuals (Engda, et. al, 2018).

Nosocomial infections are defined as hospital acquired infection developing at least 48–72 h after admission. They are the commonest complications affecting hospitalized patients but are more frequent in intensive care units where outbreaks often originate. Three types of infection account for more than 60% of all nosocomial infections: pneumonia (usually ventilator-associated), urinary tract infection (usually catheter associated) and primary bloodstream infection (usually associated with the use of an intravascular device). Antibiotic resistant Gram-positive or negative bacteria including *Staphylococci*, a wide variety of Enterobacteriaceae, *Pseudomonas species*, *Acinetobacter species* . account for up to 70% of the nosocomial infections in the ICU patients(Ahmed, et. al, 2009) .

There are approximately 2 million nosocomial infections(NI) per year in the USA, and 600 000 per year in France(Schneider, Veyres et al. 2004). Patients who develop NI are two to three times as likely to die, 60%more likely to spend time in an intensive care unit, and two to five times more likely to be readmitted to hospital than those who do not. It has been estimated that 1% of all patients with an NI die as a direct result of the infection, and that NI contribute to the death of 2·7% of all patients admitted to hospital. Thus, NI could be responsible for 6–10% of all intra-hospital deaths. The excess duration of hospitalization secondary to NI ranges from 1–4 d for urinary tract infections to 6·8–30·0 d for pneumonia(Schneider, et. al,2004).

Five to ten percent of patients admitted to acute care hospitals acquire one or more infections, and the risks have steadily increased during recent decades. Intensive care units represent only 5–15% of hospital beds and account for 10–25% of healthcare costs, corresponding to 1–2% of the gross national product of the United States(Schneider, et. al, 2004). A World Health Organization (WHO) systematic review and meta-analysis showed health-care associated infection density in adult intensive-care units in developing countries is 47.9 per 1000 patient-days, at least three times as high as densities reported from the USA(Peter Agaba,et.al, 2017). In Canada,between 1 September 2005 and 30 June 2006, collected 4180 isolates recovered from clinical specimens from patients in 19 intensive care units and found *Staphylococcus aureus* (methicillin sensitive *S. aureus* andmethicillin resistant *S. aureus, MRSA*), *Escherichia coli*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Enterococcusspecies*, *Streptococcus pneumoniae*, and *Klebsiella pneumoniae* were the most common isolates (Peter Agaba,et.al, 2017).

An extended spectrum beta-lactamase production has been observed mostly in *Entrobacteriaceae,* and theirresistance increased mainly due to the spreading of ESBL and the emergence of different genes. The frequently ESBL producing *Entrobacteriaceae* are *Escherichiacoli, Klebsiella pneumoniae* and *Proteus species*.However, all other clinically relevant *Entrobacteriaceae* species are also common ESBL producers. The distributionof ESBL depends on geographic locality, hospital wards, groups of patients and the type of infection.

The resistance patterns of ESBLs are initially considered as a problem related to nosocomial outbreak,mainly in Intensive Care Units, surgical procedures, bladder catheterization, long-term hospitalization, and frequent exposure of broad spectrum antimicrobials(Engda, et. al, 2018).

Beta-lactamase-producing bacteria may have an important clinical role in infections. These organisms can be pathogenic in causing the infection as well as have an indirect effect through their ability to produce the enzyme BL into their environment. BLPB may not only survive penicillin therapy but also may protect other penicillin susceptible bacteria from penicillins by releasing the free enzyme into their environment(Brook,et.al, 2009).Beta-Lactam antibiotics include (penicillins,cephalosporin, carbapenems & monobactams) arecommon to treat bacterial infections. The emergenceof β-Lactamases mediated bacterial resistance, are due to the irrational use of antibiotics, particularlythe third generation cephalosporins, which subsequently led to the development of ESBL producing bacteria*(Chaudhary,et.al, 2020).*

Patients infected with ESBL-producing bacteria are likely not treated with beta-lactam antibiotics owing to the risks of treatment failure leading to death and amplified infectiousness. Therefore, early detection of these bacteria is important to control and prevent nosocomial outbreaks in hospital settings(Andrew,et,al, 2017).

Prevalence of *Klebsiella* species isolated from urine specimens in Nepal revealed that *K. pneumoniae* accounted for 145 (2.3%); whereas the prevalence of *Klebsiella* species in India was 170 (4.3%), of which, 116 (68.2%) were *K. pneumoniae* and 54 (31.8%) were *K. oxytoca;* in Saudi Arabia 23.5%; Yemen 42 (24.7%); and Nigeria 14 (7.0%) were *Klebsiella pneumoniae* and 2 (1.0%) were *Klebsiella oxytoca.* In Uganda, 10/86 (11.6%) *Klebsiellapneumoniae* and 6/86 (7.0%) Klebsiella oxytoca were isolated from midstream urine of the patients; in the northeastern part of Ethiopia, Klebsiella species isolated were 40 (5.88%) among the urinary isolates; 8.1% Klebsiella spp. In Northern Ethiopia (Mekele); 29 (15.8%) K. pneumonia in Gondar; and two studies in Bahir Dar showed 13.6% K. pneumoniae and 5/7 (71.4%) K. pneumoniae, 1/7 (14.3%) K. ozaenae, and 1/3 K. rhinoscleromatis(Ameshe, Engda and Gizachew 2022). Another study in a SouthAfrican hospital, established 36% of K. Pneumoniae isolates were ESBL-producers. Outbreaks of infections due to Klebsiella strains resistant to third-generation cephalosporins have also been reported in Uganda, Nigeria and Kenya(Abubakar, et. al, 2020).

E coli accounted for most of the bacteria (74.1% to 81.0%) that produced ESBLs.E.coli is the most often isolated followed by pseudomonas aeruginosa ,entrococcus faecalis ,klebisiella pneumonia,or methicillin –resistant staphylococcus aureus(Takaba, et al, 2014).

Previous observations have confirmed that ESBL-producing production bacteria(Rubio-Perez, et. al, 2012)are not only resistant to antibiotics but a variety of disinfectants which emphasizes that their characterization is an important aspect of infection control. Furthermore, the information on the capacity of a clinical isolate to produceExtended-spectrum beta-lactamase (ESBL)-producing production bacteria would help a clinician to evaluate the measure of its virulence and devise an appropriate treatment plan for the patient. the present study will be undertaken to investigate the bacterial profile,determine ESBL-producing productionbacteria and their antimicrobial resistance pattern of catheterized patients.

ESBL-producing isolates were found to besusceptible primarily to meropenem (96.7%), amikacin(82.1%), and cefoxitin (70%). This was in close agreementwith studies done in Ghana (meropenem 100%), central India (meropenem 87.5%, amikacin 83.92%), Jimma, Ethiopia (amikacin 83.7%) , and India(meropenem 94.0%, amikacin 82.6%) . The resultsindicate that these antibiotics were the most active treatmentof choice for ESBL-producing Enterobacteriaceae(Teklu, et. al, 2019).

