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Antimicrobial Susceptibility Pattern of Bacterial Uropathogens and Associated Factors of Urinary Tract Infection Among Pregnant Women Attending Antenatal Care Clinic of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia

By:

Alemseged Workneh (B. Pharm)

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This is to certify that the thesis prepared by Alemseged Workneh entitled "Antimicrobial Susceptibility Pattern of Bacterial Uropathogens and Associated Factors of Urinary Tract Infection Among Pregnant Women Attending at Antenatal Care Clinic of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia" and Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science in Pharmacology(clinical) complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

Signed by the Examining Committee:

External examiner: Dr Solomon Gebre-Selassie (MD,MSc)

Signature:_____ date:_____

Internal examiner: Dr Prem Kumar(PhD)

Signature:_____ date:_____

Advisor: Professor Teferra Abula (PhD)

Signature:_____ date:_____

Chair person of Department of Pharmacology and Clinical pharmacy, CHS, AA

Abstract

Antimicrobial Susceptibility Pattern of Bacterial Uropathogens and Associated Factors of Urinary Tract Infection Among Pregnant Women Attending Antenatal Care Clinic of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia

Alemseged Workneh

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Urinary tract infections (UTI) are the commonest bacterial infections during pregnancy, leading to significant maternal and prenatal mortality. Moreover, the changing pattern of antimicrobial susceptibility of bacterial uropathogens is another growing problem. Therefore, this study was aimed to determine bacterial uropathogens, their antimicrobial susceptibility pattern and associated risk factors of UTI among pregnant women attending at ANC clinic of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia. Hospital based cross- sectional study was conducted from November, 2017– January, 2018 on 200 conveniently selected pregnant. Data collection involved face to face interview, urine culture, and antimicrobial susceptibility tests. Statistical models such as Bivariate and multivariate logistic regression were used to analyze the data. The overall prevalence of UTI was 15.5%. A total of 31 bacterial uropathogens were isolated. E.*coli* 45.2% was the most isolated Gram negative bacterial pathogen followed by proteus *spp,* 22.6% and K.*pneumoniae*, 16.1%. Most of the isolated bacteria showed high level of sensitivity to amikacin 96.4%, nitrofurantoin, 90.3% and gentamicin, 83.9%. In contrast, resistance of 58.1% to ampicillin, 51.6% to each of augmentin and cotrimoxazole was obtained.

Prior use of indwelling catheter (AOR: 5.348, 95% CI: 0.984, 29.075), and having previous history of UTI (AOR: 5.624, 95% CI: 2.385, 13.261).were statistically associated with the occurrence of UTI among pregnant women. In general, the early identification of bacterial uropathogens and its antimicrobial susceptibility pattern will help in patient betterment and containment of the spread of resistant bacteria in this study area. As result the clinicians need to prescribe Antimicrobial agent after culture result and hospital should establish well equipped bacteriology laboratory for culture and antimicrobial susceptibility tests.

Key Word: UTI, pregnant women, bacterial uropathogens, antimicrobial sensitivity, associated factors of UTI

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Contents

Abbreviation and Acronyms

AIDS: …….. Acquired Immuno Deficiency Syndrome

ANC:……. Antenatal Care Clinic

AOR: ……. Adjusted Odd Ratio

ASB: **…….**Asymptomatic Bacteriuria

AST: **……..** Antimicrobial Susceptibility Test

CFU:…….. Colony Forming Unit

CLED:……Cystine Lactose Electrolyte-Deficient

CLSI:**…….** Clinical Laboratory Standard Institute

COR:……..... Crude Odd Ratio

DM:**……..** Diabetes Mellitus

E.*Coli*:**.....** Escherichia Coli

FDA……...Food and Drug Administration

HFSUH:**…….....**.Hiwot Fana Specialized University Hospital

HIV: **……..**Human Immune Deficiency Viruses

Ml:**.....**. Milliliter

MDR:…….Multiple Drug Resistance

MIC: **.....**.Minimum Inhibitory Concentration

NCCL: **…….....** National Criteria for Clinical Laboratory

SPSS: **…….....**. Statistical Package for Social Sciences

USA: **.....**. United State of America

UTI:……Urinary Tract Infection

WHO: **……**.World Health Organization

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1. Introduction

1.1. Background

Urinary tract infection(UTI) is one of the most common infectious diseases diagnosed in outpatients as well as in hospitalized patients, affecting almost 50% of the population at least once in their lifetime and can lead to significant mortality and health care expenditure (1).This infection is associated with the presence and multiplications of microbial pathogens within one or more parts of the urinary tract system after bacteria overcome the natural defense mechanism of urinary tract.

