ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF MEDICAL LABORATORY SCIENCES

Bacterial profile, antimicrobial resistance patterns and the associated risk factors among cancer patients suspected with urinary tract infection in Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia.

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This is my paper to certify that partial fulfillment masters degree entitled with Bacterial profile, antimicrobial resistance patterns and associated risk factors of urinary tract infection among cancer patients attending Tikur Anbesa Hospital, Addis Ababa, Ethiopia.

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Abbreviations

AAU	Addis Ababa University
AMR	Antimicrobial resistance
ATCC	America type culture collection
BAP	Blood Agar Plate
BPH	Benign Prostatic Hyperplasia
CONs	Coagulase negative staphylococci
CFU	Colony form unit
CLSI	Clinical and Laboratory, standard Institute
ESBL	Extended spectrum beta-lactamase
GBS	Group B Streptococcus
GUC	Genitourinary cancers
LUTS	Lower Urinary Tract Symptoms
MDR	Multi Drug Resistance
MHA	Muller Hinton Agar
SOP	Standard operation procedures
SPSS	Statistical Package for Social Sciences
UPEC-	Uropathogenic Escherichia coli
UTI	Urinary tract infection

Abstract

Background*:* Bacterial infection is one of the most common life-threatening complications of cancer and cancer treatment. Ureteral tract infection (UTI) has become a serious concern in cancer patients. Therefore, the present study aimed to determine the spectrum and antibiotic resistance pattern of bacteria related to urinary tract infections among cancer patients.

Objective: The study aimed to determine antimicrobial resistance pattern, UTI bacterial profile, and their associated risk factors among cancer patients attending Tikur Anbesa Hospital, Addis Ababa, Ethiopia.

Methods: A cross-sectional study was conducted from December 2020 to May 2021 among UTI suspected cancer patients in Tikur Anbesa hospital. Study participants were recruited through a convenient sampling technique through consecutive sampling. Socio-demographic variables were collected using a pre-tested questioner while clinical variables were collected through chart review and physical examinations. A morning midstream urine sample was collected for urine culture. Colony characterization and species identification, and antimicrobial susceptibility were carried out. The data was entered and analyzed using SPSS. Descriptive statistics were presented using tables and figures. Bivariable and multivariable logistic regression analysis was done to assess the association between dependent and independent variables. A P-value less than 0.05 was considered statistically significant.

Result*:* Of the total of 272 urine sample tested , about 20.2% of the study participants were culture positive for a different type of bacterial pathogens predominantly gram-negative pathogens outnumber 45 (81.8%). *E. coli* was the predominant one reported among 26 (47.3%) of the patients followed *K. pneumonia* 9 (16.4%), *Enterococcus Spp*. 5 (9.1%). Majority of the isolates were sensitive for gentamycin 69.1%, meropenem 95.6%, nitrofatonin 84%. Incontrast, isolates were resistant to ciprofloxacin 90.7%, augmentin 88.9%, and ampicillin 96.4 %. Factors such as being female (AOR 7.86, 95% CI (3.45, 17.89)), the presence of additional comorbidity (AOR 2.4, 95% CI (1.05, 5.49)), those who had a history of catheterization (AOR 3.61, 95% CI (1.04, 12.52)) and symptomatic cancer patients (AOR 3.79 95% CI(1.84, 7.79)) had statistical significant association with more likely to develop bacteriuria

Conclusion and Recommendations: Bacteriuria among cancer patients was considerably high. Being female, having a history of catheterization, presence of additional comorbidities, and being symptomatic have been associated with bacteriuria. E. coli was the predominant bacterial isolate. Antimicrobial susceptibility patterns showed that the majority of the isolates were resistant to commonly used antibiotics such as ciprofloxacin, augmentin, and ampicillin. Thus, urine culture is very important for cancer patients to control drug resistance, to restrict and give only after doing culture and sensitivity tests.

Key Words: UTI; Cancer patient; Bacterial profile; Antimicrobial resistance

1. Introduction

1.1. Background Information

Cancer is a significant cause of death worldwide, and more than half of them occur in developing countries. The most common causes of cancer death are lung, liver, colorectal, stomach, breast cancer, cervical cancer, and leukemia (1). Infections are one of the most serious complications and the leading cause of morbidity and mortality in patients with cancer. Urinary Tract Infections (UTI) is one of the most common infection in cancer patients (2).

Urinary tract infection is one of the most common infectious diseases and the main cause of community-acquired and nosocomial infections at admission. Different microorganisms had been identified as common causes of UTI mainly; *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus saprophyticus, Enterococcus faecalis*, group *B Streptococcus(GBS*), Proteus mirabilis, *Pseudomonas aeruginosa, Staphylococcus aureus* Bahu.R et al. Patients with UTI usually presented with different clinical manifestation. Complicated UTIs are usually associated with in-dwelling catheters, urinary tract abnormalities, immunosuppression, or exposure to antibiotics (3).

Urinary tract infections (UTI) are very often observed and occur more frequently in women than in men . Infection in women is more frequent because of the close proximity of the reproductive and lower urinary tracts as Cybulski.Z et al reported . Urinary tract infections typically start with periurethral contamination by a uropathogen residing in the gut, followed by colonization of the urethra and, finally, migration by the flagella and pili of the pathogen to the bladder or kidney. Bacterial adherence to the uroepithelium is key in the pathogenesis of UTI. Infections occur when bacterial virulence mechanisms overcome efficient host defense mechanisms (4).

The prevalence of UTIs in men is significantly lower than in women, primarily urologic structural abnormalities in men are commonly associated with older adult men (5). Upper UTIs, also known as pyelonephritis, develop when uropathogens ascend to the kidneys by the ureters. Infections can occur when bacteria bind to a urinary catheter, a kidney, or a bladder stone or when they are retained in the urinary tract by a physical obstruction (6).

UTI is particularly associated with the bladder and kidney cancer in both men and women. UTI are associated with a high risk of urinary bladder cancer in postmenopausal women, especially in women. In males, the obstructive urinary symptoms induced by benign prostatic hyperplasia include difficulty in urination and urine retention, resulting in UTI caused from urinary stasis (7). A colorectal cancer is also associated with an increased risk of transitional cell cancer of the upper urinary tract. The cumulative risk is relatively low, although a subset of hereditary nonpolyposis colorectal cancer families may be exposed to a much higher risk. UTI is also common in patients with malignant neoplasms of the genitals often suffer simultaneously from inflammation of the uterus and vagina suffered from endometrial and cervical cancer (8).

Cancer patients are more susceptible to urinary infections which are directly associated with immune status. In immune-compromised cancer patients, urinary tract infection is one of the major causes of fever and morbidity. Obstructive uropathy is common in patients with solid tumors (2). Infection is a continuous and significant problem in cancer due to both direct and indirect effects on a patient's immune system. Several factors could increase the susceptibility of immunosuppressed cancer patients to infection, mainly neutropenia during aggressive therapy, altered gut flora because of frequent antibiotic administration, disruption of skin, and damage of epithelial surfaces by cytotoxic agents (9).

Risk factors associated with developing UTI include age-related changes to the genitourinary tract, comorbid conditions, and instrumentation required to manage bladder voiding (10). The prevalence also increases with advancing age, catheterization, sexual activity, menopause, and urinary obstruction problems (11).

Patients who have undergone surgery (for cancer or other reasons) may suffer an infection of the urinary tract as a complication of the surgery, catheterization, or cystoscopy. Radiotherapy, which is used alongside surgery as a standard method in the treatment of these tumors, may also be a factor increasing the risk of UTI as it causes inflammatory changes to the epithelium of the urinary bladder (12). Neutropenia is one of the most serious and common complications in oncological treatment. Patients under chemotherapy are susceptible to infections because therapy directly affects the production of neutrophils.(13) Severe immunosuppression as an adverse consequence of treatment strategies increases the risk of opportunistic infections. Although the exact mechanism of immunosuppression is still to be elucidated, reduced tumor necrosis factor-

αlevels, interleukin 10 (IL-10) induction, impairment of natural killer cells, increases in certain other cytokines, complement activation, decreased macrophage function, decreased CD4/CD8 ratio, and decreased IL-2 secretion.Reductions in these cells predispose the body to bacterial invasion and proliferation and inhibit the appearance of any inflammatory response (14).