North east Ethiopia(Desie) total of 203 Gram-negative bacteria isolates, 150 (73.9%) were suspected for ESBL production with cefotaxime zone of inhibition ≤27 mm and ceftazidime zone of inhibition ≤22 mm. Out of the 150 suspected Gram-negative bacteria isolates 108 (72%) were confirmed ESBL production by using a combination disc test(Tilahun 2022).in addis Ababa the Enterobacteriaceae isolates, 62.2% (265/426)were positive for the screening test of ESBL productionas measured with cefotaxime zone of inhibition≤27 mm and ceftazidime zone of inhibition ≤22 mm.Using the combination disk test, 92.8% (246/265) of the suspected isolates were able toproduce ESBL resulting in an overall ESBLs positivityof 57.7% (246/426)(Tekele, et. al, 2020).significant risk factors for the isolation of non ESBL K.pneumoniae strains were length of hospitalization(Rita citton,et.al,2006).

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4. SIGNIFICANCE OF THE STUDY

A number of risk factors predictive of catheter-associated urinary tract infections (CAUTI) such as being female, duration of catheterization, microbial colonization of the drainage bag and disconnection of the catheter collecting tube junction(Crouzet, et. al, 2007).The increasing prevalence of infections due to ESBL-producing bacteria creates a challenge regarding appropriate antimicrobial therapy, especially in the community setting where oral antibiotics are used(Kassakian and Mermel,et.al, 2014).

In the present study, the level of antimicrobial resistance of gram negative bacilli ranged from0–75.4%. A higher resistance level was seen to ampicillin (75.4%), amoxicillin with clavulanicAcid (64.0%), sulfamethoxazole-trimethoprim (55.6%), aztreonam and cefuroxime (48.8%),Cefotaxime (47.0%), cefepime (45.6%), ceftriaxone (44.9%) and ceftazidime (44.1%). Comparableresults were reported from studies performed in Gondar and Debre Markos inEthiopia. ESBLs producing organisms are the major cause of treatment failure, impaired clinical and microbiological responses, longer hospital stay and increased healthcare costs(Tekele, et. al, 2020).Globally, immediate needs to identify EBSL and formulate strategic policy initiatives to reduce their prevalence(Kassakian and Mermel,et.al, 2014).

ESBL producing bacteria may be reduced by using the sensitive drugs. This reduction with using antibiotics can be done based on the local antimicrobial resistance result of bacterial isolates. Hence, information about the incidence of ESBL producing Bacteria colonization by different microorganisms and their drug susceptibility pattern play an important role in treatment of such infections. In addition this to the ESBL producing bacteria and antimicrobial resistance pattern among bacterial isolates from catheter associated urinary infection in relation with catheterization is limited in the study area or not assed. Hence the study will also establish the drug susceptibility pattern of pathogens isolated from patients with an indwelling urinary catheter. The results of this study are important in terms of:

- Determining common pathogenic isolates and their drug susceptibility pattern
- Provide some data which will help improve existing infection prevention activities in the hospital

5. OBJECTIVE

5.1 General objective

- To Isolate and determine ESBL producing bacteria and their antimicrobial susceptibility

Pattern among catheterized urinary tract infection patient at Ayder Compressive Specialized Hospital and Mekelle General Hospital,

Northern Ethiopia.

5.2 Specific objective

- To determine prevalence of bacteria isolates from catheterized patients
- To determine ESBL producing bacteria from patients catheterized within dwelling urinary catheters.
- To determine antimicrobial susceptibility pattern of bacterial isolates to the commonly used antimicrobial agents.

6. METHODS AND MATERIALS

6.1. Study Area

The study was conducted at Ayder Comprehensive Specialized Hospital and Mekelle General Hospital, Mekelle, Tigray, North Ethiopia. Mekelle town which was founded around 13th century is the capital city of Tigray Regional State. Mekelle is located at 787 km North of Addis Ababa, the capital city of Ethiopia. According to 2016 census program the total population of the town was reported about 310436 (2016). Ayder Referral Hospital is the largest university hospital in the region which has about 500 beds, which is under Mekelle University. Whereas Mekelle Hospital have 200 beds and is governed by Regional Health Bureaus. These hospitals serve patients from all parts of the region and other neighborhood regions such as Afar and Amhara regional states.

6.2. Study Design and Study period

The study design was a hospital based cross sectional method. The study was conducted from October 2023 to February 2024 at Ayder comprehensive specialist Referral Hospital and Mekelle Genral Hospital.

6.3. Source Populations

The source populations were all catheterized patients that get service at both hospitals.

6.4. Study participants

The study participants were all admitted patients that undergo indwelling urinary catheterization at hospital.

6.5. Inclusion criteria

- All patients who are willing and can give written/oral consent
- All adult (≥18 years) patients catheterized with indwelling urinary catheters and admitted at Ayder referral and mekelle hospital.
- All patients with signs and symptoms of urinary tract infection prior catheterization
  Or UTI diagnosed at admission
- All catheterized patients whose indwelling urethral catheter has been removed within the previous 48 hours

Exclusion Criteria

- Critically ill patients
- Below 18 years age

6.6. Sample Size Determination and Sampling Techniques

6.6.1. Sample size determination

The sample size was computed using the following formula: (single population proportion)

Study participants: n= $(z/d)^2 \times p\ (1-p)$

Where n = sample size

z = statistic for level of confidence

p = previous prevalence

d= margin of error (degree of accuracy desired)

Considering 72% estimated previous prevalence of dessie (Tilahun 2022) 5% precision(d=0.05) and 95% level of confidence (z=1.96). The sample size is estimated to be:

= $(1.96/.05)^2 \times 0.72\ (1-0.72)$ = **310**

Therefore a total number of 310 patients catheterized with indwelling urinary catheter were included in the study.

6.6.2. Sampling technique

A non probability sampling technique was employed. Consecutive patients who were admitted and need catheterization with indwelling urinary catheter attending at Ayder Teaching Referral and Mekelle Hospital during the study period were included. Tracing of patient admission at the different wards were done by assessing each ward admission and discharge records daily and communicating with the trained data collectors on each ward. The distribution of the 310 study subjects into the two Hospitals were done based on proportion to size with respect to source population of each Hospital. Among the total source of population (all admitted patients) to Hospitals catheterized patients in two month from previous report, (4966/6190) Ayder Referral Hospital and (600/3000)Mekelle General Hospital accounts 80%and 20% respectively. By using proportion to size out of 310 study participants 248 and 62 were included from Ayder Referral Hospital and Mekelle Hospital respectively.