UTI is the commonest infection in women worldwide. Altered physiological, anatomical, hormonal changes and challenges in personal hygiene during Pregnancy and other factor makes the antenatal mother more prone to the infection of the urinary tract than non-pregnant women (2). It is a major health problem reported among 20% of the pregnant women and a common cause of admission in obstetrical wards (3). If the infection left untreated it leads maternal and fetal complication.

1.1.1. Classification of UTI

UTI described as the existence of bacterial uropathogens and it is usually classified by several methods. However, classification is mostly based on affected anatomical site, as upper UTI (pyelonephritis, infection of the kidney) and lower UTI including cystitis, urethritis, prostatitis, which are infection of bladder, urethra, and prostate gland, respectively (4).

Moreover, it can also be grouped as complicated or uncomplicated. Uncomplicated UTI is a consequence of bacterial infection in a healthy patient with normal physiology and anatomy of urinary tract. It includes the common form of the infection like cystitis and pyelonephritis (5). Such type of infection mostly occur in females of childbearing age (15 to 45 years). However, the case is scattered in male individuals.

Complicated UTI (cUTI) occurs in both men and women at any point of their life time and have ability to produce severe outcomes resulting in death. It is highly intricate and difficult to treat as well. It occurs in a patient with functional or structural abnormalities of the urinary tract as well as in patients at risk for persistent or recurrent infection and treatment failure, including, immune-suppression, diabetes mellitus (DM), hyperadrenocorticism, kidney disease, prostatitis, urinary incontinence, and altered neurogenic function of the bladder (6).

Recurrent urinary tract infection is a common phenomenon that is observed among women who have experienced uncomplicated UTIs and they are classified as re-infection and relapse. Major cases of UTIs are referred to as re-infections and the condition is encountered by the patient after several weeks of antibiotic treatment. While relapse type of UTI is less frequent which occurs due to treatment failure and the patient encounters the condition within two weeks of the previous infection (7). It's usually associated with pyelonephritis which results in renal failures, kidney impediments through kidney stones and anatomical abnormalities in men and women.

The classification of UTIs is also based on the extent of symptoms exhibited by the patients as symptomatic and asymptomatic. The bacterial count is an important parameter signifies the presence of symptomatic and asymptomatic UTI.

1.1.2. Prevalence of UTI in Pregnancy

Urinary tract infection is one of the most frequent and the second most common cause of bacteremia in hospitalized patients, accounting for 35% of nosocomial infection (8). Worldwide, it is estimated that there are 150 million UTIs per annum, with symptomatic UTI occurring in as many as 7 million, of which 100, 000 requires hospitalizations (9).

Although UTI could affect both sexes, the prevalence is much more in women than in men, at a ratio of 8:1, due to their anatomical and physiological reasons (10). Several international studies have shown that UTIs in women are very common; therefore, one in five adult women experience UTI in her life and it is highly common clinically, as well as considered as worldwide patient problem (11).

In female individuals, the closeness of urinary tract with the reproductive organs results to have pivotal relation between them. In the non-pregnant state, the uterus lies just behind and partly over the bladder while in the pregnant state the enlarging uterus affects all the tissues of the urinary tract at various times (12).

According to a survey conducted by Murtaza muzaffer among women attending at ANC clinic of Kenyatta national hospital, Nairobi, UTI was about 4–10 times more common in pregnant than in the non-pregnant women(13). This was due to a change in chemical composition of urine with increase in glucose and amino acids, which facilitate bacterial growth in urine (14).

The highest incidence of UTI occurs in the child bearing age and this has been linked to sexual activity and aging (15). As a result, the incidence of UTI during pregnancy that was reported across a globe was varied.

A study conducted by Faidah *et al.* in Makkah, the study revealed 20% prevalence of UTI (16). Another cross sectional study carried out in Kanchipuram, India by Jayachandran AL *et al.* showed that, 14(11.66%) of study participants developed UTI (17). Moreover**,** other studies performed among pregnants in Niger, Tanzania and Sudan revealed 75%, 15.5% and 14% prevalence of UTI cases, respectively (18 - 20).

