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Microbial Profile, Drug Susceptibility pattern and Associated risk factor of Urinary Tract Infection in Intensive Care Unit Patients at public Hospitals, Addis Ababa, Ethiopia

BY Hiwot Bizuayehu (Bsc, Msc Candidate)

Advisor: Adane Bitew (PhD, Associate professor)

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This is to certify that the thesis prepared by Hiwot Bizuayehu, entitled: Microbial Profile, drug Susceptibility pattern and associated risk factor of Urinary Tract Infection in Intensive Care Unit Patients at public Hospitals, Addis Ababa, Ethiopia and submitted in partial fulfillment of the requirements for Master of Science degree in Clinical Laboratory Sciences (Diagnostic and Public Health Microbiology) complies with the regulations of the University and meets the accepted standards concerning originality and quality.

Signed by the Examining Committee:

External Examiner_____ Signature _____Date _____

Internal Examiner_____ Signature _____ Date _____

Advisor _____Signature _____ Date _____

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Table of Contents

List of tables

List of figures

ABBREVIATIONS

ATCC	American Type Culture Collection
CAUTI	Catheter-associated Urinary tract infection
CDC	Centers for Disease Control and Prevention
CHR	Calgary Health Region
CLSI	Clinical Laboratory Standards Institute
DM	Diabetes millets
ECDC	European Centers for Disease Control and Prevention
EPHI	Ethiopian public health institute
HAIs	Healthcare-associated infections
HCAI	Health care acquired infection
HELICS	Hospitals in Europe for Infection Control through Surveillance
ICUs	Intensive care units
INICC	International Nosocomial Infection Control Consortium
NNIS	National Nosocomial Infections Surveillance
UTI	Urinary tract infection
WHO	World health organization

ABSTRACT

Background; Healthcare-associated urinary tract infections are one of the most common complications in hospitalized patients particularly in intensive care unit patients. Both bacteria and yeast, are implicated as the etiological agents of urinary tract infections.

Objective: To determine the spectrum of the etiology (bacterial and yeast), risk factors, and antimicrobial susceptibility patterns of urinary tract infections patients admitted in intensive care unit in public Hospitals at Addis Ababa Ethiopia.

Methods: A cross-sectional study was conducted from September 2020 to December 2020 in Addis Ababa public Hospitals' intensive care unit patients. By using convenient sampling method a total of 220 patients included. To assess Socio-demographic status and associated risk factors of participant we used a structured questionnaire. Urine specimens were collected from study participant, sent to Ethiopian public health institution for microbiological investigation and antimicrobial susceptibility testing. The data was analyzed by SPSS software version 23.

Results: Out of 220 urine samples 113 (51.4%) were culture positive of which 20.9% was bacteriuria while 19.1% was candiduria and 11.4% by mixed culture. The most common organism isolated was *Candida albican*s 29 (21.01%) followed by *Enterococcus* spp and *Candida krusei* 18 (13.1%) for each. Ampicillin, Ceftriaxone, and Cefotaxime highly resisted by most Gram-negative bacteria. Amikacin, Meropenem and, Imipenem were the most active drugs against Gram-negative bacteria. Penicillin is resisted by Gram-positive bacteria whereas Nitrofurantin best drug of choice for Gram-positive bacteria. Number of admission days in Intensive Care Unit, diabetes millets and Injury found to be risk factors for urinary tract infection. Female sex, and antibiotic use also a predisposing factor for urinary tract infection caused by yeast.

Conclusion and Recommendation: The overall prevalence of bacteriuria/ candiduria was 51.4% with high drug resistance of bacterial isolate. This implies that, UTI is a significant problem in different public Hospitals' intensive care unit patients in Addis Ababa. Thus, Hospitals may need revise their infection prevention practices to prevent the transmission of resistant bacteria in Intensive Care Unit.

Keywords: *Intensive Care Unit, Urinary Tract Infection, Bacteria, Yeast, Addis Ababa, Ethiopia*

1. INTRODUCTION

1.1 Background

A urinary tract infection is an infection in any part of urinary system - kidneys, ureters, bladder and urethra. Most infections involve the lower urinary tract, the bladder (cystitis) and the urethra (urethritis) [1]. Both Gram negative and Gram positive bacteria are implicated as the etiological agents of UTI. *Escherichia coli* remains the microorganism most frequently responsible for UTI but with different prevalence according to the characteristic of host and the epidemiology (community acquired or healthcare-associated). Hospital-acquired UTI has also been characteristically associated with a higher prevalence of *enterococci* and Coagulase- Negative *Staphylococci* [2, 3]. In addition, *Klebsiella pneumonia, Streptococcus agalactiae, Proteus mirabilis,* viridans s*treptococci, Klebsiella oxytoca, Pseudomonas aeruginosa, Citrobacter freundii, Enterobacter cloacae*, and *Staphylococci* are commonly isolated from patients with UTI [4].

A different group of yeasts has been reported to cause UTI. Species of *Candida albicans* remain the most frequent cause of UTI. However, the epidemiology of UTIs due to yeasts has been changing. Although *Candida albicans* continue to be the major species in UTI, numerous non-*albicans Candida* species are also reported in increasing frequency. *Candida* species, such as *C. tropicalis, C. glabrata,* and *C. krusei* are increasing, especially in ICU patients [5]. Laboratory analysis for UTIs includes three main tests: dipstick urinalysis, microscopic urinalysis, and urine culture. Urine culture is the gold standard for diagnosis of UTI and is considered the most appropriate screening test for asymptomatic UTI [6].

Urinary tract infection is a morbid disease in terms of loss of working days and treatment cost and also it is an important cause of sepsis resulting in high mortality rates [4].The pathogen whether from the gut or external contaminant colonize urethra and subsequent migrate to the bladder by using their pilla or flagella. Host inflammatory responses including neutrophil infiltration occur but Some bacteria evade the immune system then undergo multiplication, biofilm formation, and produce toxins and proteases that induce host cell damage, releasing essential nutrients that promote bacterial survival and ascension to the kidneys finally kidney colonization occur If left untreated, UTI can ultimately progress to sepsis by the pathogen crosses the tubular epithelial barrier in the kidneys [7, 8].

Women are more prone to UTI than men. More than 50% of all women affected by UTI at some point in their lifetime, and also more than 30% of them exposed to recurrent UTI [9, 10].This is because of different factors like shortness of the urethra with its close relationship to the anus, menopause, sexual activity and contraception [11]. In addition female sex, many other factors such as elder age, Immuno-compromise, catheterization and underline diseases specifically diabetes mellitus, are risk associated to UTI [12].

Clinically UTI classified into complicated and uncomplicated. The distinction between uncomplicated and complicated UTI is based on gender and the presence of risk factors. Acute cystitis and pyelonephritis in healthy premenopausal, non-pregnant women without urinary tract abnormality are classified as uncomplicated [13, 14]. Complicated UTI associated with factors that compromise the urinary tract or host defense including urinary obstruction, urinary retention caused by neurological disease, immunosuppression, renal failure, renal transplantation, pregnancy, and the presence of foreign bodies such as calculi, indwelling catheters, or other drainage devices [12]. Hospital-acquired UTI is always considered as complicated, because of multiple factors like indwelling of catheters, antibiotic overuse, skin breakdown, loss of urinary or bowel control and cross-contamination from patient to patients [2].

Ciprofloxacin, Trimethoprim-sulfamethoxaz, Cefpodoxime, Levofloxacin and Ceftriaxone are antibiotic recommended for treat UTI [15].

1.2 Statement of the Problem

Healthcare-associated infections (HAIs) are one of the most common complications in hospitalized patients, leading to increased hospitalization, morbidity, mortality, and associated with additional costs [16]. According to WHO 2019 report, the prevalence of HCAI was estimated in the ranges between 5.7–19.1% in low- and middle-income countries. The proportion of patients with ICU-acquired infection about 88.9% which is almost three times higher than in high-income countries [17]. HAIs were found between 1.6 and 28.7% in Sub-Saharan Africa [18].

Internationally, UTIs are the most common HAIs and one of the top-ranking microbial infections, representing 40% of HAIs, with significant consequences of health problems and substantial financial implications [19]. And relatively common in the intensive care unit. The risk of UTIs is higher in ICU than elsewhere in the hospital and it accounts for 23% of infections in the intensive care unit (ICU). Urinary catheters are associated with the majority of healthcare-associated UTIs; approximately 70% of UTIs (95% of UTIs occurring in ICUs) develop in patients with urinary catheters [20, 21]. International Nosocomial Infection Control Consortium (INICC) surveillance study from 2002 through 2007 in 98 intensive care units (ICUs) in Latin America, Asia, Africa, and Europe Show that the incidence rate of CAUTI in ICU was 6.5 with the prevalence of 0.2% [22].

In 2018, ECDC was reported 3.2% of patients staying more than two days in an ICU it accounting for an estimated total of 82,368 patients with at least one healthcare-associated urinary tract infection in ICUs each year, this means about 1.06 million days of excess ICU stay were estimated to occur each year in Europe as the consequence of ICU-acquired urinary tract infections [23]. According to HELICS (Hospitals in Europe for Infection Control through Surveillance) in 2005, the mean incidence density of UTI in patients admitted in European ICUs is 5.4 UTI episodes per 1000 patient-days and the majority of UTI (96.2%) are associated with the use of a urinary catheter [16].

In 2006, a multicenter prospective cohort surveillance study was done in 8 developing countries that are members of the International Nosocomial Infection Control Consortium (INICC), that

included 55 ICUs of 46 hospitals in Argentina, Brazil, Colombia, India, Mexico, Morocco, Peru, and Turkey the incidence rate of CA UTI was 8.9 with 4.2 prevalence [24].

In 2020 systematic review and meta-analysis done by Alemu AY *etal.* Show that, in Ethiopia, The national prevalence of healthcare-associated infection remains high. The pooled prevalence of healthcare-associated infection was 16.96%. And UTI the second most common HCAI (27.69%) and dual infections with the surgical site of infection (14.01% [25].This shows the national prevalence of healthcare-associated UTI in Ethiopia remains high but is underestimate.

In Africa, especially in Ethiopia, there is no enough research done on microbial profile and drug susceptibility UTI specifically ICU patients, so this research may give a clue to the prevalence of UTI, frequency of microbe, and associated risk factors in ICU patients.

1.3 Significance of the study

The profile of bacterial and yeasts associated with UTI particularly in ICU patients is hardly known. Determining microbial profile, patterns of antibiotic susceptibility and risk factors which are related to UTI is essential which, helps to provide physicians with current information on the level of antimicrobial resistance in local scenario. This helps them to choose suitable drugs for treatment. And also it may give clue for all health professionals to revise their infection prevention practices in institution level. It can be essential source of information for policy makers to develop prevention mechanism and effective treatment and also it could be used as a base line data for further study which are related to urinary tract infection in ICU patients in different part of Ethiopia.

2. LITERATURE REVIEW

Several studies were conducted to know the prevalence of UTI and associated risk factors. In Canada Calgary Health Region, a surveillance cohort study was conducted by Laupland k, *et al.* between 2000 and 2002. Their study was included 4465 patients who were admitted Calgary Health Region ICU hospitals for 48 hours or more. A total of 356 (8%) ICU-acquired UTIs occurred of these 290 (6.5%) CAUTI. Women are highly prone for ICU-acquired UTI with ([RR] 1.58; 95%, [CI] 1.43–1.75; $P < 0.0001$). The most common organisms isolated were *Escherichia coli* (23%), *Candida albicans* (20%), *Enterococcus* species (15%) and *Pseudomonas aeruginosa* (10%) [26].

Another cohort study was conducted in Minnesota, USA by Tedja R, *et al*. Their cohort study was included all of the patients stay in ICU between January 12012, and December 31, 2013. In this period 5,243 urine sample were taken from catheterized patients out of these 105 (2%) was culture positive. And the most common organisms identified by urine culture were yeast (50%), E. *coli* (18%), *Enterococcus spp.* (12%), and *Pseudomonas spp*. (6%) [27].

A surveillance study conducted by ECDC starting from 2008 up to 2012 show that 96.1% of UTIs were associated with the use of a urinary catheter. The result was 4.5 CAUTIs per 1 000 urinary catheter days. The most frequently isolated microorganism was *Escherichia coli* (26.3%), *Candida species* was the second most frequent microorganism representing 17.5% of isolates, followed by *Enterococcus species*, *Pseudomonas aeruginosa*, and *Klebsiella species* 16.2%, 14.1%, and 7.4%, respectively [23].