6.7 Study Variables

6.7.1 Dependent variables:

- Bacterial isolates
- Drug susceptibility pattern
- ESBL producing bacteria characteristics

6.7.2 Independent variables:

- Age
- Sex
- duration of catheterization
- underlying diseases
- site (place) of catheter insertion out of operating room
- History of previous catheterization and UTI infections

6.8 Data collection

6.8.1 Demographic and clinical profile

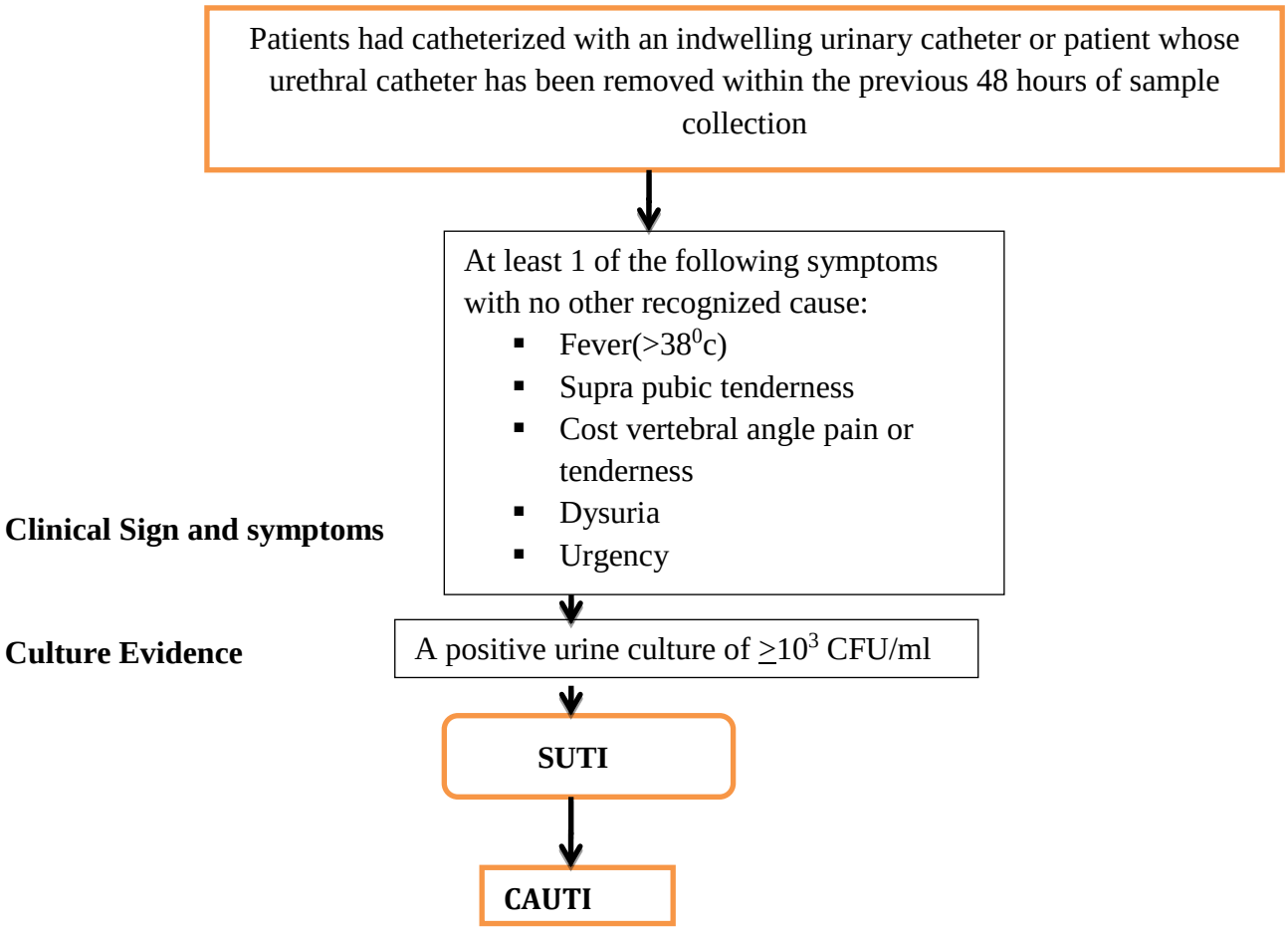
Clinical history of the study participants was collected from each patient and from patient history recording charts (MRN). Socio demographic data of the study participants was be collected by the principal investigator using the prepared structured questionnaire in local language (See Annex VII).

6.8.2 Laboratory analysis

6.8.2.1 Sample collection, handling and transportation

Urine specimen (5-10mL) from patients catheterized with indwelling urinary catheters were collected in to a sterile labeled container using a sterile syringe with needle after cleansing the out let of catheter with appropriate disinfectant (70% alcohol) or a midstream voided urine specimen from a patient whose urethral catheter has been removed within the previous 48 hours of sample collection by clean catch midstream collection Urine specimens were delivered to micro biology laboratory immediately and processed within 2hours. Samples were directly inoculated on to MacConkey agar.

Diagram 1: Identification and Categorization of CAUTI in patients with indwelling urinary Catheter



6.8.2.2 Culture and identification

Each urine sample was inoculated onto MacConkey agar plate by using a calibrated loop (0.001mL) and incubated at 37°C for 24 hours. The counted colonies yielding bacterial growth of 10^5 CFU/ml for single midstream urine is considered significant for positive bacteriuria. Isolates were preliminarily screened by their colony morphology, pigment production (pink), flat or mucoid colonies, and Gram staining reaction. Further identifications of isolates was made through a series of biochemical tests such as triple sugar iron agar, indole, Simon's citrate, and urea, and motility tests are performed by picking lactose fermented or pink colonies from MacConkey agar for identification of isolates to the species level by using the Clinical Laboratory Standards Institute (CLSI) guideline 2018(merilda,Givana et.al,2018.

6.8.2.3 Detection of ESBL

The screening (ESBL) was done using ceftazidime (≤22 mm),Agumentin(Amoxicillin clavulanic Acid)and cefotaxime (≤27 mm). More than one antimicrobial discs were used for screening to improve the sensitivity of ESBL detection as recommended by CLSI, guideline 2018. The organisms that showed zone of inhibition lower than the minimum for any of the above antimicrobial discs were considered as ESBL positive. The phenotypic confirmations were done by testing the isolated bacterial species against CAZ (30μg), AUG (30μg) and CTX (30μg/discs). In this test, an overnight culture suspension of the bacterial isolate was adjusted to 0.5 McFarland's standard. Cultures were done on the Mueller–Hinton agar (MHA) plate. The Ceftazidime, Augmentinand Cefotaxime discs were placed at 20mm apart on the agar surface. After incubating at 37°C for 24 hours, AUG ≥5mm increase in the zone diameter of inhibition in comparison to Ceftazidime is taken as indicative for ESBL positive/producer (Rani et,al 2018).

6.8.2.4 Antimicrobial susceptibility testing

Antimicrobial susceptibility pattern determination for all isolates was carried out using the standard disk diffusion method with commercial disks, on well-isolated colonies of similar appearance that are considered significant according to the guidelines. The antimicrobial susceptibility testing were done by using the Kirby-Bauer disc diffusion Method on Mueller–Hinton agar by following the CLSI guideline 2018 for ampicillin (10μg), *amoxicillin/ clavulanic*

acid (2μg), ciprofloxacin (5μg), gentamicin(10μg), cotrimoxazole (25μg), nitrofurantoin (300μg), meropenem (10 μg), ceftazidime(30μg), cefotaxime (30μg), and cefoxitin (30µg) discs.