In Ethiopia there was varied incidence of UTI among pregnant women of different regions of the country. A study performed by Agersew A *et al.* in University of Gondar Teaching Hospital, Northwest Ethiopia showed that there was 10.4% incidence of UTI among 385 pregnant women (21). While another study done in Bahir Dar, Addis Ababa and Dire Dewa showed that 9.5%, 11.6%, and 14%, respectively. (22 - 24)

UTI may manifest as asymptomatic or symptomatic bacteriuria (SB). The prevalence of symptomatic and asymptomatic bacteriuria among pregnant is very common. The existence of asymptomatic UTI has been previously reported to be 2 % to 13 % in pregnant women (25). While symptomatic UTI cases account 1–18 % during pregnancy (26).

1.1.3. Etiologic Agents of UTI

Urine is generally considered to be sterile and is believed to be germ free. Any source of possible infection occurs through the urethra initiates the incidence of the infection. Organisms causing UTI are arising primarily from the aerobic members of the fecal flora. An overwhelming majority of uncomplicated urinary tract infections (95%) are caused by a single organism. However, infections among hospitalized patients, patients with urinary catheters, or individuals with structural abnormalities of the urinary tract may be polymicrobial.

A study conducted by Wilson & Gaido (27). on diagnosis of urinary tract infections in adult patients, suggested that majority of UTIs were due to Gram-negative pathogens, particularly from the Enterobacteriaceae family including Escherichia *coli*, Proteus *mirabilis*, Klebsiella *pneumoniae*, and Enterobacter *species* .

The relative frequency of those pathogens varies depending upon age, sex, catheterization, and hospitalization (28). The most frequent uropathogens were Gram negative which made up 80.9% of all the isolates.

In Ethiopia a study conducted by Beyene and Tsegaye in Jimma university hospital showed that E.*coli* was the most common isolated bacterial uropathogen in both admitted and outpatients individuals (29).

Organisms such as Enterococcus *faecalis* and highly resistant Gram-negative rods including Pseudomonas *spp*, are comparatively more common among hospitalized patients as well as in patients with complicated UTIs. However, E.*coli* accounts for 75 - 90% of cases; Staphylococcus saprophyticus 5- 15% of cases. particularly in younger women; and enterococci and non–E.*coli* aerobic gram negative rods, like Klebsiella species and Proteus *mirabilis*, account for the remaining 5- 10% in patients with uncomplicated community-acquired UTIs (30).

1.1.4. Pathogenesis and Clinical Presentation

1.1.4.1. Pathogenesis

UTI in females results from bacteria entering the urinary tract from the nearby genital and perineum. The bacteria believed to originate from the fecal flora and the short length of the female urethra as well as its proximity to the perirectal area make colonization of the urethra likely. On the other hand massage of the female urethra and sexual intercourse allow bacteria to reach the bladder (31). Once bacteria have reached the bladder, the organisms quickly multiply and can ascend the ureters to the kidneys. In addition, contraception methods used including the use of spermicides and diaphragms promote urethral colonization (32).

Steps in the pathogenesis of UTI (33).

Step1. Contamination of the periurethral area with an uropathogens from the gut.

Step 2. Colonization of the urethra and migration to the bladder.