A three-year observational study was conducted by Duszyńska W, *et al.* At the University Hospital of Wroclaw, Poland.in ICU patients, Urine samples collected through the urinary catheter were subjected to laboratory and microbiological diagnostic tests. They used BacT/Alert kit (Biomerieux, France) and API Candida system (Biomerieux, France) for cultures/isolation of bacterial strains and fungi; the YST card was applied for yeast-like fungi. The result shows that among 1261 ICU patient 91 (7%) was culture positive. Of these hospitals acquired infection 255(36%) was CA-UTIs. The major pathogens were multi-resistant Gram-negative bacteria (64%) Namely, *Acinetobacter baumannii* (20%), *Klebsiella pneumoniae* (18%), *Pseudomonas aeruginosa* (13%), *Proteus mirabilis* (5%), other *Enterobacteriaceae* (8%) followed by Gram-positive bacteria (23%), and *Candida spp.* (13%) [28].

A cross-sectional study was carried out on Catheter-related urinary nosocomial infections in intensive care units: in North of Iran was done by Rezai M, *et al.* Urine culture preformed for 1409 patients, of these 256 (18.2%) had catheter-induced UTI. Their result shows that UTI is significantly associated with age (p=0.015) and time of catheterization (0.001). *E. coli* was the main agent for urinary infection (34.9%), followed by *Klebsiella* (15.3%), *Pseudomonas aeruginosa* (9.5%), and miscellaneous (40.3%). *E. coli* isolated were highly resistant to third-generation cephalosporin and aminoglycosides, while *Klebsiella pneumonia* highly resistant for Cefexim and Ceftriaxone and *Pseudomonas aeruginosa* showed high resistance to third-generation cephalosporin and gentamicin [29].

In Aligarh Region of India study done by Garg N, *et al*. Conducted between October 2013 and December 2014. From 100 urine samples, 20(20.0%) samples showed bacterial growth and 8(8.0%) samples showed *Candida* growth. The Prevalence of UTI was higher in female than male patients, with 18(64.2%) and 10(35.7%) respectively. 16(80.0%) of isolates Gram-negative bacilli, whereas 4(20%) Gram-positive cocci. *Escherichia coli* was frequently isolated with 8(40.0%) followed by *Citrobacter koseri, Staphylococcus aureus, Klebsiella oxytoca, Acinetobacter species, Pseudomonas aeruginosa* and *Enterococcus faecalis* with 4(20.0%), 3(15.0%), 2(10.0%), 1(5.0%), 1(5.0%) and 1(5.0%), respectively. All Gram-positive cocci were sensitive to vancomycin and cefazolin While Most of the Gram-negative bacilli were sensitive to amikacin 12(75.0%) and nitrofurantoin 12(75.0%). 3(18.7%) of Gram-negative bacteria were resistant and 13 (81.2%) were sensitive for imipenem [30].

Similarly, a study was done in India by Mangukiya J, *et al.* 2015, A total of 200 urine samples were taken from catheterized patients admitted at tertiary care hospital and culture performed, of these 62 samples were found culture positive for microorganisms. Of 200 patients, 140 were ICU patients and out of these 43 patients (30.71%) were urine culture positive. The incidence of UTI was higher in female and DM Patients and account (56.46%) and (63.33%) respectively. *E.coli* was frequently isolated (38.71%) followed by *Pseudomonas spp, Kebsiella spp, Proteus mirabilis, Acinetobacter, Candida spp, and Enterococcus spp.* (20.97%), (17.74%), (8.06%), (6.45%) (4.84%) and (3.23%), respectively. Enterobacterials found highly resist Cotrimoxazole (80%), *Peudomonas spp* highest resistance show against tobramycin (92.36%) and they also

found All *Enteroccus spp* were found susceptible for Linezoid, Livofloxacin, and Vancomycin [31].

In the same year Vyawahare C, *et al*. done at Maharashtra, India, Urine sample collected from 345 catheterized ICU patients. Out of 345 urine specimens 119 (34%) culture-positive Out of these 50(14%) fungal isolated while 69(20%) bacterial isolated. *E. coli* was the most common isolate 39 (57%) and the second most isolate was *Klebsiella spp.* 14 (20%), followed by *Pseudomonas spp*.5 (7%), Group D *streptococci* 6 (9%), *Staphylococcus aureus* 2 (5%) and Other Gram-negative bacteria were account 4% of total isolates. From fungal isolates, the most frequent isolate was *Candida glabrata* 20 (40%) followed by *C. albicans*, *Candida tropicalis*, *Trichosporon spp* and *Candida parapsilosis* 18(36%), 7(14%), 3 (6%), and 2 (4%), respectively. Both Gram-negative and Gram-positive bacteria show high resistance to antibiotics that are commonly used such as Gentamicin, Nalidixic, Cotrimoxazole, Norfloxacin. On other hand most of them sensitive for imipenem (95%) [32].

A prospective study was done in the South Indian state of Karnataka Hospital, by Verma S, *etal*. A total of 163 patient samples were collected and the prevalence of CAUTI was (15%). Duration of catheterization ≥ 5 days, Female gender, mechanical ventilation, and Diabetes were a predisposing factor for CAUTI Whereas age increasing (over 64 years) was not correlated with the development of CAUTI. CAUT caused by Bacteria account 18(69.2%) of this 50% were Gram-negative bacillus and 19.2% were Gram-positive cocci. Whereas fungal CAUIT accounts for 8(30.8%) of total prevalence. The most frequent isolate was Candida spp (30.8%), the second most frequent isolates are *E.coli*, and *Enterococcus faecalis* (19.2%), followed by *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Citrobacter freundii* 11.5%, 7.7%, 7.7%, and 3.8%, respectively. All Enterobacteriaceae isolates sensitive to Colisti but 88.9% of isolates were resistant to Cotrimoxazole, 77.8% were resistant to Fluoroquinolones and 44.4% Enterobacteriaceae were resistant to Nitrofurantoin. *Enterococcus faecalis* isolates were 100% resistant to Ciprofloxacin and sensitive to Vancomycin. Coming to yeast, All *Candida* isolates were sensitive to Amphotericin B. and 50% of isolates were sensitive to Fluconazole [33].

A study aimed to identify the risk factors and common pathogens associated with CAUTI in the ICUs of Assiut University Hospital of Egypt performed by Aly S, *et al*, the bacterial incidence

rate was 11%. *Kllebsella spp* was the most frequent isolate (50%) followed by *Enterococcus spp* (44%) and S. aureus (6%). Their finding also shows that Female sex, old age, diabetes mellitus, and prolonged duration of catheterization were found to be risk factors for the development of bacterial UTI. *Klebsiella spp* was 100% resistance for most of the drug which is used routinely which are Cefotaxime, Cefpodoxime, Ampicillin, Ceftriaxone, and Nitrofurantoin and low resistance to Amikacin and Norfloxacin and Imipenem (37.5%), (25%) and (12.5%), respectively. *Enterococcus* isolates showed 100% resistance to Tetracycline and Nitrofurantoin. It also resist (85.7%) of most antibiotics: Vancomycin Ampicillin, Ceftazidime, Cefpodoxime, Ceftriaxone, and Cefotaxime [34].

Recently study conducted in Kenya by Mwangi E, et al. from 238 participant icu patients Thirty four were 34 (14.3%) had UTI. The most common microorganisms (60.9%) causing CAUTI were Gram-negative bacteria with dominating *Escherichia coli.* Gram positive bacteria were isolated at a proportion of 33.2% among Gram positive, *Enterococcus* species were commonly isolated and *Candida albicans* was 6%. Escherichia coli was sensitive to Amikacin (76.5%), Meropenem (70.6%) and Nitrofurantoin (53%). They were resistant to gentamycin (76.5%), Amoxicillin/Clavulanic acid (82.4%), Piperacillin/Tazobactam (82.4%), Ciprofloxacin (82.4%), and Ampicillin/ Sulbactam (94.1%). The organisms were 100% resistant to Ceftriaxone, Cefepime, Cefuroxime, Cefazolin and Ceftazidime. Enterococcus species: Enterococcus faecalis were 100% sensitive to Vancomycin, Linezolid, and Teicoplanin. They were also sensitive to Nitrofurantoin and Ampicillin at 73%. These microorganisms were 100% resistant to gentamycin, Vancomycin 100%, streptomycin, levofloxacin and Benzyl penicillin. They were 73% resistant to Tigecycline. *Candida albicans* were sensitive to Fluconazole and Voriconazole (60%), Amphotericin B (40%), Fencitocine (40%), Caspofugine (40%), and Micafugin (40%) [35].

Most of the above studies show that the prevalence of UTI in hospitalized patients remains a big problem with different etiologic agents and antibiotic-resistant. Their finding also shows that female gender, DM, and duration of catheterization are the main predisposing factors.

2.1 Conceptual framework of the study

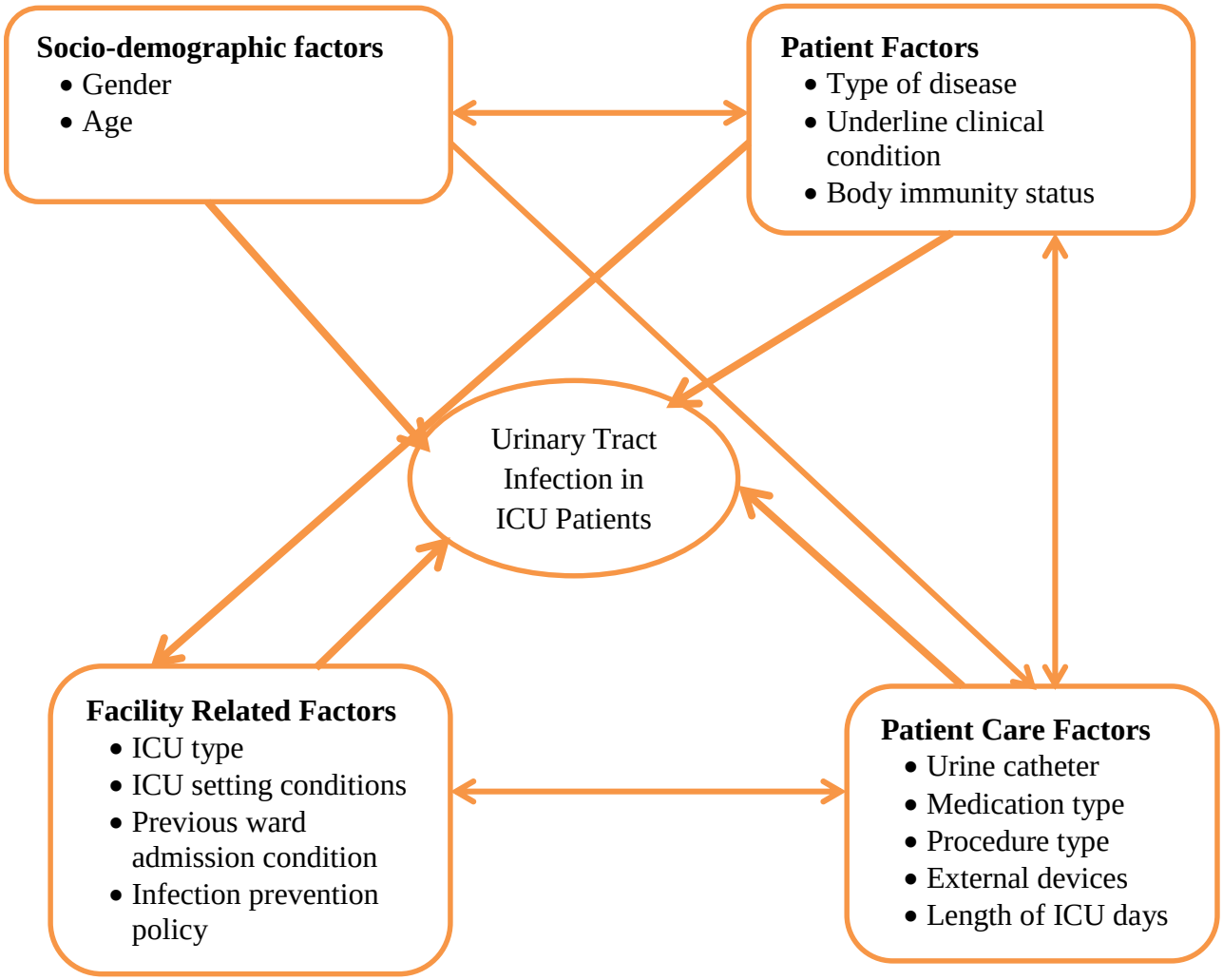


Figure 1: Conceptual framework

For the spectrum of bacterial and yeast pathogen from intensive care unit patient, the antibacterial profiles bacterial isolated and to document potential risk factors associated with UTI patients from selected hospitals of Addis Ababa developed by reviewing different kinds of literature [3, 23, 25, 27, 29, 30].