6.9 Quality control

Quality control for the new batch was performed using ATCC 25922 E. coli standard strain to check the quality of culture media and antibiotics disks. For the ESBL confirmatory test, K. pneumonia ATCC® 700603 (ESBLs positive) and E. coli ATCC® 25922 (ESBLs negative) control strains were used to check the quality of the commercially purchased antibiotics disks and in-house prepared combination disks. The data collection form were checked for its completeness and accuracy before recording the data (kasu et.al,2019).

6.10 Data management, Analysis and Interpretation

Questionnaire was checked for its completeness, unrecorded values and unlikely responses and was manually cleaned up. Laboratory result was recorded in the laboratory data result formats coded for each participant. Pre-coded data was entered Epi data version 3 and analyzed using Statistical Package for Social Sciences (SPSS) version 20. Descriptive analysis was used to determine the distribution of bacterial pathogens and their ability of ESBL production. Association of the variables was determined by calculating odds ratio and level of significance was set at $p < 0.05$.

6.11 Ethical Considerations

Ethical clearance was obtained from Mekelle University, College of Health science institutional review board (MU-IRB)(2154/2024). Permission was obtained from Regional Health Bureau, Ayder Referral Hospital and Mekelle hospital administration, where the study was carried out. Study participants and/or their relatives were informed on the procedures and significance the study. No or minimum harm is associated with the study procedures. Each data and analysis result was kept confidential and result was only communicated to clinicians assigned at the health facilities. The laboratory findings of study participants were communicated with the responsible clinicians assigned at the health facilities and patients were treated accordingly. Any participant who is not volunteer was not enforced to be included as study subject and participants were informed to refuse participating in the study at any point study stage.

6.12 Operational definitions

- CA-UTI in patients with indwelling urethral, indwelling suprapubic, or intermittent catheterization is defined by the presence of symptoms or signs compatible with UTI(fever >38^0C, urgency, frequency, dysuria, or suprapubic tenderness cloudy urine blood in the urine strong urine odor, urine leakage around your catheter pressure, pain, or discomfort in your lower back or stomach ,chills ,fever ,unexplained fatigue, vomiting) with no other identified source of infection along with $\geq 10^3$ colony forming units (cfu)/ml of in a single catheter urine specimen or a midstream voided urine specimen from a patient whose urethral catheter has been removed within the previous 48 hours of sample collection (Rubi, et.al, 2022).
- **Catheter associated asymptomatic bacteriuria**: is isolation of a specified quantitative count of bacteria from a single catheterized urine specimen in a quantitative count $\geq 10^5$CFU/mL and the absence of signs and symptoms that may suggest a urinary infection, such as: Fever, urgency, frequency, dysuria, suprapubic tenderness and costovertebral angle pain or tenderness (Crouzet, et. al., 2007)..

7 Results

7.1 *Socio-demographic characteristics of study participants*

Three hundred ten (310) patients were recruited in this study. Majority of the participants; were females 169(54.5%), and the rest were male 141(45.5%), from these participant 98(31.6%) were 18-29 age range. Most patients were admitted in medical ward; 207(66.8%). Gyn ward, surgical and ICU were 65 (21%), 19(6.1%) and 19(6.1%) respectively (Table 1).

Table 1-Distributionofparticipants by Age, gender and ward among catheterized patients at Ayder Referral Hospital and Mekelle General Hospital, Tigray, Ethiopia [October. 1/2023 to February30, 2024].(n=310)

Variable	**Category**	**Frequency**	**Percent**
Age	18-29	98	31.6
	30-39	75	24.2
	40-49	51	16.5
	50-59	30	9.7
	≥60	56	18.1
	Total	310	100
	Mean	31+2.58	
Gender	Female	169	54.5
	Male	141	45.5
	Total	310	100
Ward	Medical	207	66.8
	Gyn	65	21
	Surgical	19	6.1
	ICU	19	6.1
	Total	310	100
Duration of catheter with patient	1-5 days	195	62.9
	6-10days	93	30
	11-15days	17	5.5
	≥16	5	1.6
Treatment before catheter	Yes	46	14.8
	No	264	85.2

Key, Age category is according to WHO, ICU (Intensive care unit)

Diagnose of participants

Of the 310 participants, the major diagnose was UTI 156 (50.3%) followed by HAI 20(6.5%) Viral Hepatitis 17(5.5%) Uro Sepsis 13(4.2%) and others 68(21.9%) (Table 2).

Table 2: diagnose of admitted catheterized patient at Ayder Referal Hospital And Mekelle General Hospital [October. 1/2023 to February30, 2024](n=310)

Diagnose	Frequency	Percent
DYSPEPSIA	8	2.6
HAI	20	6.5
STROKE	11	3.5
URO SEPSIS	13	4.2
UTI	156	50.3
VIRAL HEPATITIS	17	5.5
YELLOW FEVER	6	1.9
UTI+DM	11	3.5
Others	68	21.9
Total	310	100.0

Key:UTI(urinary tract infection),HAI(health care associated infection)

7.2 prevalence of Bacteria isolated

In this study, out of 310 cultured specimens, 37 had bacterial growth.Majority 32 (84.6%) of the bacterial isolates were E.coli. followed by k.pnuemonia3 (8.1%).13 out of the 37 isolates (35.1%) were ESBL producing bacteria. ESBL production was all expressed by Escherichia coli (13/13) (Table 3)

Table 3: prevalence of Bacteria isolated from catheterized patient at Ayder Referral Hospital and Mekelle Gnenral Hosipital [October. 1/2023 to February30, 2024] (n=37)

Bacteria isolated	Frequency		Percent	
	Non-ESBL	ESBL	Non –ESLB	ESBL
E.coli	***32***	***13***	86.5	100
k.pnuemenia	***3***	***0***	8.1	0
E.coli and K.pnuemenia(mixed)	***2***	***0***	5.4	0
Total	***37***	***13***	100	100

Key:E.coli (Escherichia coli),k.pnuemonia (klebsiella pneumonia

7.3 prevalence of ESBL producing bacteria

Growth of bacteria was 37 out of 310 participant (10.9%).13 out of 37 were EBL producing bacteria .all ESBL was expressed on E. *coli* (13/13) 100%.from 13ESBL producing bacteria 5(38.5%) of the patients were female and 8(61.5%)were males. 8(61.%) were from medical wards, 3(23.1%) were from gynaecology wards and 2(15.4%) were from ICU. There was no significant association between ward and ESBL production ($p \leq 0.05$) (Table 4).