Step 3. Colonization and invasion of the bladder, mediated by pili and adhesions

Step 4: Host inflammatory responses, including neutrophil infiltration

Step 5: Bacterial multiplication and immune system subversion

Step 6: Biofilm formation

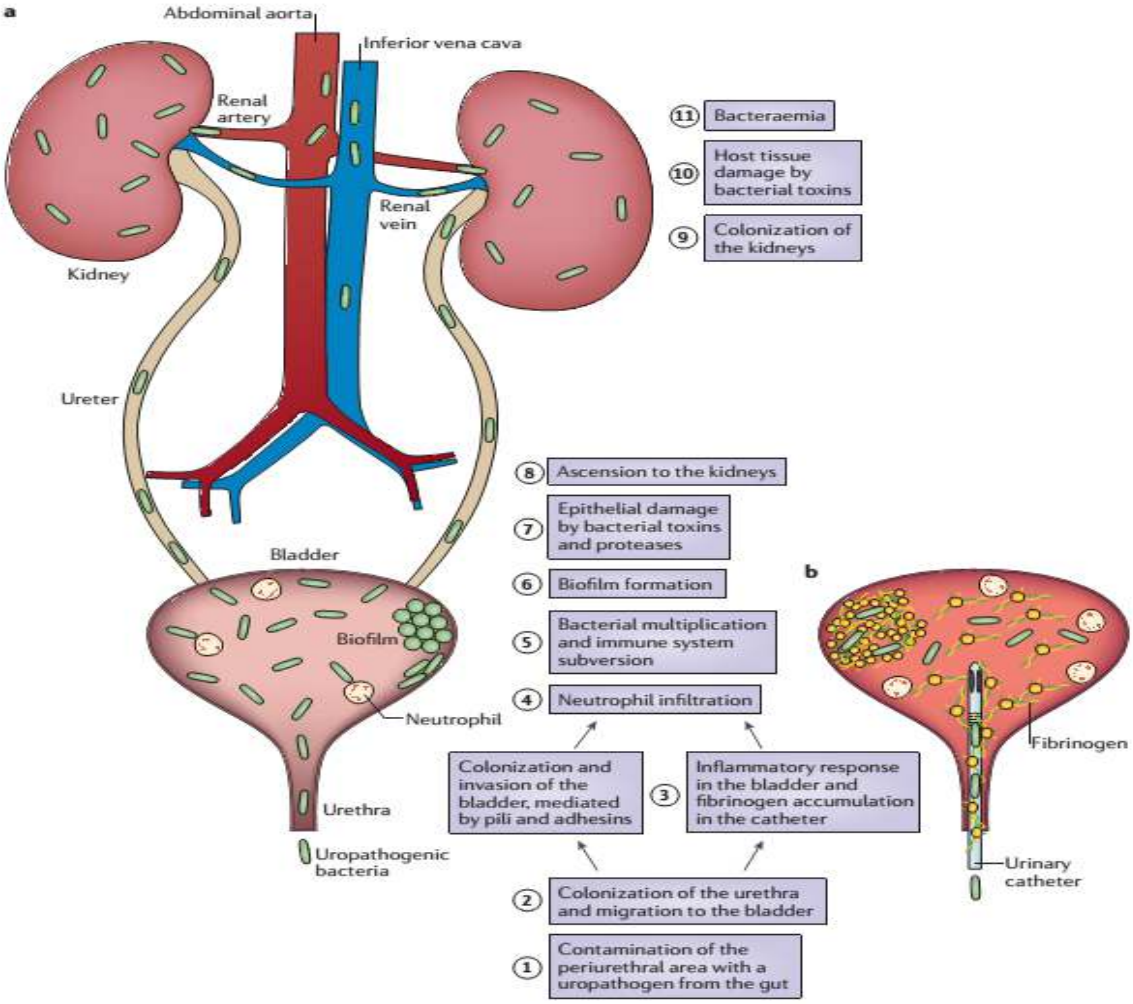
Step 7: Epithelial damage by bacterial toxins and proteases

Step 8: Ascension to the kidneys

Step 9: Colonization of the kidneys

Step 10: Host tissue damage by bacterial toxins

Step 11: Bacteraemia



Fig, 1: Pathogenesis of urinary tract infections (33)

1.1.4.2.Clinical presentation

Several studies showed that clinically, patients with UTI may have two principle presentations; symptomatic and asymptomatic bacteriuria (34).

A study done by Ferry and his colleagues, on clinical and bacteriological effects of therapy of UTI in primary health care, reported that patients with symptoms of UTI could be manifest a number of clinical signs including pain during urination (dysuria), pus in the urine (Pyuria), strong urge to urinate frequently, even immediately after the bladder is emptied, painful burning sensation, discomfort able pressure and bloody urine, which may have a strong smell (35). While, Abdominal pain and fever, back pain, new onset urinary inconsistency as well as dysuria were reported as the most reliable symptoms in older children by Shaikh, Morone and their friends (36).

Arinzon, Shabat *et.al* reported that, the clinical presentation with postmenopausal women were more sensitive than in premenopausal with urinary inconsistence and generalized unspecific symptoms (37). However, another study done by Gilbert and his friends showed that urine culture revealed significant growth of pathogen ($>10^5$ bacteria/ml) in the absence of clinical manifestation (38).