3. OBJECTIVES

3.1. General objective

To determine the spectrum of bacterial and yeast pathogen from intensive care unit patient, the antibacterial profiles bacterial isolated and to document potential risk factors associated with UTI patients who are admitted at Addis Ababa public hospitals from September to December 2020.

3.2. Specific objectives

- To determine the distribution of bacterial and yeast UTI pathogens in ICU patients admitted at Addis Ababa public hospitals
- To assess the antimicrobial susceptibility pattern of bacterial UTI pathogens in ICU patients admitted at Addis Ababa public hospitals
- To identify risk factor associate with UTI in ICU patients admitted Addis Ababa public hospitals

4. HYPOTHESIS

The prevalence, frequency of microbe isolate, drug susceptibility and associated risk factors related with UTI in ICU patients may not be different from the study conducted previously in Kenya [35].

5. MATERIALS AND METHODOLOGY

5.1. Study area

The study was conducted in public hospitals in Addis Ababa. Addis Ababa's 2021 population is now estimated 5,005,524 with an annual growth rate of 4.42[36]. The city is divided into eleven sub-cities and 116 wereda (The lowest level administrative unit in the city) Currently, Addis Ababa has 54 hospitals. Which are 14 state-run and 40 private hospitals [37]. The study conducted in public hospitals' ICU with total of 90 ICU bed which include St. Paul Hospital has six ICU bed , Menilek II Hospital six ICU bed , Yekatit 12 Hospital six ICU bed , Zewuditu memorial Hospital six ICU bed, Ras Desta Damtew memorial Hospital has six ICU bed, Alert Hospital has eight ICU bed, Toriloch Hospital has seven ICU bed, Ghandi Hospital has five ICU bed, Tirunesh Beijing Hospital five ICU bed and Ethiopian Federal Police Commission Referral Hospital six ICU bed, Aabet hospital twelve, St. Peter Hospital fourteen ICU bed.

5.2. Study design and period

A cross-sectional study design was conducted from September to December 2020.

5.3. Population

5.3.1. Source population:

All patients who were admitted to ICU.

5.3.2. Study Population:

All adult patients who were admitted to selected health facility's ICU within the study period interval.

5.4. Inclusion and exclusion criteria

5.4.1. Inclusion criteria

All patients ≥ 16 years of age, who gave informed written consent for their attendant and

Patients at least two calendar days admitted in intensive care unit was included

5.4.2. Exclusion criteria

Patients who had laboratory urine culture-positive results, and Patients with clinically confirmed UTI before admitted to ICU were excluded.

5.5. Study variables

5.5.1. Dependent variables:

- Bacterial and fungal isolates
- Antimicrobial resistance patterns

5.5.2. Independent variables:

- Socio-demographic factor: age, sex, place of residence
- ICU admission days
- Use of antibiotic
- Underline disease

5.6. Sample size calculation and Sampling method

5.6.1. Sample size calculation

The sample size calculation is based on single sample size estimation formula. The value of *P* is taken as 0.143 (14.3 % estimated prevalence) from the previous study conducted in Kenya [37]. Considering 95% confidence interval, 5% margin of error and using single sample size estimation formula the sample size is calculated as follows;

$$sample\ size\ n = \frac{z^2 * p(1-p)}{d^2}$$

Where

n = Sample size

α = level of significance

z = at 95% confidence interval Z value (a = 0.05) =>Z α/2=1.96

p = Proportion of occurrence of the event estimated 0.159

d = Margin of error at (5%) (0.05)

$$n = \frac{1.96^2 * 0.143(1-0.143)}{0.05^2}$$

n≈ 189

The initial sample size was estimated as 189 participants, and finally, by computing a 10% (19 subjects) nonresponse rate, the final sample size was consolidated as 207. We took 220 samples.

5.6.2. Sampling Method

A convenient sampling technique was used and included 220 study participants, who are admitted to ICUs of Addis Ababa public hospitals during the study period. Sampling for each hospital done based on proportional to their number of ICU bed. St. Paul Hospital, Menilek II Hospital, Yekatit 12 Hospital, Zewuditu memorial Hospital, Ras Desta Damtew memorial Hospital, Federal Police Commission Referral Hospital, each had six ICU bed, and we took fifteen study participants from each hospital. Toriloch Hospital and Alert Hospital each had eight ICU bed, and we took nineteen study participants from each hospital. Ghandi Hospital and Tirunesh Beijing Hospital each had five ICU and we took twelve study participants each hospital. Aabet hospital and St. Peter Hospital each had fourteen ICU bed and we took thirty-four study participants from each hospital.

5.7. Measurement and Data collection

5.7.1. Data collection procedure

Data was collected using a structured questioner to gain information on the socio-demographic status and associated risk factors. The Questioner was filled by a selected nurse from each hospital. The principal investigator took additional patient details from the patient card. Each nurse was informed to collect data from study participants after written consent/ assent was obtained from all patients attendant.

5.7.2. Laboratory diagnosis

A) Sample collection, transportation, and inoculation

Sample collection Urine was collected employing a catheter in an aseptic manner. This was done first clean the upper part of the tube catheter by use of 70% alcohol then clamp it at the point of the junction by using forceps after few minutes we could collect a fresh urine sample [30].

Transportation All collected urine samples were transported to Ethiopian public health institution (EPHI) bacteriology and mycology national reference laboratory. We use triple packaging sample transporting method with icebox within two hours for culture and antimicrobial sensitivity test.

Inoculation Each urine sample was inoculated onto Blood Agar base (Oxoid, Basingstoke, Hampaire, UK) to which 5% sheep blood is incorporated, MacConkey (Oxide, Basingstoke, and Hampshire, England) and Brain Heart infusion agar supplemented with chloramphenicol (100µgml^{-1}) and gentamycin (50 µgml^{-1}), Oxide, Basingstoke, and Hampshire media by using a calibrated loop with a capacity of 1 µl in Biosafety cabinet Level II. All inoculated plates were incubated at 37 °C for 24 to 48 hr aerobically and were inspected for the growth of bacteria and/or yeasts. Since our participants are critically ill, and they are catheterized patients Colony counts yielding microbial growth count at list 10^2/ml of urine was be regarded as significant for bacteriuria/candiduria [2].

B) Bacterial Identification

Pure isolates of the bacterial pathogen were preliminarily characterized by colony morphology, Gram-stain, further identification performed by conducting conventional biochemical tests: catalase, coagulase, and novobiocin sensitivity test for Gram-positive bacterial isolates and Oxidase, Citrate utilization, Indole, Gas & Glucose, LDC, Urease production, Motility, Hydrogen sulphide production and Lactose fermentation tests for Gram-negative bacterial isolates [34].

C) Yeast identification Yeasts were identified by employing conventional routine diagnostic methods such as gram stain, Germ tube test. Species identification was determined by employing chromogenic medium (CHROMagar Candida medium, bioM´erieux, France) as per the instruction of the manufacturer. It contains a chromogenic Beta-glucosaminidase substrate that reacts with species-specific enzymes to give colonies with different colours [5].

D) Antimicrobial susceptibility testing

Antimicrobial susceptibility test was carried out by Kirby Bauer disc diffusion method as per Clinical Laboratory Standards Institute (CLSI, 2020) guidelines on Muller Hinton agar (Oxoid, Basingstoke, England) [38]. Three to five pure colonies were picked from original culture plates and mix with a test tube containing 2ml of sterile saline until it becomes equivalent to McFarland 0.5 standards to obtain approximately the organism number of 1×10^6 colony forming units (CFU) per ml. A sterile swab was dipped into the suspension and the excess inoculum was removed by pressing it against the sides of the tube. Then the swab was applied to the center of Muller Hinton agar plat and evenly spread on the medium. Antibiotic discs were placed after 15

min of inoculation to Muller Hinton agar seeded with each isolate and were incubated for 24 h at 37 °C. The diameter of the zone of inhibition around the disc was measured using a ruler according to Kirby-Bauer Disk Diffusion Susceptibility Test Protocol [39]. For Gram negative bacterial isolates Antibiotics tested included Ampicilin 10µg, Cefatoxime 30µg, Ceftazidime 30µg and Ceftriaxone 30µg, Torbamicen 10µg, Gentamycin 10µg and Amikacin 30µg, ciprofloxacin 5 µg Impreneum 10µg and Meropenum 10µg, Folate cotrimoxazol 25µg, Nitrofurantion 300µg and teteracycline 30µg.

Antibiotics tested For Gram positive bacterial isolates included Vamcomicen 30µg Folate cotrimoxazol 25µg, Nitrofurantion 300µg, teteracycline 30µg, Peniciline10µg and oxacillin 1 µg Gentamycin 10µg and ciprofloxacin 5 µg. All these antimicrobial agents were selected based on current availability in addition to CLSI guidelines. The susceptibility and resistance were interpreted according to Clinical Laboratory Standards Institute (CLSI, 2020) guidelines [38].

5.8. Data Quality Assurance

A) Pre analytical phase

A questionnaire was checked for its completeness and validity before the collection of data and a pretest of the questionnaire was performed before the beginning of the actual study to assure it's a consistency to study tool. The principal investigator checked data reliability and completeness throughout the data collection process. A double data entry method was used to ensure the accuracy of data.

All urine sample was collected from ICU patients aseptically manner. By using a standardized and sterile urine sample container and each sample was also controlled and recorded by using specimen information format that contains all information starting from the collection up to the results of each urine specimen.

B) Analytical phase

All laboratory processes, material, and equipment quality was guaranteed by performing quality control (QC) activity according to the standard bacteriology laboratories SOPs., media preparation was based on the manufacturer's instruction and sterility was tested. International control bacteria strains**,** *E. coli (ATCC 25922), S. aureus (ATCC 25923) and P. aeruginosa*

(ATCC 27853) used in controlling the tests carried out. Anti-microbial disc quality control was performed based on the EPHI laboratory and CLSI protocols.

C) Post analytical phase

All urine specimen laboratory findings were checked by an experienced microbiologist and primary advisor and also the result was documented properly. Purified bacterial and yeast cultures were stored in nutrient broth with 20% glycerol at –70°C until use. These cultures may be stocked in this condition for 2 years.

5.9. Data analysis and interpretation

Data were cleaned, entered, and analyzed using SPSS, version 23. Descriptive statistics were computed for most of the study variables, and frequency distribution tables were used to describe the findings. Logistical regression was also used to estimate the crude odds ratio (COR) and adjusted odd ratio (AOR) with 95% confidence interval (CI) to the different independent variables, and *P* values less than 0.05 was taken as statistically significant when looking for associations between dependent and independent variables.

5.10. Operational definitions

Catheter-associated UTI refers to UTIs occurring in a person whose urinary tract is currently catheterized or has been catheterized within the past 48 hours [12].

Health care-associated infections, or "nosocomial" infections, affect patients in a hospital or other health-care facility, and are not present or incubating\ at the time of admission. They also include infections acquired by patients in the hospital or facility but appearing after discharge, and occupational infections among staff [40].

ICU-acquired UTI defined as those patients with a positive urine culture first identified on ICU 48 hrs or later. Patients with positive urine cultures within 48 hours of ICU discharge were also considered to have ICU-acquired UTIs [41].

Incidence density of UTI is number of urinary tract infection episodes per 1000 patient-days or Catheter-days [42].

Significant bacteriuria is defined as a urine sample containing more than 10^5 colony forming units/ml of urine (10^8/l) for catheterized patients Colony counts yielding microbial growth count

at list 10^2/ml of urine was be regarded as significant for bacteriuria/candiduria in pure culture using a standard calibrated bacteriological loop [2].

MDR microorganisms is an organism **a**cquired non-susceptibility to at least one agent in three or more antimicrobial classes [43].

5.11. Ethical considerations

The study was conducted after ethically reviewed and approved by the Institutional Review Board (IRB) of the Department of Medical Laboratory Sciences, College of Health Sciences, and Addis Ababa University. Permission letter also obtained from Addis Ababa Public health Research Decorate for the study sites hospital to collect samples. The study participants were informed about the purpose of the study and written informed consent was obtained from each participant *attendant* family or clinician.

5.12. Dissemination of the result

The study finding will be disseminated to the College of Health Science Department of Medical Laboratory Science, Addis Abba University, Addis Ababa Public Health Research and Emergency Management Directorate, Ethiopian public health institute to all study area health facilities and for different organization and the Manuscript will be submitted to peer-reviewed journals for publication.