Table 4. Result of multivariate analysis showing association between Socio-demographic characteristics and prevalence of ESBL producing bacteria at Ayder Referal Hospital And Mekelle General Hospital (N=37)

Variable		Total	ESBL character		COR	95% Confidence interval	*p* -value
			ESBL N=13	Non- ESBL N=24			
Sex	Female	19	5(26.3%)	14(73.7%)	0.558	0.306-1.419	
	Male	18	8(44.4.5%)	10(55.5%)	2.240	0.51263-8.9	0.252
Age	18-29	12	6(50%)	6(50%)	3.500	0.505-24.270	0.205
	30-39	6	2(33.3%)	4(66.6%)	1.750	0.173-17.686	0.635
	40-49	7	2(28.6%)	5(71.4%)	1.400	0.144-13.568	0.772
	50-59	3	1(33.3%)	2(66.6%)	1.750	0.099-30.837	0.702
	≥60	9	2(22.2%)	7(77.8%)	1		
Ward	Medical ward	25	8(32%)	17(68%)	0.194	0.015-2.501	0.209
	Gyn ward	9	3(33.3%)	6(66.6%)	0.400	0.026-6.176	0.512
	ICU ward	3	2(66.6%)	1(33.3%)	1		
Treatment before catheter	Yes	9	4(44.4%)	5(55.6%)	0.592	0.128-2.749	0.504
	No	28	9(32.1%)	19(67.8)	1		

Key; ESBL Extended spectrum beta lactamace, COR (crude odd ratio), ARH- ayder referral hospital,MGH- mekelle general hospital

7.4 Antimicrobial susceptibility bacteria isolate

The antibiotic susceptibility test profile of the identified bacteria was determined by modified Kirby Bauer disc diffusion method. The bacteria isolates showed highest sensitivity to Meropenem (100%), Nitrofurontion(83.8%) and Gentamycin(59.5%) respectively.Similarly high resistant rate was found againstampicillin (**64.8**%), Ampicillin sulbactam (56.8%). (Table 6)

Table 6. Antimicrobial susceptibility bacteria isolates from catheterized patients at Ayder Referal Hospital and Mekelle General Hospital (N=37)

antimicrobial agents	No of bacterial isolate=37	Susceptibility pattern		
		Sensitive No (%)	Intermediate No (%)	Resistant No (%)
Ampicillin		**2(5.4%)**	**11(29.7%)**	**24(64.8%)**
Ampicillin sulbactam		**2(5.4%)**	**14(37.8%)**	**21(56.8%)**
Agumentin		**18(48.6%)**	**17(45.9%)**	**2(5.4%)**
Cefazoline		**13(35.1%)**	**22(59.5%)**	**2(5.4%)**
Ceftriaxone		**10(27%)**	**23(62.2%)**	**4(10.8%)**
Cefotaxime		**13(35.1%)**	**20(54.1%)**	**4(10.8%)**
Ceftazidime		**20(54.1%)**	**15(40.5%)**	**2(5.4%)**
Levofloxcin		**11(29.7%)**	**15(40.5%)**	**11(29.7%)**
Cotrimoxazole		**9(24.3%)**	**18(48.6%)**	**10(27.0%)**
Gentamycin		**22(59.5%)**	**12(32.4%)**	**3(8.1%)**
Meropenem		**37(100%)**	**0**	**0**
Nitrofurontion		**31(83.8%)**	**6(16.2%)**	**0**

Key:ARH- ayder referral hospital,MGH- mekelle general hospital

7.4 Antimicrobial susceptibility of ESBL producing bacteria isolate

The antibiotic susceptibility test of the identified ESBL producing bacteria was determined by modified Kirby Bauer disc diffusion method. The bacteria isolates showed highest sensitivity to Meropenem (100%), Nitrofurontion(76.9%)and Gentamycin(53.8%). Similarly high resistant rate was found against Ampicillin (92.3%), Ampicillin sulbactam (84.6%) and Cotrimoxazole (**30.8%)**%). (Table 7)

Table 7. Antimicrobial susceptibility of ESBL producing bacteria isolates from catheterized patients at Ayder Referal Hospital and Mekelle General Hospital (N=13)

antimicrobial agents	**No of bacterial isolate=13**	**Susceptibility pattern**		
		Sensitive No (%)	**Intermediate No (%)**	**Resistant No (%)**
Ampicillin		**0**	**1(7.7%)**	**12(92.3%)**
Ampicillin sulbactam		**0**	**2(15.4%)**	**11(84.6%)**
Agumentin		**6(46.2%)**	**6(46.2%)**	**1(7.7%)**
Cefazoline		**2(15.4%)**	**8(61.5%)**	**3(23.1%)**
Ceftriaxone		**1(7.7%)**	**8(61.5%)**	**4(30.8%)**
Cefotaxime		**3(23.1%)**	**9(69.2%)**	**1(7.7%)**
Ceftazidime		**2(15.4%)**	**9(69.2%)**	**3(23.1%)**
Levofloxcin		**2(15.4%)**	**8(61.5%)**	**3(23.1%)**
Cotrimoxazole		**1(7.7%)**	**8(61.5%)**	**4(30.8%)**
Gentamycin		**7(53.8%)**	**5(38.5%)**	**0**
Meropenem		**13(100%)**	**0**	**0**
Nitrofurontion		**10(76.9%)**	**3(23.1%)**	**0**

Key; SEBL Spectrum extended beta lactamace**,**ARH- ayder referral hospital,MGH- mekelle general hospital

Table 8: Multidrug resistance pattern of isolated bacteria from catheterized patients at Ayder Referal Hospital and Mekelle General Hospital

Organism isolated	Total no. of isolates	No. of MDR (%)	Non-ESBL	EBL
E.coli	**32**	**10(31.3)**	**4(40%)**	**6(60%)**
k.pnuemenia	**3**	**1(33.3)**	**1**	**0**
E.coli and k.pnuemenia(mixed)	**2**	**0**	**0**	**0**
Total	**37**	**11(29.7)**	**5(45.5%)**	**6(55.5%)**

MDR: melti-drug resistance

8 Discussion

Strains of ESBL-producing bacteria have become a concern in the treatment of infections and infection control programs in hospital settings. Most *E. coli*and*K. Pneumonia* are resistant to Ampicillin because of the production of plasmid mediated β-lactamase enzymes. Most isolates are susceptible to Meropenem and Nitrofurontion.ESBLs-producing bacteria are a major problem in the management of certain bacterial infections and are a growing concern in those hospitals where antibiotics use is frequent and the patients are in critical conditions. ESBL-producing bacterial pathogens limit the rapeuticoptions for the treatment.

In this study, Meropenem, Nitrofurontion and Gentamycin with the susceptibility rate of (100%),(83.8%) and (59.5%) respectively were found to be the most active drug against ESBL producing bacteria isolates. Ampcillin(64.8%),Ampcillin sulbactam was found as the most resistant drug. In this study, 29.7% of the total bacteria isolates were found as MDR.