A recent study demonstrated a relationship between UTI and genitourinary cancers (GUC) and confirmed that recurrent UTI are a risk factor for urinary bladder cancer. Moreover, the relationship between UTI and other tumors is important because UTI-caused inflammatory response is a systemic symptom (15). Patients with UTI usually present with acute clinical UTI or chronic uncomplicated or complicated UTI. Complicated UTI involve individuals with a condition or more resistant pathogen that increases the risk of failing treatment with functional, metabolic, or structural abnormalities (16). Treating UTI in cancer patients is clinically challenging as many cancer patients are at high risk of AMR due to long-term chemotherapies, depressed immune systems and repeated use of antibiotics to prevent and/or treat infections (17). Understanding patterns of AMR resistance for UTI is imperative to inform clinical practice and stewardship in relation to the appropriate use of antibiotics in cancer patients (18).

Furthermore, high consumption of antibiotics and prolonged hospital stays make cancer patients vulnerable to multidrug-resistant (MDR) bacteria strains. Furthermore, without effective use of antibiotics for prevention and treatment of infections, the success of major surgeries and cancer chemotherapies would be compromised, putting them at even higher risk. Although rational use of antibiotics has been proven effective in reducing AMR frequent and irrational use of antibiotics has been linked to rising MDR bacteria among cancer patients (19, 20).

Infection is the second leading cause of death in patients with cancer. Loss of efficacy in antibiotics due to antibiotic resistance in bacteria is an urgent threat against the continuing success of cancer therapy. Antibiotic failure in patients with cancer increases the frequency of sepsis, sepsis-related mortality, and sepsis-associated costs of cares. Some of the key factors contributing to antibiotic resistance are misuse of antibiotics in humans, lack of rapid diagnosis procedures, and the presence of antibiotics in the environment (21).

Antibiotic resistance can be intrinsic or acquired due to various genetic mechanisms. Some mechanisms can lead to antibiotic resistance such as by antibiotics inactivation of ESBL-producing E. coli, Antibiotic target modification by the microorganism ; Alteration of the

peptidoglycan synthesis pathway, Mutations in DNA gyrase and antibiotic efflux which is a key mechanism of resistance in gram negative bacteria this allow the microrganism to regulate their internal environment by removing toxic substance including antimicrobial agents (22).

In Ethiopia,there is scarcity of information with regard to the over all prevalence uropathogens related among cancer patient suspected with urinary infection in Ethiopia.Hence,it was important to assess bacteriuria, their associated risk factor and antibiotic susceptibility patterns of uropathogens among cancer patients in Tikur Anbesa Specialized Hospital.

1.2 Statement of the Problem

Urinary tract infection are the most common causes of morbidity and mortality in patient with cancer . It has been estimated that 150 million UTIs occur per annum worldwide. Despite the widespread availability of antibiotics, urinary tract infection remains a worldwide therapeutic problem. Cancer patients being immunosuppressed are vulnerable to develop infections (23). It causes a significant health care burden. For instance, in the United States, UTI among men was estimated at 13,689/100,000 (24).

Cancer, with an estimated incidence of 103.7 per 100,000 population in 2018, is a major public health problem in Nepal . At least 700,000 deaths globally have been attributed to AMR each year, which is predicted to rise to 10 million deaths each year by 2050. The burden of cancer in Nepal has been increasing over the last decade, with the top cancers being lung, cervical, breast, stomach and colorectal . Hence urinary tract infection (UTI) is one of the most common infections among cancer patients due to their prolonged immunosuppression, complex cancer treatment and catherization (25).

In developing country , Infections among cancer patients are a major challenge to deal with (26). Resistant organisms have emerged owing to selective antimicrobial pressure, which further complicates the problem. percentage of deaths in cancer patients with infections was found to be 60%. It was greater in those with solid organ tumours than in those with haematological malignancies. Bloodstream infections accounted for 36.3% of the total infections. Second most common were respiratory tract infections, accounting for, 31.9%,third most common were urinary infection which accounts for 16.9% (27).

Reports showed that the overall prevalence of UTI is 62.86% among Benign Prostatic Hyperplasia. The Lower Urinary Tract Symptoms (LUTS) due to bacterial etiology are one of the common factors for the complications among the patients. LUTS are of significant importance to public health, affecting millions of older men suffering from BPH(Benign Prostatic Hyperplasia) and prostatitis. The bacterial agents in LUTS associated with BPH are primarily the *Enterobacteriaceae*, less commonly Gram-positive organisms, and *Pseudomonas aeruginosa* (28).

UTI is one of the growing problems in developing countries. In addition to the increase in UTI cases, the emergence of drug resistance is one of the most threatening factors in developing countries. Major factors for increasing antibiotic resistance and spreading ESBL-producers are mobility of ESBL genes, misuse of antibiotics, and passage of resistance genes between uropathogens play a main role in increasing drug resistance (29).

The emergence of antimicrobial resistance has become a significant problem worldwide, and cancer patients are among those affected. Treatment of infections due to multidrug-resistant bacteria represents a clinical challenge, especially in the case of Gram-negative bacilli, since the therapeutic options are often very limited (30).

In Ethiopia, there is limited data on ureteral infection in cancer patients and, the UTI problem has been magnified over time with the emergence of multidrug-resistant bacteria as well an increment of UTI due to recurrent infection. Thus, the current study aimed to assess the prevalence, antimicrobial resistance, and factor associated with UTI among cancer patients.

1.3 Significant of the Study

Urinary tract infections are the common types of infections in the community and health care settings. Despite the widespread availability of antibiotics, urinary tract infection remains a worldwide therapeutic problem. Even though it is a continuous and significant problem in cancer patients epidemiological data are limited regarding the prevalence, antimicrobial resistance, and factors associated with it. Nowadays the emergence of antimicrobial resistance has become a significant problem worldwide, especially among cancer patients. Treatment of infections due to drug-resistant bacteria represents a clinical challenge, especially in the case of Gram-negative bacilli, since the therapeutic options are often very limited. Thus, the current study was designed to assess the prevalence, antimicrobial resistance, and factor associated with UTI among cancer patients. In doing so, results from the current study generate evidence on the type of pathogens which help the physicians to select the optimal empirical treatment in critically ill patients, early diagnosis, and selection of the appropriate antibiotic which decreases drug resistance. In addition, it will help to treat the underlining disease to prevent further complications. Moreover, it serves as baseline information for those who are interested to conduct further studies in the area.

2.Literature Review

2.1. UTI in cancer patient

Urinary tract infections are the most commonly encountered infections in medical practice. It is a major public health problem and the increased risk of bacterial infections in the cancer patient is further compounded by the rising trends of antibiotic resistance in the commonly implicated organism (31). There are some literatures that showed bacterial profiles, and antimicrobial resistance pattern in cancer patients.

According to the study conducted in Virginia, USA; UTI was the most frequent type of infection with a prevalence of 30.5%. *E. coli, S. aureus,* and other Gram-negative bacteria were the most frequent microbiological isolates (32).

A retrospective analysis was conducted among 497 Indian's UTI suspected cancer patients of which 100 cases were positive. Over all, *E.coli* (40%) was the predominant isolate followed by *Klebsiella pneumonia* (25%), *Pseudomonas aeruginosa* (11%), *Enterococcus spp(11%)* and *Proteus mirabilis*(5%). Susceptibility of Gram negative bacteria to *colistin* was highest (100%) followed by the carbapenems (72%). Resistance was found to be higher to the aminoglycosides (46%), cephalosporins(67%) and fluoroquinolones (90%) (17). Similar study from India that 20.82% of the outpatients' urine samples was confirmed as having community-acquired urinary tract infection while 24.83% of the indoor patients' urine samples as hospital-acquired urinary tract infection. *Escherichia coli* was the predominant pathogen both cases with prevalence of 68% and 45%; followed by *Klebsiella spp* and Enterococcus spp. High level of antibiotics resistance was reported to fluoroquinolones and third generation cephalosporins was noted. Nitrofurantoin was found to be a reliable oral drug for treatment of most of the uropathogens (33).