6. RESULT

6.1 Demographic Characteristics

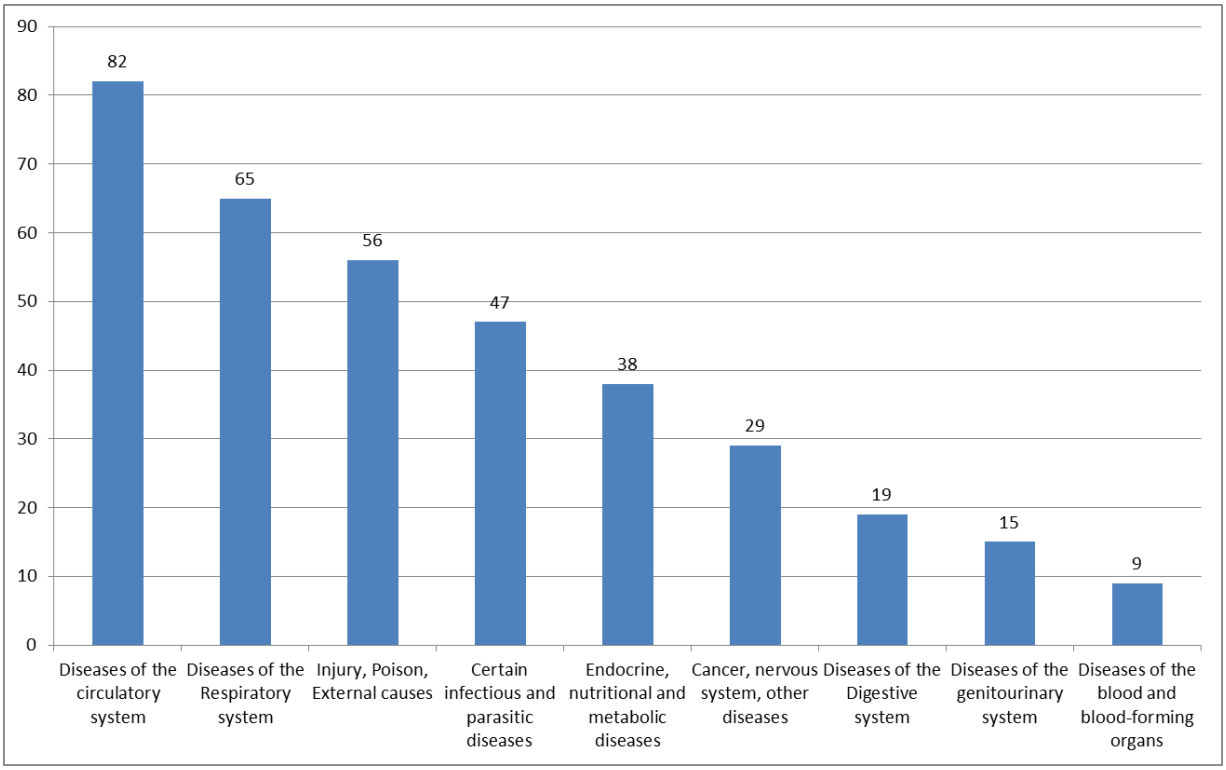
A total of 220 patients involved who fulfilled the inclusion criteria, admitted to the ICU between September and December 2020. Out of these 76 (34.5%) were female and 144 (65.5%) were male. The mean age of the participant 40.6 ± 18.4 years. One hundred fifty-six (70.9%) participants were from Addis Ababa and sixty-four (29.1%) were from out of Addis. Duration of stay in the ICU was between 2 and 50 days, with a median of 5 ± 8 days in total study patients. (Table 1)

Table 1: Demographic characteristics of ICU patients admitted at public hospitals of Addis Ababa from September 2020 to December 2020 (n=220)

Characteristics	**Response**	**Frequency**	
		Number	**Percent**
Gender	Female	76	34.5
	Male	144	65.5
Age	15-24	49	22.3
	25-64	136	61.8
	>=65	35	15.9
Place of residence	Addis	156	70.9
	Out of Addis	64	29.1
antimicrobial drug	Yes	192	87.3
	No	28	12.7
N# of ICU admission in days	>6	105	47.7
	<= 5	115	52.3

6.2 Clinical condition of study participants

The study participant had different underlying clinical conditions, the most frequent underlying diseases were Diseases of the circulatory system, Diseases of the Respiratory system, and Injury. Other clinical findings were also observed in study participants as shown in (fig 2). The majority of study participants 192 (87.3%) were taking a different type of antibiotics. as shown in (Table 1) and all of them are catheterized patients.



International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)-WHO Version for; 2016 [51].

Figure 2 Clinical condition of ICU patients admitted at public hospitals of Addis Ababa from September2020 to December 2020.

Table 2 Demographic characteristics, Clinical condition of study participants and prevalence of UTI in terms of overall growth, bacterial, and yeast isolation in ICU patients admitted at government hospitals of Addis Ababa from September to December 2020 (n=220).

Characteristics	**Frequency N=220**	**Growth 113/51.4%**		**Bacteria 66/30.0%**		**Yeast 54/24.5%**	
		No.	**%**	**No.**	**%**	**No.**	**%**
Female Gender	76	46	60.5	22	28.9	27	35.5
Male Gender	144	67	46.5	44	30.6	27	18.8
15-24 Years	49	26	53.1	19	38.8	9	18.4
25-64 Years	136	70	51.5	40	29.4	34	25.0
>=65 Years	35	17	48.6	7	20.0	11	31.4
From Addis Ababa area	156	83	53.2	46	29.5	42	26.9
Out of Addis Ababa area	64	30	46.9	20	31.3	12	18.8
On antimicrobial agents	192	97	50.5	52	27.1	52	27.1
Not taking antimicrobial agents	28	16	57.1	14	50.0	2	7.1
More than six days in ICU	105	73	69.5	41	39.0	37	35.2
Five or less days in ICU	115	40	34.8	25	21.7	17	14.8
Certain infectious and parasitic diseases	47	24	51.1	11	23.4	17	36.2
Endocrine, nutritional and metabolic diseases	38	28	73.7	12	31.6	17	44.7
Injury, Poison, External causes	56	30	53.6	25	44.6	5	8.9
Diseases of the circulatory system	82	39	47.6	21	25.6	23	28.0
Diseases of the Respiratory system	65	35	53.8	13	20.0	23	35.4
Diseases of the Digestive system	19	7	36.8	3	15.8	5	26.3
Diseases of the genitourinary system	15	8	53.3	6	40.0	5	33.3
Diseases of the blood and blood-forming organs	9	5	55.6	1	11.1	4	44.4
Cancer, nervous system, other diseases	29	14	48.3	10	34.5	5	17.2

International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)-WHO Version for; 2016 [46].

6.3 Microbial isolates

Out of 220 urine sample, 113 (51.4%) were culture positive and we had identified 138 microbes, of these 79 (57.25%) were bacterial isolates and 59 (42.75%) yeast isolates. Of 79 bacterial isolates, 50 (63.3%) were Gram-negative bacteria and 29 (36.7%) were Gram-positive bacteria. From Gram-negative bacterial isolates *Acitenobacter spp* was predominant with 30% followed by *pseudomonase spp*, *E,coli*, and *Klebsiella ozenae* 24%,16%, and 10% respectively. We found two types of Gram-positive bacterial isolates which are *Entrococcus spp* with 62.1% (18/29) and *S .epidermides* with 37.9% (11/29). Among the 59 yeast, the most frequently isolated was *Candida albicans* with 29 (48.3%), followed by *C. krusei*, *C. tropicalis*, and *Cryptococcus neoformans* 18 (31%), 10 (17.2%) and 2 (3.5%), respectively.

Over all the most common organism isolated was *Candida albican* 29 (21.01%). *Enterococcus spp* and *C. krusei* were the second most common organisms isolated 18 (13.1%), followed by *Acitinobacter spp* 15 (10.9%), *Pseudomonas spp*, 12 (8.8%), *S. epidermides* 11(8.0%), *Candida tropicals* 10 (7.3%) and *E.coli*. 8(5.8%) (As shown as table 3)

Most of the isolates identified from patients whose source of admission were Emergency and surgical ward, 83(60.14%) and 28(20.29%), respectively. From Emergency ward admission source; out of 83 isolates 55(66.1%) isolates were bacterial isolates and the most frequent bacteria was *Enterococcus spp* with 12 (14.5%). Whereas 28(33.7%) isolates were yeast isolates with *Candida albican* the most frequent isolate and it account 14(16.9%). Isolates from patients whose admission source was surgical ward account 28(20.29%) of total isolates. Of these 14(50%) bacterial isolates and 14(50%) yeast isolates. From bacterial isolates *Pseudomonas spp* 5(17.9%) and *Enterococcus spp* 4 (14.3%) were dominate. Whereas from yeast isolates *Candida krusei* and *Candida albican* frequently identified and account 6(21.4%) and 5(17.9%), respectively.

Table 3: Microbial profile of isolates from urine culture of ICU patients admitted in a governmental hospital at Addis Ababa from September to December 2020 (n=138)

Isolates	**Frequency**	**Percent**
Bacterial	**79**	**57.25**
Gram Positive	**50**	**63.3**
Acinetobacter spp	15	10.9
Citrobacter spp.	4	2.9
Enterobacter spp.	2	1.5
Klebsiella oxytaca	2	1.5
Klebsiella Pneumonia	2	1.5
E. coli	8	5.8
Pseudomonas spp.	12	8.8
Klebsiella ozenae	5	3.6
Gram Negative	**29**	**36.7**
Enterococcus spp.	18	13.1
S. epidermids	11	8.0
yeast	**59**	**42.75**
Candida *albicans*	29	21.01
Candida krusei	18	13.04
Candida tropicalis	10	7.25
Cryptococcus neoformans	2	1.45
Total	**138**	**100.0**

NB: GN; Gram Negative Bacteria **GP;** Gram Positive Bacteria

Pure and mixed isolates; Out of 138 isolates, 88(63.77%) were pure isolates and 50(36.23%) were mixed isolates. From bacterial isolates 46(58.2%) were pure and 33(41.8%) were mixed isolates. From yeast isolates, 42(71.2) pure and 17(28.8%) were mixed.

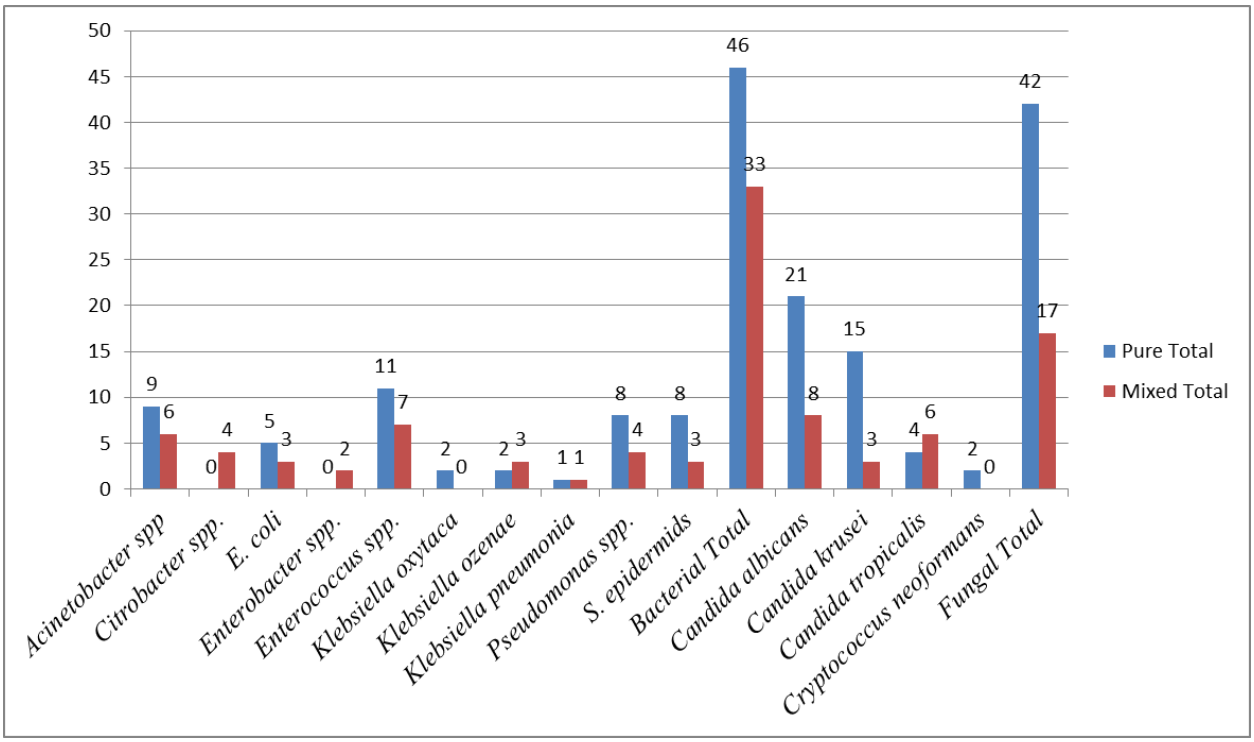


Figure 3 Frequency of pure and mixed isolate from urine culture of ICU patients admitted in a public hospital at Addis Ababa from September to December 2020

6.4 Antibiotic susceptibility testing

Most ICU-acquired uropathogenic bacteria are a high degree of antibiotic-resistant**.** The majority of the isolates were resistant to the commonly prescribed antibiotics. All Gram-negative bacteria show high level of resistance for antibiotics classes Cephem (92%), Penicillin (91.3%) Folate pathway antagonist (89.5%) Tetracycline (57.9%) and Fluoroquinolone (54%), and least resistance for Carbapenem (20%) Nitrofurantoin (17.4%). Most Enterobactrials 100% resistant for Ampicillin, Ceftriaxone, and Cefotaxaime except *citrobacters spp75*% and *enterobactr spp.* 50% resistant. *Acientobacter spp* 100% resistance for Ceftazidime and Ceftriaxone.