A study conducted by Jean Philippe and his colleagues in France suggested that asymptomatic bacteriuria was very common case during pregnancy (3-8%) with peak incidence between 9-17 weeks of gestation (39). Such condition could be found in pregnant and non- pregnant women however being pregnant enhances the progression from asymptomatic to symptomatic form which could result in pyelonephritis and adverse obstruction.

1.1.5. Risk factors of UTI

The frequency of UTI depends on many associated factors such as the existence of diabetes mellitus, advanced age, frequency of sexual intercourse, multi-parity, family history, use of contraceptives and spermicidal agent, urinary tract Obstruction immune-suppression, and neurological disorders (40). In addition, catheter-associated UTI is the most common nosocomial infection (41).

One of the factors associated with the occurrence of UTI is residence area. A cross sectional study conducted by Derese and his colleagues, among 186 pregnant women at ANC Clinic of Dil Chora Referral Hospital, Dire Dawa, Eastern Ethiopia, reported that 92.3% of UTI were exhibited from urban dwellers. The study also showed that 50% of the infection occurred among study subjects with lower family monthly income, 501-1000 birr (24).

A cross sectional study carried out by Wanyoike Gichuhi and his friends,(2015) on prevalence of urinary tract infection, microbial etiology, and antibiotic sensitivity pattern among 150 antenatal women presenting with lower abdominal pains at Kenyatta National Hospital, Nairobi, Kenya revealed that highest incidence of the UTI,62.5% and 82.5% among age group of 25-34 and married pregnant, respectively. This study also reported that 65.0% prevalence among Multi gravid individuals as well as 87.5% and 82.5% rate of UTI among those who had previous history of UTI and obstetric surgery, respectively (42).

Urinary Tract Infection (UTI) is more common in diabetics because of a combination of host and local risk factors. A number of demonstrative research studies have shown that the contribution of diabetes for the occurrence of UTI (43).

Modification of chemical composition of urine in DM patients can alter the ability of urine and support the growth of microorganism. Ramana and Chaudhury in south India, they found that autonomic neuropathy in diabetes mellitus impairs bladder emptying and subsequent urological manipulations predispose to UTI (44).

A study done in Ethiopia by Yeshitela et.al in Tikur Anbessa Specialized University Hospital showed that the rates of symptomatic and asymptomatic bacteriuria among diabetic patients were 13.6% and 10.4%, respectively (45).

Another risk factor for UTI is pregnancy. This usually begins in week 6 and peaks during weeks 22 to 24 of pregnancy due to a number of factors including urethral dilatation, increased bladder volume and decreased bladder tone, along with decreased urethral tone which contributes to increased urinary stasis and ureterovesical reflux and up to 70 % of pregnant women develop glycosuria, which encourages bacterial growth in the urine (46).

Previous history of UTI has increased risk of having a UTI during pregnancy and other risk factors for UTIs during gestation period include lower socio economic status, individual hygiene, sickle cell trait and anemia, increased parity or age, and lack of prenatal care. The functional urinary tract abnormalities and diabetes mellitus can also increase susceptibility to UTIs during pregnancy (47).

The use of an indwelling catheter frequently is associated with infection of the urinary tract and represents the most common cause of hospital acquired infection. The incidence of catheter-associated infection is related to a variety of factors, including method and duration of catheterization, the catheter system (open or closed), the care of the system, the susceptibility of the patient, and the technique of the healthcare personnel inserting the catheter. The incidence of infection from a single catheterization in a healthy ambulatory patient is 1% (48).

Patients with indwelling catheters acquire UTIs at a rate of 5% per/day (49). However, after 30 days of catheterization, there is a 78% to 95% incidence of bacteriuria despite use of a closed system (50). Therefore proper insertion and use of catheter is required

1.1.6. Diagnosis of UTI

Diagnosis of UTI mostly requires laboratory examination of the collected urine sample in addition to clinical evaluation. The gold standard for the diagnosis of a urinary tract infection is the detection of the pathogens in the presence of clinical symptoms.

The pathogen is detected and identified through urine culture (from clean catch midstream urine); it also allows estimating the level of bacteria in the urine sample. However, many guidelines indicate that the culture of urine is not required in most cases of uncomplicated cystitis (51).

The clinical diagnosis of UTI is primarily based on the medical history. Specific data may either increase or decrease the probability of an infection. According to many clinical studies a number of manifestations including, dysuria, urinary incontinence, macrohematuria, suprapubic pain, offensive' smell and turbid urine as well as others clinical sign and symptoms have been associated with infection of urinary tract (52).