Another prospective study from India reported 42/121 cases positive for cultrure. Overall *E. coli* 16 (38.09%) was the predominant pathogen followed by *Pseudomonas aeruginosa* 8 (19.04%), *Klebsiella pneumonia* 5 (11.9%), *Candida* species 5 (11.9 %), *Acinetobacter* species 4 (9.52%), *Staphylococcus aureus* 2 (4.76%), *Enterobacter* species 1 (2.3%) and *Enterococcus* species 1 (2.3%). Susceptibility to polymyxin B and colistin was highest (100%) followed by the carbapenems (90%) and piperacillin +Tazobactam (73%). Resistance was

reported for to fluroquinolones (96%), cephalosporin's (80%) and aminoglycosides (50%) was noted (34). In addition, typical study from India was conducted on the basis of 285 specimens from oncology patients; *E.coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus and Acinetobacter spp*. were the most predominant pathogens. majority of *Acinetobacter* strains were resistant to carbapenems. About 41.67% of S. aureus were methicillin resistant (35).

A cross sectional from Egypt was conducted among 343 patients where E. coli was the most frequent isolates (30%) followed by *Pseudomonas aeruginosa*(24.5%). Isolates *of Escherichia coli, Klebsiella, Enterobacter, Pseudomonas and Acinetobacter* species were resistant to most of the antibiotics including non-β-lactam antibiotics such as aminoglycosides (gentamicin) and quinolones (ciprofloxacin, levofloxacin) (36).

Another study conducted in Egypt reported gram-negative pathogens were the most commonly isolated predominantly *E. coli*. Isolates exhibited simultaneous resistance to more than one non β-lactam drug. There was significant imipenem -resistance in *Acinetobacter* (40.9%), *Pseudomonas* (40%), and *Enterobacter* (22.2%) species, and noticeable imipinem-resistance in *Klebsiella* (13.9%) and *Escherichia coli* (8%) (37).

In Ethiopia, a study conducted at University of Gondar among 216 cancer patients reported *S. aureus* (12, 28.6%), *CoNS* (11, 26.2%) and *E. coli* (9, 21.4%) as the predominant bacterial isolates. The most common isolates identified in UTI were *E. coli* and *CoNS* (9, 28.1%) each. Multidrug resistance was detected in 46.5% bacterial isolates. Methicillin resistance was detected in 25% of S. aureus and in 45.5% of coagulase negative staphylococci. Fluor quinolone resistance was detected in 33.3% of *E. coli* isolates. Cancer patients with solid tumor, started cancer therapy, and being symptomatic had higher odds of culture positivity (38). Another study form the same institution showed that the overall prevalence of asymptomatic bacteriuria in cancer patients as 23.3% and 6.7% in apparently healthy blood donors. *E. coli* (32.1%) was the commonest isolated followed by *Klebsiella species* (25.0%), *S. aureus* (21.4%), *Enterococcus species* (10.7%), *Serratia species* (7.1%), and *Enterobacter aerogenes* (3.6%). Most Gram-negative bacteria were more sensitive to ceftazidime, ceforxime, nalidixic acid, nitrofurantoin, norfloxacin, ciprofloxacin, and tobramycin, whereas highly resistant to ampicillin, penicillin, tetracycline, and ceftazidime. *S. aureus* isolates were 100% susceptible to nitrofurantoin (39)

2.2. Risk associated factor causing UTI in cancer patient

Cancer patient are more susceptible to ureteral infection due to various risk associated factors. Several factors had been postulated as a risk factor for UTI among cancer patients which includes progression of the tumor, age, diabetic mellitus, disruption of natural anatomic barriers such as the skin and mucosal surfaces, and treatment-related factors such as chemotherapy, radiation, diagnostic and/or therapeutic surgical procedures, and the increasing use of medical devices such as various catheters, stents, and prostheses. Cancer chemotherapy often damages mucosal surfaces, thereby increasing the risk of infections caused by organisms that colonize these surfaces (40).

Urinary tract infections are most frequently observed and occur in women than in men which might be due to the close proximity of the reproductive and lower urinary tracts (29). Patients with malignant neoplasms of the genitals often suffer simultaneously from inflammation of the uterus and vagina. Patients who have undergone surgery (for cancer or for other reasons) may suffer infection of the urinary tract as a complication of the surgery, catheterization or cystoscopy (41). Radiotherapy, which used alongside surgery is a standard method in the treatment of these tumors, had also been associated with increased risk of UTI as it causes inflammatory changes to the epithelium of the urinary bladder, it can irritate the bladder wall lining and muscle wall, leading to decreased bladder compliance and capacity (12).

People with cancer who are being treated with chemotherapy are more likely to get infections Chemotherapy and radiation therapy can suppress or weaken the immune system by lowering the number and/or effectiveness of white blood cells and other immune system cells. A weakened immune system results in an increased risk of infection. It is important for cancer patients to understand their risk for infection (42).

Generally, in affected patients, organisms that are typically less virulent may cause marked illness, although *E. coli* infection remains the most common organism nearly in all patient; *Klebsiella* and group *B streptococcus i*nfections are relatively more common in patients with diabetes, and *Pseudomonas* infections are relatively more common in patients with catheterized patients. *Proteus mirabilis* is a common uropathogen in patients with indwelling catheters, spinal cord injuries, or structural abnormalities of the urinary tract (43).

3. Objective

3.1 General objective

The general objective of this study is to determine the prevalence of urinary tract bacterial pathogens, antimicrobial susceptibility patterns, and associated risk factors among cancer patients at Tikur Anbesa hospital, Addis Ababa, Ethiopia.

3.2 Specific objective

- To determine the prevalence of urinary tract bacterial pathogens among cancer patients attending Tikur Anbesa hospital, Addis Ababa, Ethiopia.
- To determine antimicrobial susceptibility patterns of the bacterial isolated that causes urinary tract infection among cancer patients at Tikur Anbesa hospital, Addis Ababa, Ethiopia.
- To assess associated risk factors of UTI among cancer patient at Tikur Anbesa hospital, Addis Ababa, Ethiopia.

4. Materials and Methods

4.1. Study Area

The study was conducted at Black Lion Specialized Hospital oncology center, Addis Ababa, Ethiopia. The hospital was established in 1964 and serving as a referral and teaching hospital. Currently, the hospital had 300 undergraduate medical students and 350 residents. The hospital offers diagnosis and treatment for approximately 370,000-400,000 patients a year. The oncology center of the hospital gives service for patients from all regions of the county with an overall bed capacity of 678. The center provides chemotherapy, radiation therapy, as well as supportive and palliative, cares. The center provides diagnostic and treatment services for 85 cancer patients daily.

4.2. Study Design and Period

A cross-sectional study was conducted from December 2020 – May 2021 among cancer patients attending Tikur Anbesa Hospital at cancer treatment center.

4.3 Populations

4.3.1 Source Population

All cancer patients who visited Tikur Anbesa hospital cancer treatment center during the study period were the study population.

4.3.2. Study subjects

All cancer patients who were symtomatic for urinary tract infection in Tikur Anbesa hospital were considered as a source population.

4.4. Inclusion and Exclusion Criteria

4.4.1. Inclusion Criteria

The criteria for inclusion of individulas for cases were:

- Cancer patients who are admitted to the hospital and diagnosed with related symptom**.**
- Cancer patients who were volunteered to take part and gave written consent to take part in the study.
- All age groups who expectorate urine sample

4.4.2. Exclusion criteria

- Currentely catheterized patients
- Patients who took antibiotics currently within the last 7 days
- Critically ill patient who are unable to give sample

4.5. Study variables

4.5.1. Dependent variables

- ✓ Prevalence of bacterial isolates
- ✓ Antimicrobial resistance pattern

4.5.2. Independent variables

The independent variables were demographic characteristics (age, sex, residence, marital status), behavioral characteristics (smoking, alcohol), and clinical variables such as cancer type and stage of cancer Patients with UTI usually present with acute clinical UTI or chronic uncomplicated or complicated UTI, the associated risk factor includes types of therapy they used, co-morbidity case, history of u UTI, history of a catheter, types of drug they used, clinical sign and symptom

4.6. Sample size determinations and Sampling techniques

4.6.1. Sample size determinations

Single population proportion formula had been implemented to calculated the sample size for the current study using prevalence of 23.3% (P = 0.23) derived from previous study conducted in

Gondar. Thus, by considering 95% confidence level, 5% of marginal error (0.05), p=0.23, the sample size was calculated as follows:

$$n = \frac{(Z_{\alpha/2})^2 * P(1-P)}{d^2} \qquad \frac{(1.96)^2 * (0.23*0.77)}{(0.05)^2}$$

The final sample size become 272

Where, n- is the sample size to be determined,

$Z_{\alpha/2}$- for standard normal distribution at 95% confidence interval, is 1.96

p- Prevalence of bacterial pathogens 23.3%,

d- Is margin of error assumed to be 5%.