Cotrimoxazole 100% resisted by most bacterial isolates except *Acitenobacter spp*, *Citrobacter spp*, and *S .epdermides* which 80%, 75%, and 63.6% resistant respectively. Amikain (16%), Meropinum (20%), and Imrneum (20%) are the most effective antibiotic for all Gram-negative bacteria except *Klibsella ozoniae.* (As shown detail in Table 5)

Penicillin resisted by (89.7%) of Gram positive bacteria, Tetracycline (44.8%), Fluoroquinolone (37.9%), and Aminoglycoside (27.3%). Antibiotic resistant level of Gram-positive bacterial isolates is different, *Enterococcus spp* highly resistant for Ampcillin Penicillin, Tetracycline, Ciprofloxacin, Vancomicen.72.2%, 66.7%, 61.1%, 44.4%, 33.3%, respectively. *S. epidermidis* resist Oxacillin, Penicillin, Cotrimoxazol, Ciprofloxacin Gentamicin and Tetracycline 81.8%, 63.6%, 63.6%, 27.3%, 27.3% and 18.2%, respectively. (Table 4) Nitrofurantine best drug of choice for *Klibsella ozoniae*, resisted only 20% and for gram-positive bacteria: *Entrococcus spp*, and *S. epidermides* which resist only 22.2%, and 9.1%, respectively, (As summarized in table 4 and 5)

Table 4 Antibiotic resistance patterns of Gram-positive bacterial isolates from urine culture of ICU patients admitted in a selected governmental hospital at Addis Ababa from September to December 2020 (n=29)

	Ampcilin (10µg)	Oxacillin (30µg)	Penicillin (10µg)	Ciprofloxacn (5µg)	Cotrimoxazl (25µg)	Gentamicn (10µg)	Nitrofuranoin (300µg)	Tetracyclie (30µg)	Vancomyn (30µg)
Enterococcus spp. (18)	13 (72.2)	ND	12 (66.7)	8 (44.4)	ND	ND	4 (22.2)	11 (61.1)	6 (33.3)
S. epidermids (11)	ND	9 (81.8)	7 (63.6)	3 (27.3)	7 (63.6)	3 (27.3)	1 (9.1)	2 (18.2)	ND
Total Gram positive (29)	**13 (72.2)**	**9 (81.8)**	**19 (65.5)**	**11 (37.9)**	**7 (63.6)**	**3 (27.3)**	**5 (17.2)**	**13 (44.8)**	**6 (33.3)**

NB ND; not done

Table 5 Antibiotic resistance patterns of Gram-Negative bacterial isolates from urine culture of ICU patients admitted in a selected governmental hospital at Addis Ababa from September to December 2020(n=50).

	Ampcilin (10µg)	Ceftazidime (30µg)	Ceftriaxone (30µg)-	Cefotaxime (30µg)	Ciprofloxacin (5µg)	Cotrimoxazol (25µg)	Gentamicin (10µg)	Tobramycin (10µg)	Amikacin (30µg)	Imipenem (10µg)	Meropenem (10µg)	Nitrofurantoin(300µg)	Tetracycline (30µg)
Acinetobacter spp (15)	ND	15 (100)	15 (100)	13 (86.7)	8 (53.3)	12 (80)	5 (33.3)	5 (33.3)	3 (20)	5 (33.3)	5 (33.3)	ND	7 (46.7)
Klebsiella oxytaca (2)	2 (100)	2 (100)	2 (100)	2 (100)	1 (50)	2 (100)	2 (100)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)
Klebsiella pneumonia (2)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	1 (100)	1 (50)	0 (0)	0 (0)	1 (50)	1 (50)
E. coli (8)	8 (100)	3 (37.5)	8 (100)	8 (100)	5 (62.5)	8 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (57.1)
Pseudomonas spp. (12)	ND	10 (83.3)	ND	ND	7 (58.3)	ND	5 (41.7)	5 (41.7)	2 (16.7)	2 (16.7)	2 (16.7)	ND	ND
Klebsiella ozenae (5)	5 (100)	3 (60)	5 (100)	5 (100)	3 (60)	5 (100)	3 (60)	3 (60)	2 (40)	3 (60)	3 (60)	1 (20)	5 (100)
Citrobacter spp. (4)	3 (75)	1 (25)	3 (75)	3 (75)	1 (25)	3 (75)	1 (25)	1 (25)	0 (0)	0 (0)	0 (0)	2 (50)	2 (50)
Enterobacter spp. (2)	1 (50)	0 (0)	1 (50)	1 (50)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)
Total Gram negative (50)	**21 (91.3)**	**36 (72)**	**36 (94.7)**	**34 (89.5)**	**27 (54)**	**34 (89.5)**	**18 (36)**	**17 (34)**	**8 (16)**	**10 (20)**	**10 (20)**	**4 (17.4)**	**22 (57.9)**

NB 100; 100% resistant, 0.0; 100% susceptible, ND; not done, only two isolates were intermediate, we consider as susceptible.

6.5 Multidrug resistance pattern of bacterial isolates

Multidrug resistance level was very high, Out of 79 bacterial isolates, 76(96.2%) were MDR. From 50 Gram-negative bacterial isolates 49(98%) were MDR. From 29 gram-positive isolates, 27(93.1%) exhibited as MDR. All Gram-negative bacteria exhibited as 100% MDR except *pseudomonas spp.* with 91.7% MDR. (As shown as table 7)

6.6 Risk factor associated with urinary tract infection

Culture positivity rate was higher in the female with 46 (60.5%) than male 67(46.5%) but statistically is not significant (p=0.05). Age, residential status are not correlated with Culture positivity rate (as shown in table 9). Based on underlying diseases the highest Culture positivity rate shown Endocrine, nutritional and metabolic diseases with 28(73.7%) followed by Diseases of the blood and blood-forming organs 5(55.6%), Diseases of the Respiratory system 35(53.8%), Injury, Poison, External causes 30(53.6%) Diseases of the genitourinary system 8(53.3%) (As shown as Table 2). But none of them predisposing factor for UTI except Diabetic millets and Injury.

Longer ICU stay was a significant risk factor for the development of UTI (p=0.00, COR 5.08). Female in gender and Diabetes millets significantly correlated Candiduria (p=0.01, COR 2.56) and (p=0.01, COR3.83), respectively. Multivariate analysis, which incorporated independent variables in the stepwise logistic regression model, Number of ICU days > 6 is predisposing factors for both Candiduria (p=0.00) and Bacteriuria (p=0.00) UTI. Injury significant relationship (p=0.00) with Bacteriuria and (p=0.04) Candiduria whereas Female in gender and Antibiotic use (p=0.02) and Diabetic millets (p=0.01) highly correlated with UTI caused by yeast. (As shown as Table 7)

Table 6 Multidrug resistance patterns of bacterial isolates from urine culture of ICU patients admitted in a selected governmental hospital at Addis Ababa from September to December 2020.

Bacterial Isolate (n)	**Level of Resistance (N/%)**									**MDR**	
	R0	**R1**	**R2**	**R3**	**R4**	**R5**	**R6**	**R7**	**R8**	**No**	**Yes**
Acinetobacter spp(15)	0 0.0	0 0.0	2 13.3	7 46.7	4 26.7	1 6.7	1 6.7	-- --	-- --	0 0.0	15 100
Citrobacter spp(4).	0 0.0	0 0.0	1 25.0	0 0.0	2 50.0	1 25.0	0 0.0	0 0.0	0 0.0	0 0.0	4 100
Enterobacter spp.(2)	0 0.0	0 0.0	1 50.0	1 50.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	2 100
Klebsiella oxytaca (2)	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	1 50.0	1 50.0	0 0.0	0 0.0	0 0.0	2 100
Klebsiella pneumonia (2)	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	2 100.0	0 0.0	0 0.0	0 0.0	2 100
E. coli(8)	0 0.0	0 0.0	0 0.0	2 25.0	3 37.5	3 37.5	0 0.0	0 0.0	0 0.0	0 0.0	8 100
Pseudomonas spp.(12)	1 8.3	2 16.7	6 50.0	2 16.7	1 8.3	-- --	-- --	-- --	-- --	1 8.3	11 91.7
Klebsiella ozenae (5)	0 0.0	0 0.0	0 0.0	0 0.0	2 40.0	0 0.0	0 0.0	2 40.0	1 20.0	0 0.0	5 100
Total Gram-negative (50)	**1 2.0**	**2 4.0**	**10 20.0**	**12 24.0**	**12 24.0**	**6 12.0**	**4 8.0**	**2 4.0**	**1 2.0**	**1 2.0**	**49 98.0**
Enterococcus spp. (18)	1 5.6	3 16.7	4 22.2	6 33.3	4 22.2	0 0.0	-- --	-- --	-- --	1 5.6	17 94.4
S. epidermids (11)	1 9.1	3 27.3	2 18.2	1 9.1	4 36.4	0 0.0	0 0.0	-- --	-- --	1 9.1	10 99.9
Total Gram positive (29)	**2 6.9**	**6 20.7**	**6 20.7**	**7 24.1**	**8 27.6**	0 0.0	0 0.0	-- --	-- --	**2 6.9**	**27 93.1**
Total (79)	**3 3.8**	**8 10.1**	**16 20.3**	**19 24.1**	**20 25.3**	**6 7.6**	**4 5.1**	**2 2.5**	**1 1.3**	**3 3.8**	**76 96.2**

R0*:* Sensitive to all antibiotic class***;*** **R1:** resistance to **one, R2:** resistance to **two R3** resistance to **three, R4:** resistance to **four, R5:** resistance to **five, R6:** resistance to **six, R7:** resistance to **seven, R8:** resistance **eight** antibiotic classes.

Table 7 Risk factors associated with urinary tract infection among patients admitted in a selected governmental hospital at Addis Ababa from September to December 2020.

Characteristics	**Growth**			**Bacteria**			**Yeast**		
	P	**COR**	**95% C.I.**	**P**	**COR**	**95% C.I.**	**P**	**COR**	**95% C.I.**
Sex	0.05	2.15	1.11-4.17	0.97	1.01	0.51-2.00	0.01	2.56	1.23-5.33
Age (15-24)	0.66			0.24			0.55		
Age (25-64)	0.36	0.70	0.32-1.51	0.11	0.54	0.25-1.16	0.35	1.60	0.60-4.25
Age (>=65)	0.64	0.78	0.27-2.26	0.19	0.46	0.15-1.47	0.30	1.91	0.56-6.58
Residential status	0.37	0.72	0.36-1.46	0.31	0.68	0.32-1.44	0.89	0.94	0.40-2.23
ICU days	0.00	5.08	2.66-9.71	0.01	2.58	1.32-5.05	0.00	3.29	1.56-6.91
Antibiotic	1.00	1.00	0.40-2.49	0.16	0.53	0.22-1.29	0.04	5.52	1.10-27.70
Certain infection	0.67	1.19	0.52-2.74	0.83	0.91	0.37-2.21	0.12	2.04	0.83-5.04
DM	0.00	4.98	1.92-12.89	0.35	1.53	0.62-3.80	0.01	3.83	1.47-10.02
Injury	0.09	2.45	0.88-6.78	0.03	3.31	1.13-9.73	0.54	0.66	0.17-2.55
Circulatory	0.41	0.73	0.35-1.54	0.87	1.07	0.48-2.36	0.98	1.01	0.45-2.27
Respiratory	0.47	1.32	0.62-2.79	0.31	0.65	0.28-1.50	0.11	1.95	0.85-4.46
Digestive	0.83	1.14	0.35-3.67	0.78	0.82	0.20-3.38	0.52	1.55	0.41-5.81
Genitourinary	0.87	0.90	0.25-3.21	0.32	1.96	0.53-7.26	0.58	1.48	0.37-5.88
Anemia	0.61	1.51	0.31-7.40	0.32	0.33	0.04-2.96	0.24	2.55	0.54-12.04
Cancer/other	0.87	1.08	0.42-2.77	0.22	1.84	0.69-4.95	0.56	0.70	0.21-2.36
	P	**AOR**	**95% C.I.**	**P**	**AOR**	**95% C.I.**	**P**	**AOR**	**95% C.I.**
Sex	---	---	---	---	---	---	0.02	2.22	1.11-4.43
ICU days	0.00	4.39	2.46-7.84	0.00	2.66	1.43-4.94	0.00	3.38	1.68-6.80
Antibiotic	---	---	---	---	---	---	0.02	6.60	1.41-30.78
DM	0.00	3.38	1.48-7.71	---	---	---	0.01	3.01	1.30-6.98
Injury	---	---	---	0.00	2.85	1.46-5.54	0.04	0.35	0.12-0.98

Reference groups: Male, Age (15-24), Out of Addis, <=5 ICU days, and Underline condition (No), Antibiotic therapy (No)

NB: **COR**; Crud Odds Ratio, **AOR**; Adjusted Odd Ratio "**---**"Adjusted odd ratio not calculated because *p*-value is not significance

7. DISCUSSION

ICU sees an important number of hospital infections with a high incidence of multidrug resisted microorganisms. UTI is the most common infection particularly associated with catheterization in ICU patients [24]. ICU-acquired UTI result in increased cost of hospitalization among patients who develop these infections [20, 42].