1.1.7. Treatment of UTI

Treatment of UTI is often started empirically and therapy is based on information determined from the antibiotic resistance pattern of the urinary pathogens (53). A study conducted by Bonadio et.al showed that the occurrence of antimicrobial resistance among urinary pathogens has been increasing worldwide due to inappropriate use of Antibiotics in clinical practice (54).

The emergence of antibiotic resistance of UTIs is a serious public health issue, particularly in the developing world where apart from high level of poverty, ignorance, and poor hygienic practices, there is also a high prevalence of fake and spurious drugs of questionable quality in circulation (55). This, make empiric antibiotic selection very difficult, particularly when previous antibiotic therapy has been administered to the patient (56).

Distribution of urinary pathogens and their susceptibility to antibiotics varies regionally so it becomes necessary to have knowledge of distribution of these pathogens and their susceptibility to antibiotics in a particular setting (57). The estimation of local etiology and susceptibility profile could support the most effective empirical treatment (58). E. *col*i is the most commonly isolated uropathogens (59). Both E.*coli* and K.*pneumoniae* as well as other uropathogens, are capable of producing extended-spectrum β-lactamases (ESBL) which result in resistance to many antibiotics that are typically used in the treatment of UTIs (60).

Carbapenems are considered the most reliable treatment for infections caused by ESBL-producing bacteria (61). Despite their utility, resistance has emerged, placing a focus on finding alternative antibiotics for UTIs so that carbapenems can be reserved for more serious infections (62). Antimicrobials that may prove useful for this purpose include nitrofurantoin, fosfomycin, amikacin, cefepime, and piperacillin/tazobactam.

Unlike non pregnant women with ASB, in whom intervention is not recommended, pregnant patients with ASB will go on to develop pyelonephritis if left untreated. Treatment of ASB can be accomplished with a variety of FDA category B drugs that has a relatively low adverse-effect potential and is safe for the mother and baby. The administration of sulfonamide, amoxicillin, amoxicillin-clavulanate, cephalexin, or nitrofurantoin is effective in 70% to 80% of patients. A seven day course for amoxicillin or cephalexin, five day course for nitrofurantoin, or one time dose for fosfomycin is recommended, with follow-up urine cultures to document sterile urine. Persistent bacteriuria requires re-treatment guided by sensitivities and then consideration of suppressive therapy, usually with nitrofurantoin (63). Tetracycline should be avoided because of teratogenic effects, and sulfonamides should not be administered during the third trimester because of the possible development of kernicterus and hyperbilirubinemia. In addition, the available fluoroquinolones (FDA Category C) should not be given because of their potential to inhibit cartilage and bone development in the newborn. A follow up urine culture 1 to 2 weeks after completing therapy and then monthly until gestation is complete is recommended.

1.1.8. Antimicrobial susceptibility pattern of bacterial uropathogens

According to WHO (2015) report, antimicrobial resistance is greatest challenges to global public health today, it has been detected in all parts of the world and the problem is increasing. Although the development of antimicrobial resistance is a natural phenomenon, its development and spread are being accelerated by misuse of antimicrobial medicines, inadequate or non-existent programs for infection prevention and control, poor-quality medicines, weak laboratory capacity, inadequate surveillance and insufficient regulation of the use of antimicrobial medicines (64).

According to the finding documented in a study conducted by Jayachandran AL and his friends in Kanchipuram, India showed that E.*coli* had sensitivity of 20% to ampicilline, 40% to each of amikacin, ciprofloxacin, nitrofurantoin and 60% to ceftazidime. However, 100% sensitivity was observed to cotrimoxazole. And 100% sensitivity was reported to Klebsiella *spp* among patients taking cotrimoxazole and amikacin.

Among isolated Gram positive microorganism, S.aureus showed that 100% sensitivity to each of ceftazidime, cotrimoxazole and nitrofurantoin and 75% sensitivity to ampicillin and amikacin (17).

Another cross sectional study done by Faidah *et.al* in Makkah, Saudi Arabia exhibited that 15.8%, 10.5% and 5.3%, resistance of isolated bacterial uropathogens to ceftriaxone, augmentin and amikacin occurred respectively. Those pathogens showed sensitivity of 97.4%, 84.2% and 73.7% to norfloxacin, gentamicine and cotrimoxazole respectively (16).