4.6.2. Sampling techniques

Convenient sampling techniques was employed to recruit the study participants. All the consecutive cancer patients suspected to have urinary tract infection visiting Tikur Anbesa Specialized Hospital who were volunteer to participate were recruited.

4.7. Data collection procedure

4.7.1. Socio-demographic characteristics

Socio-demographic variables (mainly age, sex, residence) were collected using structured questionnaires via face-to-face interviews. On the other hand, clinical variables were collected through patient chart review to collect secondary data from patient cards and physical examinations was also performed .

4.7.2. Specimen collection and Laboratory procedure

A 5 ml midstream urine sample had been collected using clean, leak-proof sterile plastic cups for routine microbiological tests and culture..Urine culture had been done by inoculation of midstream urine on MacConkey (MAC) and 5% sheep blood agar plate (BAP. Incubate aerobically at 36 ^{o}C for 24 hr for bacterial isolation. Identification of bacteria were done using colony characteristics and biochemical tests following standard bacteriological procedure. Colonies were counted to check the presence of significant (Annex).

4.7.3. Antimicrobial susceptibility testing

An antimicrobial susceptibility test was carried following the preparation of a suspension of a pure colony from each confirmed culture isolate was prepared by using 0.85% sterile normal saline, and the suspension was adjusted at 0.5% MacFarland standard. It was carried out by Kirby Bauer disc diffusion method as per Clinical Laboratory Standards Institute (CLSI, 2020) guidelines on Muller Hinton agar. Identified bacterial isolates were tested for susceptibility using different antibiotics mainly for 12 antibiotics such as Amikacin (AK- 30µg), Ciprofloxacin (CIP-5µg), Ampicillin (AMP-10µg), Gentamicin (CN-10µg), Amoxycillin- Clavulanic acid (Aug -20µg), Ceftriaxone (CTR-30µg), Nitrofurantoin (NIT-300 µg), Co-trimoxazole (Trimethoprim-Sulfamethoxazole) (25 µg), Piperacillin-Tazobactam (16µg), Ceftazidime ((CAZ-10µg), and Meropenem((10µg).cefuroxime (CXM), (CLSI 2020) 30th edition.

The suspension was swabbed uniformly over the entire surface of a sterile Muller Hinton Agar (MHA) plate. The antibiotics discs were placed on an inoculated plate no closer than 15mm from the edge and 24mm from center of the discs. The plates were then left at room temperature for 15 Minutes for pre-diffusion and then incubated at 36˚C. Diameter of the zone of inhibition around the disc was measured to the nearest millimeter using a metal caliper and the isolate was classified as sensitive, intermediate, and resistant according to 30th edition CLSI,2020 guidelines. Isolates were considered as multidrug-resistant (MDR) if bacterial isolates are non-susceptible to Greater than or equal to three or more antimicrobial categories Standard quality control ATCC strains with known minimum inhibitory concentration Including *S.aureus* ATCC 25923, *E.coli* ATCC 25922, and *P.aeruginosa* ATCC 27853 was included in each

4.7.4. Operational Definitions

- Suspected for UTI was defined in the presence of at least 1 of the following signs or symptoms: chills or rigors associated with fever or hypothermia, flank pain (pyelonephritis) or pelvic pain (cUTI), dysuria or urinary frequency/urgency by a physician based on the information obtained from history, physical examination (44).
- According to guidelines of the Infectious Diseases Society of America significant bacteriuria will be defined when colony count yielding bacterial growth of $\geq 10^5$ CFU/Ml of urine (45).

- Multiple Drug Resistant (MDR) was defined as a bacterial isolate, which is resistant to three or more antibiotics in three or more classes of antimicrobials agents (39).

4.8. Data Quality Assurance

The questioner was prepared in English language and translated to Amharic then translated the English language to check for consistency. The urine sample had been assessed for contamination and adequacy of the sample. Data was collected after consent was secured from each study participant to make them fully concerned about their response. The collected data were assessed for completeness, consistency, and accuracy on daily basis. Culture media were tested for sterility and performance. In addition sterility of culture, media was assured following overnight incubation at 35–37°C without specimen inoculation. Moreover, standard reference strains of *E. coli* (ATCC 25922), *S. aureus* (ATCC 25923), and *P. aeruginosa* (ATCC 27853) had been used for quality control throughout the study for culture and antimicrobial susceptibility test.

4.9. Data analysis and interpretation

The data were entered into an excel sheet after checking for completeness then the data were exported to SPSS version-20 for analysis. The descriptive result was summarized using frequencies, mean, median, standard deviation and presented using figures and tables. Both bivariate and multivariate logistic regression was used to determine the association between dependent and independent variables. In all cases, a P value less than 0.05 was considered statistically significant.

4.10. Ethical consideration

The research was conducted after ethical clearance was obtained from the department of medical laboratory science, college of medicine and health sciences, Addis Ababa university ethical review committee. In addition, a permission letter was obtained from Tikur Anbesa hospital cancer treatment center. Moreover, informed consent, and assent were secured from each study participant. Code had been used and confidentiality of patient data was kept.

4.11. Dissemination of finding

Results obtained from the current study will be presented and submitted to the department of medical laboratory, college of medicine and health sciences, Addis Ababa University. In

addition, a copy of the result will be submitted to Tikur Anbesa hospital's cancer treatment center. Besides, it will be presented at different annual conferences and will be disseminated through publication in peer-reviewed journals.

5.Results

5 .1. Socio-demographic characteristics

A total of 272 study participants which comprises 133 (48.9%) male and 139 (51.1%) female patients were included in the current study. The mean age of study participants was 39.57 ± 21.55 years, range 1–80 years. The majority of the study participants (51.1%) were female. About 183 (67.3%) of the study participants came from the rural part of the country (Table 1).

Table 1: Socio-demographic characteristics of study participants attending in Tikur Anbesa hospital, Addis Ababa, Ethiopia (n=272)

Variables		**Frequency (N)**	**Percentage (%)**
Age in years	< 17	56	20.6
	18- 44	94	34.6
	45- 64	87	32
	> 65	35	12.9
Gender	Male	133	48.9
	Female	139	51.1
Residence	Rural	183	67.3
	Urban	89	32.7
Marital Status	Married	164	60.3
	Single	48	17.6
	Divorced	2	0.7
	Widowed	11	4
	NA for infants and toddler	47	17.2
Educational status	Unable to read and write	78	28.7
	Attend primary school	52	19.1
	Attend secondary school	57	21
	Attend college and above	42	17.3
	NA for infants and toddler	43	15.8
Occupation	Student	35	12.9
	Employed	50	18.4
	Self-employed	56	20.6
	Unemployed	91	33.5
	NA for infants and toddler	56	20.6

5.2. Clinical characteristics of study subjects

Of the total 272 cancer patients, the majority 232 (85.3%) were solid tumors while the rest 40 (14.7%) them were hematological malignancy patients. Most of the cancer confirmed patients, 48 (17.6%), had colorectal cancer followed by cervical cancer, 39 (14.3%). Almost all 249 (91.5%) of the patients were on therapy. About 35 (12.9%) of the patients had a previous history of UTI (Table 2)

Table 2: Clinical characteristics of UTI suspected cancer patients at Tikur Anbesa hospital, Addis Abeba, Ethiopia (n=272)

Variables		**Frequency (N)**	**Percentage (%)**
Type of cancer	Hematological	40	14.7
	Solid	232	85.3
Solid	Cervical	39	14.3
	Colorectal	48	17.6
	Breast	29	10.7
	Prostate	12	4.4
	Other	144	52.9
Stage of the disease	Stage I	5	1.8
	Stage II	55	20.2
	Stage III	61	22.4
	Stage IV	126	46.3
	Undifferentiated	25	9.2
Initiation of therapy	Yes	249	91.5
	No	23	8.5
Duration of treatment follow-up	< 1 year	209	76.8
	> 1 year	63	23.2
Presence of additional comorbidity	No	210	77.2
	Yes	62	22.8
History of UTI	Yes	35	12.9
	No	237	87.1
History of antibiotics	Yes	145	53.3

	No	127	46.7
Previous history of catheterization	Yes	13	4.8
	No	259	95.2
Disease Condition	Symptomatic	70	25.7%
	Asymptomatic	202	74.3