Our findings show that the prevalence of UTI in ICU patients was 51.4 % which was comparable with the study done in Indonesia with the prevalence of UTI (44.4%) [45]. However, this value was much higher than studies done perversely in different countries. In Iran, (18.2%) [29], In India (15%) [33] and Egypt (11%) [34]. All these studies show that the prevalence of UTI among ICU patients lower than current study. The differences in the distribution of uropathogens may result from different environmental conditions, host factors, healthcare and education programmers, socioeconomic standards and hygiene practices in each country [46].

The etiology of UTI is varied and many of these pathogens are part of a patient's flora but can be acquired by cross-contamination from other patients, hospital personnel, or by exposure to contaminated equipment [32].

In this finding, *Candidia spp* the most frequent isolate and it accounts for about 42% which agrees with other researches done in India by Verma S, *et al* 30.8% of finding was *candida spp.* [33].This finding also agrees with other study in USA and Egypt the most frequent isolate was *candida spp* but slightly higher than our result it accounts for 50% of the total finding. [27, 47]. The frequency of UTIs caused by *Candida* spp. has increased considerably in recent years, especially in hospitalized patients [45]. For critically ill patients, candiduria, whether symptomatic or asymptomatic, should be considered a precursor of disseminated candidiasis. Candidemia is common in this setting, and 46%–80% of persons with candidemia will have accompanying candiduria [48, 49].

Among bacterial isolate we found that *Enterococcus spp* the most common 18 (13.1%), followed by *Acitinobacter spp* 15 (10.9%) which was similar to a study conducted in Poland, The main pathogens were *Enterococcus spp.* (22%) and *Acinetobacterspp* (20%) [28].Unlike our finding many other studies done in different countries; Canada (55%), India (38.71%), Indonesia (44.6%) and Dessie *(*60.29%) of uropathogenic bacterial isolate was is *E. coli.* [26, 31, 50, 51] Variation may be caused by epidemiological variation of etiologic agents (community acquired

or healthcare-associated). Hospital-acquired UTI has also been characteristically associated with a higher prevalence of enterococci and Coagulase- Negative Staphylococci [2, 3].

Most bacterial pathogens were found to be resistant to most of the tested antimicrobials. Current study show that 81.75% of bacterial isolates were resistant to Penicillin supported by other study conducted in Addis Ababa 80% [52]. Folate pathway antagonist, Fluoroquinolone, Aminoglcoside and nitrofurantion had overall resistance rates of 76.5%, 45.95%, 31.65% and 17.3% respectively supported by studies conducted in Dessie regional laboratory [53].

Penicillin resisted by 89.7% of Gram positive bacteria which confirmed by study conducted in Iran 90.9% [54] whereas Nitrofurantin was the most powerful antibiotic for these bacteria which were resisted only 17.2%. This result supported by other study conducted in Bangladesh [46]. *Enterococcus spp*. was the most frequent bacterial isolate and showed high resistance to Ampicillin (72.2%) Similarly study done in Egypt, (85.7%) of *Enterococus spp* was resistant to Ampicillin [44]. 33.3% of *Enterococus spp* was Vancomicen resistant. Which is higher than studies done in Ethiopia (0%) [55]. Difference may due to variation of study participant. Nitrofurantoin low resisted by *Enterococus spp* (22.2%), supported by Verma S, *etal*. only (20%) of *Enterococus spp* show resistance [33].

In this study Gram negative bacteria resisted Ampicillin 91.3% in Libya was 90%. [54], Arsho Advanced Medical laboratory in Addis Ababa 78.3% resistance [62]. Current study show that Gram negative bacteria resistance to Ceftazidime 72%, Ceftriaxone 94.7%, Ciprofloxacin 54% this consistent with study done Nigeria 67.7%, 81.8% 68%, respectively [57]. In our findings, *Acientobacter spp* was the second most isolated from bacterial isolates followed by *Pesudomonas* spp. and with high rate of resistance for Ceftazidime 100% and 83.3%, respectively. In agreement with study done in Uganda 100% of none fermenter Gram negative bacterial isolates were resistance for ceftazidime [58]. Gram negative bacilli show low resistance for Amikain 16% and Meropinum (20%), In agreement with other studies done, in India 25% and (8.7%), respectively [30].

Our findings show that only three isolates found to be susceptible to all class of antibiotics tested. 76(96.2%) were MDR of these isolates 27(93.1%) were Gram-positive and 49(98%) were Gram-negative bacterial isolates exhibited as MDR. This finding consistent with previous studies

conducted in Egypt 85.7% [34], Dessie 92.7% [59]. Hawassa 80.3% [60], Ambo and Dire Dawa 100% of uropathogenic bacterial isolates were MDR [61, 62].

The high resistance rate among the isolates observed in our study may be our study population were patients from ICUs. These patients generally undergo various antimicrobial therapy, so they expose to develop infections by resistant pathogens [33]. The emergence of multidrug-resistant pathogens in the hospital environment specifically in ICU has much reason including Inappropriate and extensive use of antibiotics in addition to the huge ability of the organism to acquire resistance genes. Because of these, options for treating infections caused by these organisms are becoming limited [34, 46].

It was observed that the incidence of UTI was more in females (60.5%) as compared to males (46.5%) although the difference did not reach statistical significance. Our findings support by other studies done in India and Sudan [31, 63], their findings show that majority of the pathogens were isolated from females. In agreement with a study done in Iran by Behzadi P, *et al.* our findings show that there is a significant association between the female gender and UTIs caused by yeast [64]. Females prone for UTI because of different factors like shortness of the urethra with its close relationship to the anus, menopause, sexual activity and contraception [11].

This finding shows that age is not a predisposing factor for UTI, supported by other studies [33] [69]. Whereas other studies were done in Egypt, Indonesia, and Bangladesh that the prevalence of UTI higher in elder age [34, 45, 50].

The present study shows that the use of antibiotics is a predisposing factor for UTI caused by yeast. This is because using broad-spectrum antibiotics for the long term or frequently is likely that antibiotics contribute to colonization *candida spp*. by suppressing endogenous bacterial flora [67, 66].

In our findings show that, injury is risk factor for bacterial UTI (p=0.00), which is comparable with study conducted in Japan and USA showed that injury is significantly associated with UTI (p= 0.026) and (p= 0.038) respectively [67, 68].This result disagrees with studies conducted in Switzerland and Tigray region of Ethiopia [69, 70].This variation may be due to the type and severity of the injury.

A significant association between ICU length of stay and development of UTI was observed with (p=0.00) supported by study done in china [71]. Since all our study participants catheterized patients before 48 hours, this result may related to catheterization. Prolonged duration of catheter use led to an increased rate of UTI. This occurs because, catheter serves as a portal of entry for the pathogen if not aseptically inserted and it causes the biofilm development between the catheter and urethral mucus thus, preparing the environment for bacterial attack and proliferation [29, 33, 34].

In this study, a significant correlation was found between UTI and diabetes mellitus Confirmed by studies done in India [31, 33] and Tigray [72]. Diabetic patients experienced an increased rate of infection, with the UTI being the most frequent infection site [29, 31, 66, 70]. This is because of various impairments in the immune system, poor metabolic control of diabetes, and incomplete bladder emptying due to autonomic neuropathy, which may all contribute to the pathogenesis of UTI in diabetic patients [29, 72].

8. STRENGTH AND LIMITATION OF THE STUDY

8.1 Strength of the study

Based on our knowledge, this study is the first multi-center study done in different public hospitals' ICU in Addis Ababa, Ethiopia on UTI and we took relatively larger number of sample size so it can be representative for the population. It identify both bacterial and yeast pathogen which are main causative agent of UTI in ICU patients it also identify multi drug resistance bacterial isolates. It included information about participants such as clinical condition, antibiotic therapy and duration of ICU admission days which complete our study.

8.2 Limitation of the study

Lack of Vanomycin minimum inhibitery concentration test for Oxacillin resistance *S. epidermids* isolates.and antifungal susceptibility test for yeast isolate.

9. CONCLUSION AND RECOMMENDATIONS

9.1 Conclusion

The overall prevalence of UTI was 51.4% with frequently isolates were *Candida spp* and *Enterococus spp* this may give a clue microbial profile of UTI changing specifically critically ill patients. Risk factor for UTI varies depending on demographic characteristics and Clinical condition of patients. In our findings, Number of ICU admission days, Injury and DM main risk factor UTI. Female sex, and antibiotic use also a predisposing factor for urinary tract infection related with yeast. Amikain, Meropinum, and Imrneum are the most effective antibiotic for most Gram-negative whereas Nitrofurantin best drug of choice for Gram positive bacteria. 96.2% of bacterial isolates were exhibited as MDR. High prevalence UTI with high antibiotic-resistant bacterial isolates implies that, UTI is a significant problem in different ICU hospitals in Addis Ababa.

9.2 Recommendation

- Prevalence of UTI and rates of antibiotic resistance microbe can vary enormously depending on geographic location. Therefore, antimicrobial resistance surveillance should be established to develop treatment guideline.
- Hospitals may need revise their infection prevention practices to prevent the widespread transmission of these resistant bacteria around hospital environments specifically in ICU.
- For proper management of UTI in ICU, need further updated information for different health professionals about the prevalence of the causative agents and their antimicrobial resistance patterns in the country, the town as well as institution-specific ICUs.
- Further studies are needed for better understanding of the distribution microbial agents of UTI and their antibiotic resistance pattern in different hospitals' ICU at different parts of country.

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11. ANNEX

Annex I: Participants information sheet [English version].

Introduction/Purpose: My name is Hiwot Bizuayeu. I'm studying for my second degree at Addis Ababa University. Now, I'm researching the Microbiological Profile of Urinary Tract Infection in Intensive Care Unit Patients at different Hospitals, Addis Ababa, Ethiopia. This information will help to develop prevention mechanisms and effective treatment.

Procedures: the procedure followed in this study includes a brief questionnaire that will seek to gather socio-demographic and general clinical condition-related information from an attendant physician, followed by urine sample collection for microbiological analysis.

Risk: There is no risk and serious invasive procedure at the beginning as well as at the end of the study

Benefits: Participants will not be paid for participating in this study. But the patient will know their urinary tract microbiological status including antimicrobial profiles. The laboratory finding will be reported to the attendant clinician as soon as possible.

Confidentiality: The results of the laboratory findings will be kept confidential and could only be accessed by the researcher and the responsible physician. There will be no personal information to be attached to your data.

Voluntary participation and withdrawal: Taking part in this study is voluntary. We will respect your decision if you, later on, change your mind and you can refuse to participate or withdraw from the study at any time. Refusal to participate will not result in loss of medical care provided or any other benefits. You can get the results of the analysis.

Contact person: If you have any questions about the study, I will be happy to answer now. Please let me know if anything I have stated is not clear and I will be happy to explain it further to ensure you understand. If you have further questions related to this study, you can call and contact me.

Principal Investigator: Mrs Hiwot Bizuayehu,

Mobile N# 0911904482, **e-mail hiwimd2@gmil.com**

Informed consent [English version]

Consent for study participant patients' attendant clinician/family

Do you understand the purpose of the study, procedure, risks, and benefits of participation, right to refuse or withdraw, confidentiality and privacy, and who to contact if you have any questions?. Yes ☐ No ☐

If yes, do you accept that your patients (for the attendant clinician) /relatives (for attendant family) who admitted to this ICU participate in urinary tract infection assessment that will include taking socio-demographic data, general clinical condition related information, and urine sample collection for microbial investigation ?. Yes ☐ No ☐

If you are willing that your patient/family participates, please put your signature or thump print in the space provided below.