In this study, the proportion of participants who were confirmed to have urinary tract infection was 37 out of the 310(11.9%). This relatively low proportion of participants with UTI was probably due to the fact that there are different nonbacterial conditions that can manifest with UTI like symptoms. In this study lower prevalence with the findings from different studies which include; in Uganda with a prevalence of (27%), [1], in India with a prevalence of (29.4%) [22], in Senegal by with a prevalence of (26.7%) [23], in India with a prevalence of (12.65%) [24] And in West Bengal India with a prevalence of (27.75%) [1].

The proportion in this study was higher compared to those from different studies which include; in Uganda which was (10%) (Mwaka A el al 2011) and in Bangui, Central African Republic which was (10.9%) (Bercion R el al.2009).This indicates there is a varied prevalence of urinary tract infection in different areas due to socio-economical differences but UTI is still a challenge to the current health care system. The most common uropathogens that were isolated were Escherichia coli.

This was probably due to the fact that normal flora and more pathogenic in humans as compared to other isolates and if introduced in the urinary tract they can cause UTI depending on one'simmune status. Since most of the participants were female, the anatomical closeness of the anal opening and urethral opening together with poor hygienic practices may facilitate the introduction of the pathogens in the urinary tract. Other common uro pathogens isolated in this study included;k.pneumenia and mixed (E.coli and k.pneumenia). My finding is similar to those that were showed by a study in Central African Republic and a study in Uganda which indicated that Escherichiacoli was the most common uropathogens that caused UTI.

In this study, uropathogens that were Extended Beta Lactam Producers had a frequency of 13 isolates out of the 37 isolates (35.1%). ESBL production is increasingly becoming a problem especially due to the factthat gram negative bacteria have many resistance mechanisms, due to erroneous use of drugs inempirical treatment and lack of appropriate infection control strategies, which may result in increased prevalence of resistant organism in the community. This proportion was lower than Nepal, 55.6% [26], Cameroon, 55.3% [27]; and India 54.3% [28]. However, it was higher than the Bahir Dar Ethiopia 24.8%, [29] France 25% [30], Nepal (28.2%) [31], Qatar 26% [31] and Israel 21.4% [32]. This variation was probably due to the difference in the sample size and the nature of participants recruited.

In this study, all the ESBL producing bacteria were Gram negative bacteria with Escherichia coli having the highest proportion of 13 out of 13 isolates (100%). The results of this study were different from the study done at Kabale Regional Referral Hospital where Klebsiella species predominated with 52%, followed by Escherichia coli (44%)[1,5] but similar to those in the study done in Cameroon where Escherichia coli (50.9%) [1] Was the most common pathogen.

9 Conclusion and Recommendations

This study showed that most common uro-pathogens that were responsible for urinary tract infections at MGH/ACSH were Escherichia coli. A number of uro-pathogens isolated were ESBL producing, and all ESBL producing uro-pathogens were Gram negatives with Escherichia coli showing the highest proportion. Therefore, such UTI patient should be managed based on microbiological analysis, including antibiotic susceptibility testing results, rather than just on clinical grounds and empirical treatment.

Catheterized infections due to ESBL-producing bacteria, amarked increase in healthcare-associated infections, we found high levels of Cefazoline,Ceftaxime and Cotrimoxazole

Resistance. This has implications regarding empiric therapy for urinary tract infections sincethese frequently utilized antibiotics in the outpatient setting are ineffective for such pathogens. Another important finding is the susceptibility of ESBL-producing E. colito Meropenem. Further elucidation of underlying genetic makeup of ESBL-producing pathogens will assistin better understanding the epidemiology of these emerging infections.

There is need for sensitization of the community and the health workers about urinary tract infections and the existence of drug resistance among uro-pathogens.The laboratories need to be well equipped with necessary materials for proper diagnosis of urinary tract infection and detection of ESBL production. This will help in the management of ESBL producing uropathogens and UTI at large.

There is need for improving on laboratory surveillance systems to help in the monitoring of the Emergence of Extended Spectrum Beta Lactam producing pathogens routinely.

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11 ANNEXES

Annexes I: Patient information sheet form (English version)

My name is G/giorgis Assefa and I am MSc student in microbiology atMekelle University College of Health science department of Immunology and Medical Microbiology. I am doing a research on isolation, determination of ExtendedSpectrumbeta –lactamase (ESBL)producing bacteria and antimicrobial susceptibility of bacterial pathogens from patients catheterized with indwelling urinary catheter.

Purpose- planned to conduct a study to determine the distribution, Extended Spectrumbeta –lactamase (ESBL) producing bacteria and their antimicrobial susceptibility patterns of bacterial pathogens in patients with indwelling catheter. Since type of micro-organisms and associated antimicrobial susceptibility pattern in patients with indwelling catheter are different, the result of this study is believed to contribute for appropriate management of CAUTI.

Participation: I am asking you to participate voluntarily in this study, if you agree to participate you will be asked to respond to short questionnaire interview, to undergo physically examination and to provide urine sample for laboratory examination.

Risks associated: With this study, there are no risks associated during sample collection procedures.

Benefits: If there is any positive finding in laboratory examination the result will be reported to your physician for appropriate treatment and management.

Confidentiality: All information you give and data obtained from laboratory analysis will be kept confidential and will be communicated only to responsible figure. Formats containing data will be kept locked.

Sharing the result: Report will be written about the finding of the study, either through publication or any other means. The result will not bear any information relevant to your personality in anyway.

Contact Address

If you have any question or doubt you can contact:

G/giorgis Assefa

Institute of Biomedical sciences unit of Immunology

And Microbiology, Mekelle University

Tel: - 0914112224, E-mail:- glab2343@gmail.com

Annexes II: Patient information form (Amharic version)

ግ/ጊዮርጊስ ኣሰፋ እባላሎህ፡፡ የመቐሌዩኒቨርስቲ የሕክምና ማይክሮባዮሎጂ የማስተርስ ዲግሪ ማለትምየ2ተኛ ዲግሪ ተማሪ ነኝ፡፡ በሰዉነታችንሽንትመሸኛክፍልላይበሚደረገዉ ለመሸኛየሚያግዝ ቱቦምክንያት ወደሰዉነታችን የሚገቡትንባክተርያየተባትሉትንበሽታኣምጪ ነገሮችስርጭታቸዉን ለማወቅ የሚካሄድ ጥናትነዉ፡፡

<u>የጥናቱተሳታፊዎችየመረጃቅጽ</u>

ሀ.