5.3. Bacterial profiles of study subjects

Out of 272 patients, 55 (20.2%) of them were culture positive for different types of bacterial pathogens. *E. coli* was the predominant one reported among 26 (47.3%) of the patients followed *K. pneumonia* 9 (16.4%), *Enterococcus Spp*. 5 (9.1%). (Table 3)

Table 3: Bacterial profiles of UTI suspected cancer patients at Tikur Anbesa hospital, Addis Abeba, Ethiopia (n=272)

Variables		**Frequency (N)**	**Percentage (%)**
Culture result	Positive	55	20.2
	Negative	217	79.8
Bacterial Isolate	*E coli*	26	47.3
	K. Pneumonia	9	16.4
	K. Oxytoca	4	7.3
	Enterococcus	5	9.1
	Pseudomonas Spp	3	5.5
	S. aureus	4	7.3
	Others	4	7.3

**others include: - citrobacter Spp, providencial stuarti, and coagulase negative staphylococci*

5.4. Antimicrobial susceptibility

Bacterial antimicrobial susceptibility tests were performed for bacterial isolates; the result showed that majority of the isolates were sensitive for gentamycin 69.1% (73.1% for *Escherichia coli*, 88.9% for *Klebsiella Pneumonia*, and 100% for *Pseudomonas species*), meropenem 92.2 % (100% for *Escherichia coli*, 77.8% for *Klebsiella Pneumonia*, 100% for *Pseudomonas species*, 100% for S. aurous) and Amikacine 92.1% (92.3% for *Escherichia coli*, 100% for *Klebsiella Pneumonia*, 100% for *Pseudomonas species*, 100% for S. aurous) (nitrofatonin 85.5% (92.3%

for *Escherichia coli*, 100% for *Enterococcus*, 100% for *Pseudomonas species*, 100% for S. aurous). On the other hand, isolates were resistant to ciprofloxacin 90.7% (96.2% for *Escherichia coli*, 66.7% for *Klebsiella Pneumonia*, 75% for S. aurous, and 100% for *Pseudomonas species*), augmentin 88.9% (88.5% for *Escherichia coli*, 88.9% for *Klebsiella Pneumonia*, and ampicillin 96.4 % (100% for *Escherichia coli*, 88.9% for *Klebsiella Pneumonia*, (Table 4)

Table 4: Antimicrobial susceptibility pattern of UTI suspected cancer patients at Black lion specialized hospital, Addis Ababa, Ethiopia

Bacterial isolates		Antimicrobial susceptibility pattern																									
		AMP		Aug		GM		CIP		MEN		FM		CXM		CAX		TZP		COT		AK		CAZ		Vanc	
		R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S
E coli		26		23	3	17	19	25	1	-	26	2	24	16	10	20	6	7	19	9	17	2	24	12	12	-	-
K. Pneumonia		8	1	8	1	1	8	6	3	2	7	4	5	6	3	7	2	5	4	2	7	-	9	2	6	-	-
K. Oxytoca		4	-	4	-	1	3	4	-	-	4	2	2	1	3	1	3	-	5	1	3	-	4	1	2	-	-
Enterococcus fecalis		5	-	-	-	-	-	5	-	-	-	-	5	-	-	-	-	-	-	-	-	-	-	-	-	2	3
Pseudomonas Spp.		3	-	3	-	-	3	3	-	-	3	-	3	-	-	3	-	-	3	1	2	-	3	2	1	-	-
S. aureus		4	-	-	4	2	2	3	1	-	-	-	-	1	3	-	4	-	-	2		-	4	1	3	-	-
Citrobacter fecalis		1	1	1	1	-	2	1	1		2	-	2	1	1	1	1	-	2	1	1	-	2	-	2	-	-
Providencial stuarti		1	-	1	-	-	1	1	-	-	1	-	-	-	1	1	-	-	3	-	1	-	1	-	1	-	-
CoNs		1	-	-	1	1	-	1	-	-	-	-	1	-	1	1	-	-	-	-	1	1	-	1	-	-	-
Total	(N)	53	2	40	5	22	38	49	6	2	43	8	42	25	22	34	16	12	36	16	32	3	47	19	27		
	(%)	***96.4***	***3.6***	***88.9***	***11.1***	***40***	***69.1***	***90.7***	***9.3***	***4.5***	***95.6***	***14.5***	***84***	***53.2***	***46.8***	***68***	***32***	***25***	***75***	***33.3***	***66.6***	***7.9***	***92.1***	***41.3***	***58.7***		

N.B: - ***CoNs:*** *coagulase negative staphylococci* ***AMP****: ampicillin;* ***Aug****: Augmentin;* ***GM****: gentamicin;* ***CIP****: ciprofloxacin;* ***MEN****: Meropenem;* ***FM****: Nitrofurantoin;* ***CXM:*** *Cefuroxime;* ***CAX****: Ceftriaxone,* ***TZP****: Piperacillin-Tazobactam,* ***COT*** *co-trimoxazole,* ***AK****: Amikacine;* ***CAZ****: Ceftazidime.*

5.4.1. Prevalence of Multidrug-Resistant Isolates

Among the isolates, about 19 (7%) of the study participants had shown MDR. The majority 12 (63.2%) of them were associated with *E. coli* whereas the rest were *K. pneumonia* 2(10.5%), *K.oxytoca* 1(5.3%), *S. aureus* 1(5.3%), and *CoNs* 1(5.3%) (Table 5).

Table 5: Multiple drug resistance patterns of bacteria isolates among UTI suspected cancer patients at Black lion specialized hospital, Addis Ababa, Ethiopia

Bacterial isolates	Antibiogram Pattern (N)						
	R0	R1	R2	R3	R4	MDR	
						(N)	(%)
E coli	0	4	10	10	2	12	63.2
K. Pneumonia	1	2	4	2	0	2	10.5
K. Oxytoca	0	0	3	1	0	1	5.3
Enterococcus	0	0	5	0	0	0	0.0%
Pseudomonas Spp	0	0	1	2	0	2	10.5
S. aureus	0	1	2	1	0	1	5.3
Citrobacter Spp	1	0	1	0	0	0	0.0%
Providencial stuarti	0	0	1	0	0	0	0.0%
CoNs	0	0	0	0	1	1	5.3
Total	2	7	27	16	3	19	0.0%

Note*:* **Ro***:sensitive for all class of antibiotcs,* **R1***:resistance for one class of antibiotics*, **R2***: resistance of two class of antiobiotics,* **R3***: resistant for three class of antiobiotics,* **R4***:resistant for four class of antibiotics,* **MDR***:multi-drug resistance.*

5.5. Risk Associated factors with UTI

Both bivariate and multivariate logistic regression analyses have been used to determine factors associated with the outcome variable. In bivariate logistic regression analysis; gender, the presence of additional comorbidities, history of catheterization, clinical symptoms of the disease, and use of antibiotics were significantly associated with bacteriuria. However, in multivariate analysis; gender, the presence of additional comorbidity, history of catheterization, and clinical symptoms of the disease remain statistically significant (Table 6).

Table 6: Risk associated factors with of UTI infection among UTI suspected cancer patients at Black lion specialized hospital, Addis Ababa, Ethiopia

Characteristics of study subjects		**Culture result**		**COR (95% CI)**	**p-value**	**AOR (95% CI)**	**P-Value**
		Positive	**Negative**				
Age in year	< 17	9	47	1			
	18- 44	20	74	1.41 (0.59, 3.36)	0.44		
	45- 64	17	70	1.27 (0.52, 3.08)	0.6		
	> 65	9	26	1.81 (0.64, 5.12)	0.26		
Gender	Male	11	122	1			
	Female	44	95	5.14 (2.52, 10.5)	<0.001	7.86(3.45,17.89)*	< 0.001
Residence	Rural	40	15	1.38 (0.72, 2.66)	0.34		
	Urban	143	74	1			
Education	Unable to read and write	15	63	0.88 (0.36, 2.16)	0.78		
	Attained primary school	15	37	1.5 (0.6, 3.77)	0.39		
	Attained secondary school	9	48	0.7 (0.26, 1.88)	0.47		
	Attained collage and	10	37	1			

	above education						
Occupation	Student	6	29	1			
	Employed	11	39	1.36 (0.45, 4.12)	0.58		
	Own private work	12	44	1.32 (0.45, 3.91)	0.62		
	Unemployed	20	73	1.32 (0.48, 3.63)	0.58		
Type of cancer	Hematological	7	33	1			
	Solid	48	184	1.23 (0.51, 2.95)	0.64		
Initiation of therapy	Yes	50	199	1			
	No	5	18	1.11 (0.39, 3.12)	0.85		
Duration of therapy	< 1 year	40	169	1.32 (0.67, 2.59)	0.42		
	>1 year	15	48	1			
Presence of additional comorbidities	No	37	137	1			
	Yes	18	44	1.91 (0.99, 3.68)	0.05	2.40 (1.05, 5.49)*	0.038
Previous history of catheterization	Yes	6	7	3.67 (1.18, 11.42)	0.02	3.61(1.04,12.52)*	0.043
	No	49	210	1			
History of UTI	Yes	9	26	1.44 (0.63, 3.27)	0.39		
	No	46	191	1			
Disease Condition	Symptomatic	26	44	3.53 (1.89, 6.58)	0.03	3.79 (1.84, 7.79)*	< 0.001
	Asymptomatic	29	137	1			
History of Antibiotics	Yes	34	111	1.55 (0.84, 2.83)	0.16	0.97 (0.48, 1.99)	0.946
	No	21	106	1			

NB: ** indicates statistically significant association*

6. Discussion

Cancer patients are more susceptible to several bacterial infections, particularly urinary tract infections. Cancer patients are known to be susceptible to various infections due to the destructive complications of cancer treatment on their immune system (46).