Attendant Family/ Clinician: Signature:_____Date: _____

Name of Data collector _____.Signature_____Date _____

Part I Socio-Demographic data			
No.	Question and/or Characteristics	Possible Response	Skip
01	Participant ID/Code	[_____]	
02	Patient location: Hospital name/code	[_____]	
03	Room N# [_____]	Bade N# [_____]	
03	Gender	01 Female ☐ 02 Male ☐	
03	Age In Years [____]	01]15 – 25 □, 02]26 – 35 □, 03]36 – 45 □, 04]46 – 55 □, 05]56 – 65 □ 06] > 66 □.	If < 15 stop
04	Residential Status	01 Addis ☐ 02 Out Addis ☐	

Part II General ICU admission information of the patient			
201	Duration of ICU admission in days [_ _ _ _]	01] < 3 days ☐, 02] 3 – 33 ☐ 03] 34 – 63 ☐ 04] 64 – 93 ☐ 05] 94 – 123 ☐ 06] > 124 ☐	If < 3 days stop
202	The patient has developed Health Care Acquired Infection after Two days of admission.	01] Yes ☐ 02] No ☐	
203	If yes for Q. 202, could you specify it?	01] Urinary tract infection ☐ 02] Diarrhea ☐ 03]Acute febrile illness ☐ 04] Surgical site infections ☐ 05] Pneumonia (lung infections) ☐ 06] Bloodstream infection ☐	
204	Primary/Major reason/disease for ICU admission?	Infectious: 01] Acute☐, 02] Chronic☐. Please specify Non-Infectious: 04] Acute☐, 05] Chronic☐. Please specify	
205	Final/any additional clinical diagnosis of the patient (from the record).		

206	Is the patient referred from another health care facility and admitted directly to ICU	01] Yes ☐ 02] No ☐	If No skip to 207
207	If Q 206 Yes, could any possibility to know, where the department/unit was? The duration of admission		
208	Is the patient transferred from another ward/unit of this facility?	01] Yes ☐ 02] No ☐	If No skip to 209
209	If Q 208 yes, Please specify the ward/unit	01] Emergency☐ 05] TB:☐ 02] Medical:☐ 06] HIV:☐ 03] Surgical:☐ 07] Other☐ 04] Gyn-obes:☐	
210	The patient is on a urine catheter	01] Yes ☐ 02] No ☐	If No skip to 211
211	If yes, frequency of catheter exchange in days [_____]		
212	Is there any antimicrobial drug previously or currently given to the patient	01] Yes ☐ 02] No ☐	If No skip to 213
213	If Q 212 is yes, Please specify the name/type, dose,		

	administration route, duration, and frequency of the drug given			
214	Is there any clinical specimen collected from the patient for any kind of microbiological/culture investigation		01] Yes ☐ 02] No ☐	If No skip to 215
215	If Q 214 is yes, could you specify the finding if any? From lab result	Specimen type Name of isolated organism/s List antimicrobial used and indicate [R] for resistant, [I] intermediate & [S] for sustainable results		
216	Urine specimens were collected from the patient for the purpose of this study.		01] No ☐ 02] Yes ☐ and from:- Catheter: ☐ or Mid-stream urine: ☐ Date of Collection: __ /__ Time __:__	
217	Any additional comments or notes			

Annex II Participant information and consent form [Amharic Version]

የለጥናቱን አላማ፤ ይዘት ማስተዋወቂያና የጥናቱ ተሳታፊዎችን ፍቃደኝነት መጠየቂያ የአማርኛ ቅጂ ቅጽ፡፡

ጥናቱን የምታጠናው፤ ሀይወት ብዙአየሁ በአዲስአበባ ዩኒቨርሲቲ ጤናሳይን ስኮሌጅ የህክምና ላቦራቶሪ ሳይንስ ትምህርት ክፍል፡፡

የጥናቱ አላማ፤ በጽኑ ህሙማን መንከባከቢያ ክፍል ውስጥ ተኝተው ህክምናቸውን በመከታተል ላይ በሚገኙ ህሙማን ላይ የሚከሰት የሽንት ቧንቧ አንፌክሽን መጠንና ስርጭትን ለማወቅ፤ በሽታዉን አመጪ የሆኑትን ተዋስያን አይነት በላቦራቶሪ ምርመራ ለመለየትና የተለማመዱትን የመድኃኒት አይነትም ለማወቅ የጠቅማል፡፡

የጥናቱ መንገድ፡ ስለ ታካሚው/ዋ እንድ አንድ መረጃዎች ለምሳሌ እንደ ፆታ፤ እድሜ፤ ለምን ያክል ወቅት በክፍሉ እነደቆዩ፤ መክፍሉ ለመተኛት ወና መንስኤ ምን ነበር እና የመሰሰሉትን ለጥናቱ አጋዥ የሆኑ ጥያቄዋችን ከታካሚው የቅርብ ሃኪም ወይም ተንከባካቢ ነርስ ጋር በመሆን ከህክምና ካርድ፤ ከ ባለሞያ ወይንም ከቤተሰብ መረጃ ከተሰበሰበ በኋላ ለ ላብራቶሪ ምርመራ የሚሆን 20 ሚ.ሊ. የዉሃ ሽንት የምንወስድ ይሆናል፡፡

በጥናቱ ተሳታፊዎች ላይ ያለው ጉዳት፤በጥናቱ መጀመሪያም ይሁን መጨረሻ በዚህጥናት ላይ በመሳተፍዎ ሊደርስብዎ የሚችልአንድም ጉዳት አይኖርም፡፡ በጥናቱ ምክንያት የሚያባክኑት ተጨማሪ ጊዜም አይኖርም፡፡

ለጥናቱ ተሳታፊዎች ያለው ልዩ ጥቅም፤ በጥናቱ ለሚሳተፉ ፍቃደኛ ተሳታፊዎች ምንም አይነት የገንዘብ ክፍያ የለውም ነገርግን ከጥናቱ የሚገኘው ውጤት ለህመምተኛው ህክምና ተጨማሪ መረጃ ለማግኘት በተመሰሳይ ለመድሃኒት ልምምድ ያደረጉትን ካላደረጉት በመለየት ውጤታማ የሆኑትን መድሃኒቶች ይጠቁማል፡፡

የመረጃ ሚስጥራዊ አጠባበቅ፣የሚሰጡት መረጃ በጥናቱ ወቅትም ሆነ ከዚያ በኋላ ባሉት ጊዜያት ሙሉ በሙሉ ሚስጥራዊነቱ የሚጠበቅና መረጃውም የሚያዘዉ በስም ሳይሆን በመለያ ቁጥር ይሆናል፡፡ በጥናቱ

ላይ ያለመሳተፍ መብት አለዎት። ይህመረጃ በጥንቃቄ የሚያዝ ይሆናል።በመጨረሻም የጥናቱ ውጤት ለሚመለከተዉ አካል ለጥናቱ አላማና ለህክምና ባለሙያዎች ብቻ የሚገለፅ ይሆናል።

የዋና ተመራማሪ አድራሻ፤ ስለዚህ ጥናት ማንኛዉንም መረጃ ለመጠየቅ ከፈለጉ ከታች በተቀመጠው ስምና አድራሻ መጠቀም ይችላሉ፡-

ሂወት ብዙአየሁ ስልክ ቁጥር፡- 0911904482 ኢሜይል hiwimd2@gmil.com

ከላይ የተዘረዘሩትን የጥናቱን አላማና ይዘት፤ በጥናቱ በመሳተፎዎ ታካሚዎ፤ቤተሰብዎ በጥናቱ በመካተታቸው የለዉን ጥቅምና ጉዳት እነብበው ወይንም አድምጠው ተረድተዋል አዎ ተረድቻለው አልተረዳሁም መልስዎ አዎን ተረድቻለሁ ከሆነ በጥናቱ ለመሳተፍ ፍቃደኝነተዎን ታከሚዎ፡ ቤተሰብዎ በጥናቱ እንዲካተቱ ፍቃደኛ መሆንዎን ለመግለጽ ፊርማዎትን ከታች ባለው ቦታ የስቀምጡልን። የታካሚው/የቅርብ ተንከባካቢው ባለሞያ/የቅርብ አስታማሚ ቤተሰብ

ፊርማ ---------- ቀን----------

መጠይቁን የሞላው ፊርማ ---------- ቀን ----------

ክፍል 1 ስለተሳታፊው ጠቅላላ መረጃ			
ተ.ቁ.	ጥያቄዎች	የሚጠበቁ መልሶች	ዝለል
01	የተሳታፊው/ዋ መለያ ቁጥር	[_____]	
02	ታካሚው የሚገኝበት ተቋም ስም/መለያ ቁጥር	[_____]	
03	የክፍል ቁ. [_____]	የአልጋ ቁ. [_____]	
03	ጾታ	01 ሴት ☐ 02 ወንድ ☐	

03	እድሜ በአመት [_ _ _ _]	01]15 – 25 □, 02]26 – 35 □, 03]36 – 45 □, 04]46 – 55 □, 05]56 – 65 □ 06] > 66 □.	ከ15 አመት በታ ለሆኑ አያካትትም
04	መኖሪያ አካባቢ	01 ከተማ☐ 02 ገጠር ☐	
ክፍል 2 በጽኑ ህሙማን ክፍል ውስጥ ተኝቶ ከመታከም ጋር ተያያዥነት ያላቸው ጠቅላላ መረጃዎች			
201	ተኝተው የታከሙበት ቀን ብዛት [_ _ _]	01] < 3 ☐, 02] 3 – 33 ☐ 03] 34 – 63 ☐ 04] 64 – 93 ☐ 05] 94 – 123 ☐ 06] > 124 ☐	< 3 ቀን ጥናቱ አያካትትም
202	ታካሚው በክፍሉ በተኙ በ ሁለት ቀናት ውስጥ በጤና ተቋም ውስጥ ተኝቶ በመታከም ምክንያት የሚመጣ በሽታ ታይቶባቸዋል?	01] አዎ ☐ 02] አይ ☐	
203	ለጥያቄ ቁ 202 መልሱ አዎ ከሆነ. ቢያብራሩለን ?	01] የሽንት ቧንቧ ኢንፌክሽን☐ 02] ተቅማጥ ☐ 03] ድንገተኛ ትኩሳት ☐ 04] የቀዶ ጥገና ቦታ ኢንፌክሽን ☐ 05] የሳንባ ምች ☐ 06] የደም ስር ኢንፌክሽን ☐	
204	በጽኑ ህሙማን ክፍል ታካሚው/ዋ እነዲተኙ ያደረጋቸው ዋና መንስኤ	ተላላፊ: 01] አጭር ጊዜ የቆየ ☐, 02] ርጅም ጊዜ የቆየ☐. በአጭሩ ቢገለጽ	

	ምን ነበር?	ተላላፊ ያልሆነ: 01] አጭር ጊዜ የቆየ ☐, 02] ርጅም ጊዜ የቆየ☐. በአጭሩ ቢገለጽ	
205	ተጨማሪ የሃኪም ምርመራ ድምዳሜ ካለ ከታከሚው ካርድ ላይ የሚወሰድ መረጃ		
206	ታካሚው/ዋ ከሌላ ተቋም ተዛውረው በዚህ ጽኑ ህሙማን አስተኝቶ ማከም ከፍል በቀጥታ እነዲኙ የተደረጉ ናቸው	01] አዎ ☐ 02] አይደለም ☐	መልሶ አይደለም ከሆነ ቁጥር 207ይዝለሉት
207	ለጥያቄ ቀ. 206 መልሱ አዎ ከሆነ ታካሚው ህክምናቸዉን ሲከታተሉበት የነበሩበት ተቋም ተቅላላ ሁኔታዉን ማወቅ ከተቻለ ቢገለጽ ለምሳሌ የትኛው የስራ ክፍል ህክምናቸዉን እነደተከታተሉ ተኝተው ከነበረም ለምን ያክል ጊዜ እንደሆነ ቢታወቅ?		
208	ታካሚው/ዋ ከዚሁ ተቋም ሌላ ክፍል የተዛወሩ ናቸው	01] አዎ ☐ 02] አይደለም ☐	መልሶ አይደለም

			ከሆነ ቁጥር 209ይዝለሉት
209	ለ ጥያቄ ቁ. 208 መልስዎ አዎ ከሆነ ተጨማሪ መረጃ ቢሰጡን	01] ድንገተኛ☐ 05] ሳንባ ነቀርሳ:☐ 02] ዉስጥ ደዌ:☐ 06] ኤድስ:☐ 03] ቀዶ ማከም:☐ 07] ሌላ☐ 04] ማዋለጃ:☐	
210	ታካሚው/ዋ የሽንት ማስወገጃ ቱቦ ተቀጥሎላቸዋል?	01] አዎ ☐ 02] አይደለም ☐	መልሶ አይደለም ከሆነ ቁጥር 211ይዝለሉት
211	ለ ጥያቄ ቁ. 210 መልስዎ አዎ ከሆነ የሽንት ማስወገጃው በየስንት ጊዜ ይቀየራል? [_ _ _] በቀን		
212	ተካሚው/ዋ ለባክቴሪያ ማከሚያነት የሚውል መድኃኒት ወስደዋል/ አሁንም እየወሰዱ ይገኛሉ?	01] አዎ ☐ 02] አይደለም ☐	መልሶ አይደለም ከሆነ ቁጥር 2013 ይዝለሉት
213	ለጥያቄ ቀ. 212 መልስዎ አዎ ከሆነ በአይነት በመጥንና ልምን ያህክል ጊዜ የሚለው በገለጽ?		