In our country, most bacterial uropathogens showed various degrees of sensitivity and resistance to some commonly prescribed antimicrobials. A cross sectional study conducted by Derese and his friends among pregnant women attending at ANC clinic of Dil Chora Referral Hospital, Dire Dawa, Ethiopia, revealed that isolated Gram negative pathogens had highest rate of resistance, 89.5% and 73.7% to ampicillin and amoxicillin respectively. Whereas the isolated Gram positive organisms showed that 100% sensitivity to gentamicine (24).

Another study conducted by Getachew Ferede among 200 pregnants attending the ANC clinic of Gondar University Hospital showed that 91.7% and 79.2% resistance of isolated pathogen to ampicillin and amoxicillin, respectively.

Of these isolated pathogens E.*coli* was 100% resistance to aforementioned drugs. While the lower percentage of resistance 12.5% were reported among patients taking to each of ceftriaxone and gentamicine. And the overall multidrug resistance (MDR) reported in this study was 91.7% (65).

1.2. Statement of the problem

Urinary tract infection is one of the most common infectious diseases diagnosed in outpatients as well as in hospitalized patients, affecting almost 50% of the population at least once in their lifetime and can lead to significant mortality and health care expenditure (1). It's the most commonly encountered infectious diseases in developing countries.

Even though the infection affects all age groups and both sexes, the prevalence is higher in females. UTIs is the commonest infection encountered among women in which, one in five adult women experience the disease in her life time and it is highly common clinically, as well as considered as worldwide patient problem (11). The incidence of the infection among HIV/AIDS individual was higher 18% on the study area excluding pregnant women (66). The prevalence of the infection is higher among pregnant than non-pregnant women and it's a major health problem reported among 20% of the pregnant women and a common cause of admission in obstetrical wards (67). If the infection is left untreated, it results in low birth weight fetus, intrauterine growth retardation, preterm labor and premature babies, intrauterine fetal death, and increased prenatal mortality and morbidity as well as maternal complications including anemia, preeclampsia, renal failure, septicemia, and adult respiratory syndrome (68). The incidence varies from place to place. In the developed world like United States of America (USA) and Europe, it is declining because of awareness on the risk factor and prevention strategies with high socioeconomic status; but in developing countries, it is on the rise due to malnutrition, low socioeconomic status as well as inappropriate use of antibiotics.

Antibiotics are widely prescribed in the hospital setting on emperical basis. Rates of antimicrobial resistance among hospital and community pathogens have increased considerably during the past decade (69).

This could result, increased human illness, suffering, side effects from the use of multiple and more powerful medication as well as resulting in a greater economic and emotional burden on the families and health care system.

Due to the limited microbiology laboratory setup, routine culture and antibiotic susceptibility testing are not performed and the treatment is on empirical basis. Physicians in the study area prescribe different drugs without the guidance of culture and antibiotic susceptibility tests to treat patients with presumptive diagnosis of UTI which could lead to the overuse of antibiotics and development of resistant microbial species.

Thus up-to-date information on microbial resistance needs to be available at national and local level to guide the rational use of the existing antimicrobials. Therefore, this study will be carried out to determine most encountered uropathogens of UTI, risk factor and their antimicrobial susceptibility profiles among pregnant women attending at Antenatal care of Hiwot Fana specialized University Hospital, Harar, Eastern Ethiopia.

1.3. Significance of the study

UTI is a common public health problem among pregnant and an important cause of fetal complication in developing countries. The disease is associated with low birth weight fetus, intrauterine growth retardation, preterm labor and premature babies, intrauterine fetal death, and increased prenatal mortality and morbidity as well as maternal complications including anemia, preeclampsia, renal failure, septicemia, and adult respiratory syndrome (67).

Many studies have been conducted on bacterial etiologic agents of urinary tract infections; risk factor and susceptible pattern of UTI showed different results from region to region the difference might be due to climate, patient population, Collection and processing techniques of specimens as well as prior use of antibiotics. Moreover, indiscriminate use of antibacterial agents has been associated with the change in bacteriological resistant pattern and emergence of multiple drug-resistant strains. Information regarding the common pathogens responsible for UTI and the susceptible pattern is essential in the selection of the most appropriate treatment regimen and can minimize disease and pregnancy complications. Therefore, evaluation of bacteriological pattern, risk factor and their antibiotic sensitivity in local area become helpful in the prevention of diseases, to recommend prescribing antibiotics for successful treatment of UTI and thus minimizing its complications and emergence of resistant strains.