The current study aimed to assess the bacterial profiles, antimicrobial susceptibility patterns, and factors associated with UTI among cancer patients. According to the current study, the overall prevalence of MDR was 19 (7%). Our result was lower than previous reports from Gondar which reports the prevalence as 46.4% (39) and 46.5% (38) as well Addis Ababa 33% (2). Among the isolated bacteria, *E. coli* was the principal MDR strain. This was consistent with previous studies from Addis Ababa (2) and Gondar (39) and (38). The difference might be attributed to differences in study population, and the extent of use of antibiotics. Treating UTI in cancer patients is clinically challenging as many cancer patients are at high risk of AMR due to long-term chemotherapies, depressed immune systems and repeated use of antibiotics to prevent and/or treat infections (47).

Our study revealed that the overall prevalence of bacteriuria was 20.2% which was consistent with previous studies from Gondar ranging from 19.4% - 23.3% (38, 39), Nepal 24% (48), India (17), and Iran 24% (49). On the other hand, it was higher than the Addis Ababa study 6.3% (2). However, it was lower than reports from India 34.7% (50) and Iran (51). The possible reason for the discrepancy might associate with the differences in geographical location as temperatures rise the morbidity attributable to urinary tract infection may increase in the study by Simmering.JE.et al., study population, and use of a sensitive blood culture system (BD Phoenix automated microbiology system, Waldorf, Germany) which might increase culture positivity rate.

According to the current study, *E. coli* was the predominant isolate reported among 47.3% of the patients followed by *K. pneumonia* 16.4%. A similar result has been reported from Gondar (38, 39), Nepal 24% (48), India (17), Addis Ababa (2), India 34.7% (50), Iran (51), and the USA. In contrast study from Egypt had reported *K. pneumonia* as the predominant type of bacterial isolates with a prevalence of 31.2% (37). This might be due to since *E. coli* is a normal flora of the gastro-intestinal area and a common cause of both community and hospital-acquired UTI. As a result of the disease by itself as well as the nature of therapy cancer patients is more likely immunocompromised cancer thus, these patients are easily colonized by the bacteria.

In general, UTI typically start with periurethral contamination by a uropathogen residing in the gut, followed by colonization of the urethra and, finally, migration by the flagella and pili of the pathogen to the bladder or kidney. Bacterial adherence to the uroepithelium is key in the pathogenesis of UTI. Infections occur when bacterial virulence mechanisms overcome efficient host defense mechanisms (4).

According to our findings, the majority of the study participants were resistant to ciprofloxacin 90.7% (96.2% for *Escherichia coli,* 66.7% for *Klebsiella Pneumonia,* 75% for *S. aurous,* and 100% for Pseudomonas species), augmentin 88.9% (88.5% for *Escherichia coli,* 88.9% for *Klebsiella Pneumonia,* 100% for *S. aurous,* and 100% for Pseudomonas species), and ampicillin 96.4 % (100% for *Escherichia coli,* 88.9% for *Klebsiella Pneumonia*, 100% for *S. aurous,* and 100% for Pseudomonas species). Where as sensitivity was noted for gentamycin 69.1% (73.1% for *Escherichia coli,* 88.9% for *Klebsiella Pneumonia,* and 100% for *Pseudomonas* species), meropenem 92.2 % (100% for *Escherichia coli*, 77.8% for *Klebsiella Pneumonia*, and 100% for Pseudomonas species), nitrofatonin 84% (92.3% for *Escherichia coli,* 100% for *Enterococcus,* 100% for *S. aurous,* and 100% for Pseudomonas species). A similar finding had been reported previously from Addis Abeba (2), Gondar (38), and Nepal 24% (48). Mechanism of action and under-usage of Nitrofurantoin had been postulated as a reason for its sensitivity and recommended as an alternative antibiotic for the management of UTI in cancer patients. But it could not be used to treat UTI in complicated and febrile infants, because it is excreted in the urine and does not achieve therapeutic concentrations in the bloodstream (38). E. coli was resistant for ampicillin (100%), Augmentin (88.5%), ciprofloxacin (91.2%), ceftriaxone (79.2%) and ceforxamine (61.5%). The reason for increasing antibiotic resistance might be due to misuse of antibiotics and passage of resistance genes between uropathogens (29).

Bacterial antimicrobial susceptibility tests were performed for bacterial isolates; the result showed that majority of the isolates were sensitive for gentamycin 69.1% (73.1% for *Escherichia coli,* 88.9% for *Klebsiella Pneumonia,* and 100% for *Pseudomonas species*), meropenem 92.2 % (100% for *Escherichia coli,* 77.8% for *Klebsiella Pneumonia,* 100% for *Pseudomonas species,* 100% for S. aurous) and Amikacine 92.1% (92.3% for *Escherichia coli,* 100% for *Klebsiella Pneumonia,* 100% for *Pseudomonas species,* 100% for S. aurous) (nitrofatonin 85.5% (92.3%

for *Escherichia coli*, 100% for *Enterococcus*, 100% for *Pseudomonas species*, 100% for S. aurous). On the other hand, isolates were resistant to ciprofloxacin 90.7% (96.2% for *Escherichia coli*, 66.7% for *Klebsiella Pneumonia*, 75% for S. aurous, and 100% for *Pseudomonas species*), augmentin 88.9% (88.5% for *Escherichia coli*, 88.9% for *Klebsiella Pneumonia*, and ampicillin 96.4 % (100% for *Escherichia coli*, 88.9% for *Klebsiella Pneumonia*.

The emergence of bacterial strains that are resistant to commonly used antibacterial agents, becomes a potential public health problem, particularly among cancer patients. The increasing rates of antimicrobial resistance among bacterial pathogens isolated from cancer patients have been documented in many hospitals (52). According to our findings, the majority of the study participants were resistant to ceftriaxone (78.2%), Augmentin (90.9%), ciprofloxacin (89.1%), and ampicillin (96.4%). On the other hand, sensitivity was noted for gentamycin, Meropenem, co-trimoxazol, amikacine, and Nitrofurantoin. A similar finding had been reported previously from Addis Abeba (2), Gondar (38, 39), and Nepal 24% (48). Mechanism of action and under-usage of nitrofurantoin had been postulated as a reason for its sensitivity and recommended as an alternative antibiotic for the management of UTI in cancer patients. But it could not be used to treat UTI in complicated and febrile infants, because it is excreted in the urine and does not achieve therapeutic concentrations in the bloodstream (38). E.coli the predominant resistant strain with resistance pattern of ampicillin (96.4%), Augmentin (90.9%), ciprofloxacin (89.1%), ceftriaxone (78.2%) and cefoxamine (60.8%). The reason for increasing antibiotic resistance might be due to misuse of antibiotics and passage of resistance genes between uropathogens (29). The differences in susceptibility pattern of the isolates might also be due to the differences in the management of antibiotics which might leads to the development of specific mechanisms of resistance through time.