214	ከታካሚው/ዋ ለ ላቦራቶሪ/ካልቸር ምርመራ ናሙና ተውሰዱዋል?	01] አዎ ☐ 02] አይደለም ☐	መልሶ አይደለም ከሆነ ቁጥር 215ይዝለሉት
215	ለጥያቄ ቁ. 214 መልሰዎ አዎ ከሆነ ውጤቱንና ተያያዥ የሚሉዋቸዉን መረጃዎች ቢሰጡን?	የተወሰደው የናሙና አይነት የተለየው ተዋስ/ጀርም በጥቅም የዋሉትን የመዳኒት ዝርዝር እስከ ውጤቱ ቢገልጹለን	
216	ከታካሚዉ/ዋ የሽንት ናሙና ለዚህ ጥናት አላማ የሚዉል ተውስዱዋል?	01] አይ ☐ 02] አዎን ☐ እና:- ከሽንት ማስወጫ ቱቦ: ☐ ወይም ቀጥታ ከሚወርድ ሽንት: ☐ የተሰበሰበበት ቀን: __ /__ ሰዐት __:__	
217	ተጨማሪ ማንኛዉም ስለ ታካሚው/ዋ ጠቃሚ የሚሉት መረጃ ካለና ለዚህ ጥናት ያግዛል የሚሉትን እዚህ የጻፉልን		

ስላደረጉልን ማንኛውም ትብብርና ምላሽ እናመሰግናለን

Annex IV. Laboratory analysis data collection form.

1. Sample ID _____

2.

Name of media used	Colony characteristics

3. Gram stain result _____

_____

4. Biochemical test pattern

Test	Result	Test	Result
Catalase		H_2S	
Coagulase		Gas & Glucose	
Lactose		Citrate	
Indole		Motility	
Urea		LDC	
Mannitol		Other	

5. Organism Isolated _____

6. Antimicrobial susceptibility profile

Disc used / Result																				
Sus																				
Inter																				
Res																				

Annex V. Procedure for sample collection and processing.

A. Collection and transportation of urine specimen.

1. A minimum, 10 ml of urine specimen will be collected directly from the catheter tube by using a sterilized urine specimen collection cup from study participant ICU patients.

To avoid contamination, the specimen is collected by disinfecting a portion of the catheter tubing with alcohol & puncturing the tubing directly with a sterile syringe with a needle, and aspirating the urine.

2. The sample cup shall be labeled with the patient code number

3. Transportation to the laboratory, by using triple packaging sample transport system

4. It should be cultured as early as possible after collection, within 2 hours. In case of delay, it may be refrigerated up to a maximum of 24 hours before plating.

B. Processing of urine specimen:

Calibrated loop technique: The recommended procedure uses a calibrated plastic or metal loop to transfer 1µl of urine to the culture medium (MacConkey agar with crystal violet, CLED, and non-selective blood agar)

1. Shaking the urine gently, then with a 1 µl inoculating loop touch the surface so that the urine is sucked up into the loop.
2. Deposit 1µl of the urine on a blood agar plate and MacConkey agar and streak the plate
4. Incubate the plates up to 24 h in an air incubator at 35 ˚C and colony count
5. Interpretation of quantitative urine culture results:

<10000 CFU/ml	INSIGNIFICANT bacteriuria; UTI-unlikely
10000- 100,000 CFU/ml	PROBABLY SIGNIFICANT bacteriuria; UTI probable
> 100,000 CFU /ml	SIGNIFICANT bacteriuria; UTI certain

If ≤ 2 pathogens and ≥100,000 CFU /ml, perform identification & susceptibility on each If >2 pathogens, report .mixed flora.

6. Identification of isolates based on colony characteristics, Gram stain reaction, and morphology, for Gram negative, rode using a biochemical profile

7. Performing susceptibility testing

C. Bacterial Identification Tests.

Catalase

1. USING a sterile wooden stick or loop, pick a colony of the test organism. Avoid carry-over of blood agar, which can cause false positives.
2. PLACE the colony on a clean glass slide.
3. ADD one drop of 3% H_2O_2 over the organism on the slide. DO NOT reverse the order of the procedure as false-negative results may occur. Do not mix.
4. OBSERVE for immediate bubbling (gas liberation)
   - Positive = immediate bubbling
   - Negative = no immediate bubbling or no bubbling
5. DISCARD the slide into a sharp container/box or disinfectant solution.
6. RECORD results

Coagulase (Slide Method)

1. USING sterile transfer pipette, place one very small drop (10-20 µl) of sterile deionized water on a slide.
2. EMULSIFY several colonies of the test organisms into the water to obtain a smooth milk-colored suspension.

Note: If clumps occur and the organism does not suspend in the water, the slide test cannot be performed. Perform the tube test instead.

3. USING sterile loop, add rabbit plasma. Mix and observe for clumping immediately, not to exceed 10 seconds.
4. OBSERVE for clumping
   - Positive = presence of clumping within 10 seconds
   - Negative = absence of clumping
5. DISCARD the slide in a sharps container or disinfectant bucket.
6. RECORD results

Coagulase (Tube Method)

1. ADD 0.5ml of Rabbit's plasma into a test 12 x 75mm tube.

2. INOCULATE the tube with one colony of the test organism growing on SBA.
3. INCUBATE at 35˚C without CO^2 for up to 4 hours and observe hourly for clot formation. Do not agitate the tube; rather gently tip to observe the clot. If the test is negative after 4 hours continue to incubate the test for 24 hours.
4. After 24 hour incubation, OBSERVE for clot formation
    - Positive test = complete clot formation or any degree of clot formation
    - Negative test = lack of clot formation
5. RECORD results

**QC organisms: S. aureus (+) and S. epidermidis or any CNS (-) on SBA*

Spot Indole Test

1. MOISTEN a piece of Whatman No. 1 filter paper with a drop of indole reagent.
2. USING a sterile wooden stick or disposable loop, pick a colony from a pure culture of test organism on SBA.
3. RUB a portion of a colony onto a small area of the moistened filter paper OR
4. TOUCH the colony with a cotton swab and add a drop of the reagent onto the swab.
5. OBSERVE for color change
    - Positive = Blue color (cinnamaldehyde reagent) OR brown-red to purple red color (benzaldehyde reagent) within 20 seconds
    - Negative = Colorless or slightly yellow
6. RECORD results

**QC Organisms: E. coli (+) and P. aeruginosa (-) on SBA*

Oxidase Test

1. MOISTEN a piece of Whatman No. 1 filter paper with a drop of the reagent.
2. USING a sterile wooden stick or disposable loop, pick a colony from a pure culture of test organism on SBA.
3. RUB a portion of a colony onto a small area of the moistened filter paper OR
4. TOUCH the colony with a cotton swab and add a drop of the reagent onto the swab.
5. OBSERVE for color change
    - Positive = deep blue to purple color in 10 to 30 seconds
    - Negative = no color change in 60 seconds
    - Development of the color in 30 – 60 seconds is a weak positive reaction

- Do not read after 60 seconds

6. RECORD results

**QC Organisms: P. aeruginosa (+) and E. coli (-) on SBA*

Wet Mount (for suspected yeast)

1. ADD a drop of sterile normal saline solution to a slide.
2. USING sterile stick or loop, emulsify one colony of suspected yeast.
3. APPLY a coverslip and examine under the low power objective and high power objective.
4. OBSERVE for yeast cells (Present/Absent)
5. RECORD results

**QC organisms: C. albicans, C. glabrata, S. epidemidis*

Germ tube test for *C. albicans*

1. USING a sterile transfer pipette, place 0.5 ml fetal bovine serum in a 12 x 75mm tube.
2. LIGHTLY touch a suspect yeast colony with a wooden applicator stick.
3. SUSPEND colony in serum.
4. INCUBATE at 35˚C without CO2 for 2.5 to 3 hours.
5. PLACE a drop of suspension on a microscope slide.
6. PLACE a coverslip over the suspension.
7. EXAMINE under high power objective for presence or absence of germ tubes.
8. INTERPRETATION
    - Positive test = presence of germ tube
    - Negative test = absence of germ tube
    - A minimum of five germ tubes should be observed before calling the isolate positive
    - A germ tube appears as a short lateral extension from the yeast cells and does not have a constriction (septum) where it meets the yeast cell
    - A constriction where the lateral extension meets the yeast cell is produced by pseudo hyphae or budding cells
9. RECORD results

D. Antimicrobial Susceptibility Testing Procedure.

Kirby Bauer Disk Diffusion Test

1. PREPARE a standardized inoculum from an 18 to 24-hour old pure culture of an organism to be tested.

- Select 3 - 5 well-isolated colonies of the same morphologic type from an agar plate culture
- Touch the top of the colonies with a loop
- Transfer growth into a tube containing 4 - 5 ml of NSS
- Compare the standardized inoculum density to 0.5 McFarland standard

2. LABEL plates of MH agar and streak each plate for confluent growth with the standardized inoculum of each organism using a sterile swab
    - Dip a sterile cotton swab into the standardized bacterial suspension
    - Rotate the swab several times and press firmly on the inside of the wall of the tube above the fluid level to remove excess fluid from the swab
    - Inoculate the dried surface of an MH plate by streaking the swab over the entire agar surface. Repeat this procedure by streaking two more times, rotating the plate 60 degrees each time to ensure an even distribution of inoculum. As a final step, swab the rim of the agar.
3. SELECT the appropriate antibiotic disks for the organism that is being tested and dispense the disks to the surface of the agar using clean forceps. Disks should be placed to allow adequate space for the diffusion of the agents. Tap the disk with forceps to assure contact with the agar. *The disks must be added within 15 minutes of the time the inoculum was streaked on the MH plate.*
    - No more than 12 disks should be placed on a 150mm Petri dish
    - No more than 5 disks should be placed on a 100mm Petri dish
    - Disks must be distributed evenly so they are no closer than 24 mm from center to center
    - Do not place disks close to the edge of the plate
    - A disk should not be relocated once it has come into contact with the agar surface. Instead, place a new disk in another location.
4. INVERT the plates and incubate at 35°C for 16-18 hours in an ambient air incubator. A full 24 hours is recommended for testing *S. aureus* against oxacillin/cefoxitin. *The plates must be placed in the incubator within 15 minutes of the time the disks were added to the agar*.

Reading AST Plate and Interpreting Results

1. EXAMINE the plates following incubation
    - If the plate was satisfactorily streaked and the inoculum was correct, the resulting zones of inhibition will be uniformly circular and there will be a confluent lawn of growth
    - If individual colonies are apparent, the inoculum was too light
2. MEASURE the zones of inhibition
    - Use a ruler in a well-lit room to read the zone size
    - Measure the diameters of the zones of complete inhibition, as judged by the naked eye, including the diameter of the disk
    - Measure the zones to the nearest whole millimeter
    - Hold the Petri plate a few inches above a black, non-reflecting background illuminated with reflected light
    - For cefoxitin disk, read the zone of diameter with reflected, not transmitted light
    - The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye
    - With *Proteus spp*., ignore the thin veil of swarming growth inside the obvious zone of inhibition
    - With trimethoprim and sulfonamides, disregard slight growth (20% or less of the lawn growth), and measure the more obvious margin to determine the zone diameter
3. INTERPRET the zones of inhibition by referring to zone diameter interpretive standard (CLSI M100) and report the organism as Susceptible (S), Intermediate (I), and Resistant (R)
4. RECORD results

DECLARATION

I, the undersigned, declare that this M.Sc. thesis is my original work, has not been presented for a degree in this or any other university and that all sources of materials used for the thesis have been duly acknowledged.

M.Sc. candidate: Hiwot Bizuayehu (B.Sc.)

Signature: _____

Date of submission: _____

This thesis has been submitted with our approval as an advisor.

Advisor: Adane Bitew (PhD, Associate Professor)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.