<u>የጥናቱዓላማ</u>፡ባክቴሪያየተባሉትንረቂቅህዋሳትበሽንትማውጫትቦበተደረገበሰዉነታችንላይየሚ ያመጡትንችግርናስርጭታቸውንለማጥናትናለህዋሳቱተመራጭየሆኑትመዴሃኒቶችለመምረጥነ ው፡፡

ለ. <u>ፈቃደኝነት</u>፡- እርስዎን በጥናቱ በሙሉ ፍቃደኝነት እንዲሳተፉእየጠየቅንበጥናቱላይለመሳተፍፍቃደኛከሆኑለሚቀርብሌዎትንመጠይቅምላሽከሰጡ በኋላየሽንትናሙናእንዱሰጡይጠየቃሉ::

ሐ. <u>የሚያገኙትጥቅም</u>፡-

በሽታኣምጪተህዋሳያንበላቦራቶሪመኖራቸውከተረጋገጠበኋላተገቢውንመደሃኒትእንዲወስዱው ጤቱለሀኪምተልኮመዴኒኑቱንበሀኪምትዕዛዝይሰጥዎታል፡፡

መ.<u>የሚያሰከትለዉጉዳት</u>: በዚህ ጥናት በመሳተፍዎ በእርስዎ ላይየሚያስከትለዉ ችግር የለም፡፡

ሠ. <u>ሚስጥራዊነት</u>፡-የእርስዎየግልመረጃበሙሉሚስጥራዊነቱየተጠበቀይሆናል፡፡

ረ. <u>ውጤቱንስለመጠቀም</u>፡-

ከዚህጥናትበኋላየበሽታውንስርጭትበተመለከተሪፖርትይፃፋል፡፡ሆኖምየእርስዎንማንነትየሚገ ልፅመረጃየማይካተትሲሆንችግሩንለማሳወቅብቻየሚውልነው፡፡

አድራሻ

ማንኛውምጥያቄወይምጥርጣሬካለዎትይህንንአድርሻይጠቀሙ፡

የዋናውተመራማሪአድራሻ

ግ/ጊዮርጊስ ኣሰፋ

ባዮሜዲካልኢንሰቲቱትማይክሮባዮለጂእናኢሚዮኖሎጂክፍል፡፡

መቀለዩኒቨርስቲ

ሞባ-0914112224

- Glab343@gmail.com

Annex III:Patient information form (Tigrigna version)

ን/ጊዮርጊስ ኣሰፋ እየ ዝባሃል፡፡ ናይ መቐለ ዩኒቨርስቲ ናይ ሕክምና ማይክሮባዮሎጂ ናይ ማስተርስ ዲግሪ ወይ ካዓ 2ይ ዲግሪ ተማሃራይ እየ፡፡ ኣብ ናይ መሸነይ ኣካል ዝግበርሓጋዚቱቦ ተተሓሒዙ ዝመፁ ባክተርያዝበሃለሁዋሳት ኣብ ሰባት ዘልዎ ዝርገሐ እንታይ ከምዝመስል ንምፍላጥ ፅንዓት እናካየድኩ እየ፡፡

ሀ. <u>ናይዚምርምርዕላማ</u>:-

ኣብናይሰውነትናመሸኒትቦዝግበርናይመሸነይሓጋዚተተሓሒዙዝመፀባክተርያዝበሃለሁዋሳትን ምፅናዕዝዐለመእዩ፡፡

ለ. <u>ናይ ምስታፍ ድልየት</u>:-

ንሶምንካልኦትንኣብቲምርምርብምለእድልየትወይብፍቃዶምንክሳተፉእሓትት፡፡እንድሕርደኣ ኣብቲምርምርንክሳተፉወሲኖምነቲምርምርዝተደለወመሕትትመልሲይሃቡብተወሳኽናይሽንቲ ናሙናውንይሃቡ፡፡

ሐ. <u>ዝረክብዎጥቅሚ</u>:-

ኣብናይሽንቲቱቦሕማምከምፅኡዝክእለተህዋሳትምህላዎምብላብራቶሪምስተረጋገፀግቡእመድ ሓኒትንክወስዱናይምርመራውፅኢቶምናብሓኪምተላኢኩመድሓኒትብሓኪሞምትእዛዝንክወሃቡ ምክግበርእዩ፡፡

መ. <u>ዘሰፅቡ ጉድኣት</u>:- ኣበዚ ምርምር እዚብምስታፎም ኣብኦም ዘስፅቡ ጉድኣትየለን፡፡

ሠ.<u>ሚስጥርምህላው</u>:- ናቶምናይግሎምሓበሬታብዝግባእሚስጥርዝተሓለወእዩ፡፡

ረ. <u>እቲዝተረክበውፅኢትምጥቃም</u>:-

ኣብዚምርምርእዚናይቲሕማምንዝርጋሐንዘምፅእዎተህዋስያንፀብፃብክፀሓፍንናብዝምልከቶም ኣካልትብምቅራብናይኣሰራርሓለውጠንክግበረሉንእዩ፡፡እንተኮነግናናቶም/ተንማንነትዝገለፅ መረዳእታዘይሓውስንጥራሕእቲችግርንምፍላጥዝውዕልእዩ፡፡

Annexes IV: Consent form (English version)

(To be translated in to the patient's language (Amharic and Tigrigna)**)**

I, the undersigned, confirm that, I give consent to participate in the study with a clear understanding of the objectives and conditions of the study.

I_____ hereby give my consent for giving the requested information and urine specimen because the proposal has been explained to me in the language I understand.

Name of the patient_____ Patients signature_____

Date_____

Name of the researcher_____ researchers signature_____ Date_____

Annexes V: Consent form (Amharic version)

እኔ/ተማሪ/አቶ/ወ.ሮ/ወ.ት_____

የተባልኩየሽንትማውጫትቦበሽታአምጪ የሆኑት

ባክቴሪያየተባሉትንረቂቅተህዋሳያንለመመርመርበሚረዳውምርምርለምርምሩየሚያስፈልጉመ

ጠይቆችናመረጃዎችየሽንትናሙናለመስጠትበሚገባኝቋንቋየተብራራልኝበመሆኑበጥናቱለመሳ

ተፍበሙለፍቃደኝነትየተስማማሁመሆኔንበፊርማዬአረጋግጣለሁ፡፡

የህመምተኛውስም__----------የህመምተኛውፊርማ----------__ቀን_----------

--------የተመራማሪውስም----------_የተመራማሪውፊርማ----------

_____

ቀን----------

AnnexesVII: Questionnaire (English Version)

Mekelle University College of Health Science Institute of Biomedical Science

Unit of Microbiology and Immunology

Questionnaire for the study of bacterial isolation, determination of ExtendedSpectrumbeta – lactamase (ESBL)producing bacteria and drug susceptibility patternofbacterial pathogens from patients Catheterized with indwelling urinary catheter at Ayder Teaching and Referral Hospital and Mekelle hospital, Ethiopia. I request kindly to give appropriate response for each question. Your response will be kept confidential.