Moreover, result from our logistic regression showed that female patients were eight times (AOR; 95% CI: 7.86 (3.45, 17.89)) more likely to develop bacteriuria as compare to males. This was signtifically explained that lower UTIs, also known as cystitis, are significantly more prevalent in women due to anatomic differences, mainly associated with having a shorter urethral length and moist periurethral environment in women (38). On the other hand, the presence of additional comorbidity (AOR; 95% CI: 2.4 (1.05, 5.49)), patients who had a history of catheterization 3.61 (1.04, 12.52) and symptomatic cancer patients (AOR; 95% CI: 3.79 (1.84,

7.79)) were more likely to develop bacteriuria. A similar result had been reported from Gondar (38). Long-term catheterization, and the extensive use of medical devices such as stents, shunts and central venous catheters had been identified as a risk factors for the the acquisition of UTI among cancer patients (2).

Moreover our result revealed that majority of the cases were reported among solid tumor cancer patients as compared to the hematological one even though it was not found statistically significant (COR; 95% CI: 1.23 (0.51, 2.95)). Patients with solid tumors should be considered as a distinctive population as they are predisposed to developing infections, specially infection, due to a variety different of mechanisms: an often progressive catabolic state, malnutrition, ulcerating lesions in the skin and mucosal surfaces, obstructive processes, invasive procedures and indwelling devices, and immune suppression due to chemotherapy, radiation and/or the malignancy itself. Moreover, surgery had been also found as another risk factor for infection in patients with solid tumors (53).

7. Limitations of the study

As the limitation of this study, since cancer patient are immunocompromised patient the fungal agents especially Candidia are the most common etiological agent of UTI,we did not test for the fungal agents as the causative agent of UTI due to lack of laboratory consumables. Inaddition,we did not test extended betalactamase producing bacterial isolates which are the main sources of drug resistances.Due to budget issue and lack of antibiotics, drug sensitivity patterns including extended-spectrum β-lactamase and carbapenemase-producing isolates.

8. Conclusion and Recommendation

8.1. Conclusion

The overall prevalence of bacterial isolates among cancer patients was 20.2% which is a common problem. Being female, having a previous history of catheterization, presence of additional comorbidities, and being symptomatic have been associated with bacteriuria. *E. coli*, *K. pneumonia*, and *Enterococcus species* were the predominant bacterial isolates. Antimicrobial susceptibility patterns showed that the majority of the isolates were sensitive for gentamycin, Meropenem, Nitrofatonin, Pip.tazobacerium, Trimethoprime-sulfamethaxazol, Amikacine, and Ceftazidine while resistant for ceftriaxone, Augmentin, ciprofloxacin, and ampicillin.

8.2. Recommendations

Based on the finding of the study,current antibiotic use/prescription patterns for UTI and antibiotic resistance patterns among cancer patients in a representative sample of health facilities that provide cancer care in the country. Second, we recommend the implementation of standard protocols for systematic screening of cancer patients for UTI, standardized proforma for requesting urine cultures containing the relevant clinical details of the patients, systematic testing of bacteria for antibiotic drug susceptibility testing, recording and periodic reporting of drug resistance patterns and rational use of antibiotics in cancer patients. There is urgent need for an AMR stewardship program to educate and create awareness among health care professionals and the community on the rationale use of antibiotics

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Annex

Annex I: English Version of information sheet

Dear participants

I am Etabez Duga from department of microbiology, college of medicine and health sciences, Addis Ababa University conducting research on research on assessment of bacterial profiles, antimicrobial susceptibility pattern and factors associated with UTI among UTI suspected cancer patients.

The main purpose of this study is to find out the prevalence of urinary tract infection in cancer patient. This study will be carrying using self-administered questioners by which participants should be expected to answer individually. The benefits of the finding are if you are found to have urine infection you will be referred to the doctor for treatment and it may help with recommendations that may reduce for further complications related to these infections. Participation on this research project is entirely voluntary. If you decide not to participate or to withdraw from the study, the decision will have no effect on any services or treatment you are currently receiving. You can withdraw from the study at any stage without prejudicing any services you may be receiving.

If you have any question you can contact the principal investigator at any time by using the following address.

Name of the principal investigator: Etabez Duga

Mobile Phone number: +251910155874, E-mail taby.duga@gmail.com.

Annex II: English Version of consent form

Code number: _____

I undersigned below have been requested to participate in this study. I have read the information sheet (or it has been read to me) and I have understood that this study is aimed to assess the prevalence and UTI pathogens, antimicrobial susceptibility and factors associated with it among UTI suspected cancer patients. I gave my consent freely to participate in the study, and I hereby to approve my agreement with my signature.

Signature of the participant: _____

Date: _____

Annex III: English Version of Assent form

I have read the information above, or it has been read to me. I have been given the opportunity to ask questions and my questions have been answered to my satisfaction. I voluntarily consent that my child participates in this study provided he/she gives assent to give his/her urine and be a participant in this study and understand that I have the right to withdraw my child from the study at any time

Signature of the participant: _____

Date: _____

Annex IV: English Version of Questioner

I. socio demographic data

Study number _____ Study date _____

Sex _____ age _____

1.Educational status

a.no formal education c. secondary school

b. elementary d. College/university degree

2. Occupational status

a. Employed b. self-employed c .Not employed

3.Marital status

a. Married c. Divorced

b .Unmarried d. Widowed

4. Residence

a.. Rural _____

b. Urban _____

II. clinical data

5. Type of cancer _____, Mention as which type of tumor benign or malignant _____

6. Cancer treatment follow-up

a. < 1 year b. 1- 2 year c. > 2 years

6. Stage of cancer

a. Stage I _____ b. Stage II _____

c. Stage III _____d. Stage IV _____

e. Unknown stage _____

7. Started cancer therapy

a. Yes _____

b. No _____

8. If yes what type of therapy used

a. Chemotherapy _____ d. Chemotherapy with surgery

b. Surgery _____ e. Chemotherapy with Radiotherapy

c. Radiotherapy_____ f. Three of them

9. Cycle of chemotherapy

a. First diagnosis (no chemotherapy) d. 3rd cycle

b.1st cycle e. 4th cycle

c.2nd cycle f .5th cycle G.>6 th cycle

10. Recent surgery

a. Yes b. No

11. Other co-morbidity case if yes mention the coexistence disease ----------

12. History of urinary obstructive disease or urinary tract infection

a. Yes b.No

13.How often do you use water intake daily

a. less water intake per day c. three glass of water per day

b. no intake per day d. 1 liter of water per day

14. Use of antibiotics

a. Yes b .No

15. If yes what type of antibiotics used ----------16. Smoking status

a. Never b. former c. Current

17. History of catheter use

a. Yes b. No

18. History of hospitalization

a. yes b. No

19. Urine voiding habit

a. Infrequent c. Day time frequency of urination ≤ times /day

b. frequently d delayed voiding e. difficulty voiding

20. clinical signs and symptoms of UTI

a. Symptomatic cases _____

b. Asymptomatic cases_____

21. Type of specimen. Urine

22. Culture and biochemical test identification

……

……

23. Antibiotic resistance/sensitivities'

……

Name of PI…….

Signature ……. date……

Annex IV: Amharic version of information sheet

የተሳታፊዎች ፈቃድና መተማመኛ ቅፅ

መግቢያ

በአዲስ አበባ ዩኒቨርሲቲ ጤና ሳይንስ ኮሌጅ የሕክምና ላቦራቶሪ ት/ክፍል በማስተርስ ድግሪ ተማሪ የመመረቂያ ጥናት ላይ እዲሳተፉ ተጋብዘዋል፡፡ እባክዎ በዚህ ጥናት ለመሳተፍ ከመስማማትዎ በፊት ከዚህ ቀጥሎ የሚገኘዉን ምንባብ በጥሞና ያንብቡና ግልጽያልሆነልዎትን ማንኛዉም ሃሳብ ይጠይቁ፡፡

የጥናቱርዕስ

Antimicrobial resistance pattern, UTI bacterial profile and fungal pathogen and their associated risk factor among cancer patient suspected to have urinary tract infection at Black Lion Hospital, Addis Ababa, Ethiopia**.**

የጥናቱ ባለቤት፡ እታበዝ ዱጋ

የምርምር መረጃ

የተከበሩ ተሳታፊዎች በዚህ የምርምር ፕሮጀክት እንዲሳተፉ እጋብዝዎታለሁ። የጥናቱን ፕሮጀክት መቀላቀል ሙሉ በሙሉ በውሳኔ ምርጫዎ ላይ የተመሠረተ ነው ፣ ከመወሰንዎ በፊት ጥናቱ ለምን እንደ ተደረገ እና ለእርስዎ ምን እንደሚያካትት እነግርዎታለሁ ፡፡ የዚህ ጥናት ዋና ዓላማ በካንሰር ህመምተኛ ውስጥ የሽንት ኢንፌክሽን መኖር ለማወቅ ነው ፡፡

የምርመራው ጥቅሞች የሽንት ኢንፌክሽን ካለብዎ ለህክምና ወደ ሐኪም ይላካሉ እናም ከእነዚህ ኢንፌክሽኖች ጋር ለተያያዙ ተጨማሪ ችግሮች ሊቀንሱ በሚችሉ ምክሮች ላይ ሊረዳ ይችላል ፡፡ የእርስዎ ተሳትፎ ሙሉ በሙሉ በፈቃደኝነት ነው።

Annex IV: Amharic version of consent form

የተሰጠኝን መረጃ አንብቤ ተረድቼዋለሁ ፡፡ ስለዚህ ከዚህ በታች ፊርማዬ ሽንት ለማቅረብ በዚህ ጥናት ውስጥ ለመሳተፍ ፈቃደኛ መሆኔን ያሳያል

የተሳታፊ ፊርማ _____

ቀን : _____

- ማንኛውንም ጥያቄ ካለዎት የሚከተሉትን አድራሻዎች በመጠቀም ዋናውን መርማሪን ማግኘት ይችላሉ

የዋና መርማሪ ፣ **እታበዝ ዱጋ** ስልክ ቁጥር +251910155874 ፣ ኢ-ሜል taby.duga@gmail.com

Annex IV: Amharic version of assent form

ጥያቄዎችን የመጠየቅ እድል ተሰጥቶኛል እና ጥያቄዎቼ ተመልሰዋል ፡፡ ልጄ ሽንት ለመስጠት እና በዚህ ጥናት ውስጥ ተሳታፊ ከመሆን እና ልጄን ከጥናቱ በማንኛውም ጊዜ የማስወረድ መብቴ እንደገባኝ በመገንዘቤ ልጄ በዚህ ጥናት ውስጥ እንዲሳተፍ በፈቃደኝነት እስማማለሁ ፡፡

የተሳታፊ ፊርማ _____

ቀን : _____

- ማንኛውንም ጥያቄ ካለዎት የሚከተሉትን አድራሻዎች በመጠቀም ዋናውን መርማሪን ማግኘት ይችላሉ

የዋና መርማሪ ፣ **እታበዝ ዱጋ** ስልክ ቁጥር +251910155874 ፣ ኢ-ሜል taby.duga@gmail.com

Annex IV: Amharic version of questioner

I. አጠቃላይ መረጃ

የጥናት ቁጥር _____ የጥናት ቀን _____

ጾታ_____ ዕድሜ _____

2.ከፍተኛ የትምህርት ደረጃ

1. መደበኛ ትምህርት የለም _____

2 .የመጀመሪያ ደረጃ ትምህርት ቤት (1-8) _____

3. ሁለተኛ ደረጃ ትምህርት ቤት (9-10) _____

4. የኮሌጅ / የዩኒቨርሲቲ ዲግሪ _____

3, መኖሪያ

1. ገጠር _____

2. ከተማ _____

4.ካንሰር አይነት _____

5.የካንሰር ደረጃ

1. ደረጃ I _____ 2. ደረጃ II _____

3. ደረጃ III _____4። ደረጃ IV _____

5. ያልታወቀ ደረጃ _____

6.የተጀመረው የካንሰር ሕክምና

1 . አዎ _____

2. የለም ____

7.የቅርብ ጊዜ ቀዶ ጥገና

1. አዎ 2. አይ

8. አንቲባዮቲኮችን መጠቀም

1. አዎ 2. አይ

9. መልስዎ አዎ ከሆነ ምን አይነት አንቲባዮቲኮች ተጠቅመዋል

10.የካቲተር ተጠቀምዋ

1.አዎ 2. አይ

11. ተጉዳን ችግሮች ካለቦት ……

12. ህመም ሁኔታ ምልክት አለ

1. አለመኖር 2. መኖር

Annex V: SOP for urine culture

1. Aim

To isolate, quantify and permit presumptive identification and differentiation of the major microorganisms causing urinary tract infections (UTIs).

2. Principle

All urines undergo a dipstick test and/or microscopy to look for the presence of white blood cells, red blood cells, nitrites and bacteria. A known volume of urine is cultured in order to allow quantification of the number of organisms in the original urine, although because of imprecisions in the method this is usually referred to as 'semi-quantitative' culture

3. Method

Specimen collection

Urine specimens will be collected in several ways:

Morning Mid-stream clean-catch specimen

Wherever possible a specimen of urine should be collected aseptically directly into a sterile universal container following cleaning of the perineal area.

4. Specimen transport and storage

Specimens should ideally be stored and transported in sealed plastic bags. Laboratory processing should occur as soon as possible after specimen collection. Specimens should be refrigerated if delays in processing over two hours are unavoidable.

5. Specimen processing

Reception

Log the specimen in the appropriate specimen book and assign a specimen number.

Pre-culture examination

Perform a urine dipstick and microscopy on all urine samples arriving in the microbiology laboratory.

Microscopy of urine

Tip the closed urine pot over to mix carefully then use a capillary tube to place unspun urine into slide, leave the slide on the bench for one minute for the cells to settle.

Using a low power microscope objective (x40), count the RBC or WBC cell numbers in 36 small grids, unless obviously >100 (i.e. >1 per small grid). SOP for microscope

Culture

- Turn the urine pot over to mix it carefully and remove the top of the container.
- Dip the end of a sterile 1μL loop into the urine and remove it vertically making sure that there is no urine up the loop (as this would mean that a greater volume was cultured).
- Spread the entire volume over the surface of both in sheap blood agar and mackonckey agar plate by making a single streak across the centre. Spread the inoculum evenly at right angles to the primary streak. If many samples are being processed use half a plate per sample.
- Incubate the plate aerobically at 35-37°C for at 18-24 hours.
- After inoculation, estimate the number of bacteria by counting the number of colonies on the surface of the media. One colony = 1,000 cfu/mL ($1x10^6$ cfu/L).

Interpretation

- ❖ Colony count and quantity of bacteria in the urine specimen

Colony count	**Number organisms per mL of urine**
<10	$<10^4$ cfu/mL
10-100	$10^4 – 10^5$ cfu/mL
>100	$>10^5$ cfu/Ml

- ➢ If there is a pure growth of 10-100 or over 100 colonies, sub culture the isolate for identification and antimicrobial susceptibility testing.
- ➢ For cultures that contain two organisms, one in low numbers (<100 colonies) and the other over 100 colonies, then only sub-culture the predominant organism because the

organism of lower numbers is unlikely to be causing disease. If both are present at over 100 colonies, sub-culture both organisms.

- If more than two organisms are isolated, then do not sub-culture / identify any of them since this is highly likely to be a contaminated specimen.

Antimicrobial susceptibility testing

In Kirby-Bauer testing, bacteria are placed on a plate of solid growth medium and antibiotics are added by using Muller Hinton agar (MHA) plate. After allowing the bacteria to grow overnight, areas of clear media surrounding the disks indicate that the antibiotic inhibits bacterial growth. The concentration of antibiotic that diffuses into the media decreases with increasing distance from the source. Therefore, the more sensitive the bacteria are to a given antibiotic, the larger the clear bacteria-free zone that forms around the disk containing that antibiotic. The zone sizes are looked up on a standardized chart to give a result of sensitive, resistant, or intermediate

Interpretation

A "susceptible" result indicates that the patient's organism should respond to therapy with that antibiotic using the dosage recommended normally for that type of infection and species.

Conversely, an organism with a MIC or zone size interpreted as "resistant" should not be inhibited by the concentrations of the antibiotic achieved with the dosages normally used with that drug.

An "intermediate" result indicates that a microorganism falls into a range of susceptibility in which the MIC approaches or exceeds the level of antibiotic that can ordinarily be achieved and for which clinical response is likely to be less than with a susceptible strain.

Declaration

I, the undersigned agree to accept responsibility for the scientific ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the research publications office.

I certify that all the information given here are true.

Principal Investigator	Signature	Date
Etabez Duga	_____	_____

This research proposal has been submitted with our approval as academic advisors.

Principal Advisors	Signature	Date
Kassu Desta (MSc, PhD Fellow)	_____	_____
Dessie Abera (MSc, PhD Fellow)	_____	_____