Questionnaire to be filled

Patient code No (given by principal investigator) _____

I. Socio-demographic data

1. Patient MR No_____

2. Age_____

3. Gender

- ❑ Male
- ❑ Female

4.Date of admission_____

5. Admission Ward:

- ❑ Surgical ward
- ❑ Adult intensive care unit(ICU)
- ❑ Gyn & ObS Ward
- ❑ Medical Ward

6. Reason for admission/ Dx at the time of admission_____

7. Duration/length of catheterization: _____

8.Catheter status during specimen collection

- ❑ Present
- ❑ Removed prior 48 hours

9.Indication for catheterization

- ❑ Postoperative
- ❑ Bladder out flow obstruction
- ❑ intestinal obstruction
- ❑ cerebrovascular disease
- ❑ Urologic Surgery
- ❑ Others_____

10. History previous antibiotic treatment

- ❑ Yes
- ❑ No

11. Where was the catheterization performed?

- ❑ Ward
- ❑ ICU
- ❑ Emergency ward

❑ Operating room

❑ Outpatient clinic

❑ Others_____

12. Patient clinical history

S. No	**Clinical Signs and symptoms**	**Frequency**		**Remark**
		YES	**NO**	
1	Fever (>38^{0}c)			
2	Dysuria			
3	Urgency			
4	Costo-vertebral angle pain (tenderness)			
5	Suprapubic tenderness			
6	Frequency			
	Others			

AnnexVIII:Questionnaire(Tigrignaversi)

ናይ መረዳእታ መእከቢ መሕትት

(ፎርም)

መቐለ ዩኒቨርሲቲ

ጥዕና ሳይነስ ኮሌጅ

ናይ ማይክሮባዮሎጅን ኢሚኖሎጅን

ክፍሊ

እዚቅጥዒእዚባክተርያዝተባሃለ·ተሃዋስያንሕማምከምፅኡዝኽእለ·ጠንቅታ·ትኣድላይዝኾነሐበሬ ታንምእካብ ኣብ ዓይደርሪፈራልን መቐለ ሆስፒታልንዝካየድ እዩ፡፡ነቶምሕቶታ·ትብትኽክልንብቅንዕናንክትምልስዎምይላበወኩም፡፡መልስኹምብሚስጥርዝ ተሓለወእዩ፡፡

ናይታ·ሓካማይፉለ·ይመለለይ (ብዋናተመራማሪዝወሃብ) _____

I) ሓፈሻዊማሕበረሰባዊኩነታት

1. ናይተሓካማይቁፅሪካርዲ _____
2. ፆታኣንተባ ☐ ☐
3. ዕድመ---------- _____
4. ዝደቀስለ·/ላክፍሊሕክምና

☐ መጥባሕቲክፍሊመዋልዳንማህፀንሕክም☐ክፍሊ

☐ ብፅኑዕዝሐመሙ·ሕክምናክፍሊውሽጣዊ☐ማትሕክምናክፍሊ

5. ናብቲሆስፒታልዝኣተውለ· (ዝደቀስለ·/ላ) ዕለት----------

_____

6. ዝደቀስለ·/ላምክንያትሕማምእንታይእዩ? ----------_____
7. እቲናይሽንቲመሸነይሓ·ጋዚትቦንክንደይመዓልቲምስኦም/ኣንፀኒሑ? ----------

_____

8. ኣብ እዋን እቲ ናሙና ሙ·ዒሳድ እቲ ናይ ሽንቲ ቱቦተግይሩሎም/ን ዶ ኣሎ?

☐ እወ ☐ የለን

9. እቲናይሽንቲመሸነይሓ·ጋዚትቦንክግበረሎም/ንምክንያትዝኮነሕማምእንታይእዩ?

☐ጥባሕቲ

☐ይሽንቲትቦምፅባብ

☐ንቲዘይምቁፅፃር

☐ኢእግለፅ _____

10. ቅድሚእቲናይሽንቲመሸነይሓ·ጋዚትቦምጥቃሞምመከላከሊረክሲተዋሂብዎም/ ነይሩዶ?

☐ዋሂሁኒኣይተውሃነንን ☐

11. እቲናይሽንቲመሸነይትቦኣበየናይክፍሊሕክምናእዩተግይሩሎም/ን?

☐ንተኛክፍሊመጥባሕ☐ፍሊብፅኑዕ ዝሐመመ☐ክምናክፍሊ

☐ሽጣዊሕማማትሕክምናክፍሊካሊእእነ☐ዩይገለፅ _____

12.ኣብታ·ሓካማይዝርኣይዎምልክታ·ት·ንወይዝተሰመየምስምዒት·ንእን·ታ·ይእዮም?

☐ኒልዕሊ 38^{0}c ☐ ክሸኑዘይምክኣልሽንቲ☐ቲምባል

☐ንዛ ኣብ ት·ሕቲ ሕምብርቲካሊእእነ☐ዩይገለፅ

_____

Annex VX:LABORATORY DATA RECORDING FORMAT

Code No _____

A. Date and time of specimen collection_____

B. Specimen appearance _____

C. Specimen type_____

D. Urine Microscopy

Gram stain Result of urine _____

E. Cultures and Identification

I) Colony count

- ❑ <10^3CFU/ml
- ❑ 10^3CFU/ml
- ❑ 10^4CFU/ml
- ❑ ≥10^5 CFU/ml

II) Significant bacteruria:

- ❑ Yes
- ❑ No

Annex X:ANTIMICROBIAL SUSCEPTIBILITY TESTING

A suspension of pure colony from each confirmed growth is inoculated into sterile normal salineand incubated at 37°C for 15 to 30 minutes. The suspension is adjusted to 0.5% McFarland standard. A sterile cotton applicator stick is used to uniformly distribute the suspensionon Mueller–Hinton agar. Afterincubation at 37°C for 24 hours, the zones of inhibition will be measured using a caliper. Results will be measured, recorded,and classified as susceptible, intermediate, and resistant byusing the CLSI 2018 performance standard for antimicrobialsusceptibility testing interpretation. Here, the MDR isolates will be defined as isolates which acquired nonsusceptibilityto at least one agent in ≥3 classes of antimicrobials

11.1 :DUMMY TABLE

Table 2: Clinical signs and symptoms of UTI in catheterized patients at the two hospitals

UTI sign and symptoms	**Hospital**		**Total No (%)**
	Mekelle hospital No (%)	**Ayder Referral hospital No (%)**	
No signs and symptoms			
Fever (>38^0c)			
Dysuria			
Urgency			
Suprapubic tenderness			
Frequency			
Others			

Table 3: Distribution of underlying diseases in catheterized patients

Indication For catheterization	**Number of patients (Percentage)**	**Hospital Type**	
		Mekelle hospital No (%)	**Ayder Referral hospital No (%)**

Table 4: Distribution of Bacterial isolates in patients with indwelling urinary catheters

Bacteria Isolated	**Types ward**		**Total Frequency NO (%)**
	Mekelle hospital No (%)	**Ayder Referral hospital No (%)**	
Total			

Table 5: ESBL characteristics of the bacterial isolates

Bacterial Isolates	**ESBL producer No (%)**		**Non-ESBL producer No (%)**		**Total No (%)**
	Mekelle hospital No (%)	**Ayder Referral hospital No (%)**	**Mekelle hospital No (%)**	**Ayder Referral hospital No (%)**	
Total					