However, in Ethiopia, particularly in the Harar area, there is a scarcity of recent data that indicate the magnitude of the problem among pregnant women. Thus this study was designed to identify bacterial isolates, risk factor and to determine their drug susceptibility patterns from pregnant attending at ANC clinic of HFSUH. This knowledge is very important for the clinicians for appropriate management of the cases and to prevent or minimize the occurrence of complications. Study participant who were returned back for their result during the study period were communicated about their result and got appropriate antibiotics treatment of the cases after the result, it will also contribute in preventing the emergence of resistant strains in the community.

Furthermore, the overall antimicrobial susceptibility profile of isolates would be compiled and provided to the physician and nurses who would use it as a local guideline for selection of effective antibiotics and contribute for national guidelines development on the treatment option for UTI. Giving such information would also serve as baseline data for future studies.

2. Objectives

2.1. General objective

- To determine the bacterial profile, antimicrobial susceptibility pattern and associated factors of UTI among pregnant women attending at ANC clinic of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia from November,2017 – January,2018

2.2. Specific Objectives

- To determine the bacterial profile of urine isolate among pregnant women.
- To determine the antimicrobial susceptibility pattern of bacterial uropathogens among pregnant women.
- To identify risk factors associated with UTI

3. METHODS AND MATERIALS

3.1. Study Area

The present study was undertaken at Antenatal care Clinics of Hiwot Fana Specialized University Hospital. It is found in the Harari Regional State, Harar, Eastern Ethiopia. The region is found at 525 km from Addis Ababa. It is divided into nine districts with three of them are rural and six are urban. The urban districts are subdivided into nineteen kebeles, and the rural districts into seventeen peasant associations (which is equivalent to kebele in urban case). The region has a total population of 250,903 of these urban population comprises of 146,913 and women with reproductive age (15-49 years) accounts 65,486 with expected pregnancy of 7,753 . There are six hospitals (4 governmental and 2 private) and eight public health centers in the region.

Currently, the hospital is affiliated with Haramaya University College of Medicine and Health sciences. It's the training center for postgraduate and undergraduate health professionals and serves as a referral hospital for the entire eastern part of the Ethiopia.

Figure 2: Location of the study area (Source: Culture, Tourism and Social Affair of Harare Regional State Bureau, 2017).

3.2. Study design and Period

Hospital based cross sectional study design was used from November, 2017 to January, 2018.

3.3. Source and Study population

3.3.1. Source Population

All pregnant women attending antenatal care clinic of HFSUH during the study period.

3.3.2. Study population

All pregnant women attending antenatal clinic of HFSUH and met the eligibility criteria, within the study period were consecutively recruited in the study.

3.4. Eligibility criteria

3.4.1. Inclusion Criteria

- Being pregnant and have follow up in ANC clinic of HFSUH.
- Willingness to participate in the study after informed verbal and written consent.

3.4.2. Exclusion criteria

- Who received antibiotics within 15 days before ANC follow up.
- Who were treated for another infection

3.5). Sample size Determination and Sampling technique

A single population formula was used to calculate the sample size using the following parameter, 14% incidence rate of UTI among pregnant women attending at antenatal clinic of Dil Chora referral Hospital, Dire Dewa Ethiopia (24). Tolerable or margin of error (d) = 5%, Z score for 95% confidence interval, with 10% non-response rate

$$n = \frac{z2\ p\ (1-p)}{d2}$$

Where: z = Z score for 95% confidence interval = 1.96,

P= prevalence,

d = margin of error (5%).

$$n = \frac{z2\ p\ (1-p)}{d2} = = \frac{1.962*0.14\ (1-0.14)}{0.05*0.05} = 185$$

Non-response rate = 185 * 10% = 18.5 ~ 19

Total sample size was = 185 + 19 = **204**

All pregnant women attending antenatal clinics of HFSUH and that fulfilled the inclusion criteria until the required sample size attained were selected using convenient sampling technique.

3.6. Variables of the study

3.6.1, Dependent variables

- ✓ Significant Bacteriuria
- ✓ Antimicrobial susceptibility patterns

3.6.2. Independent variables

- Socio- demographic characteristics of the patients: Age, residency, marital Educational status, occupation
- Diabetes mellitus
- Catheterization
- History of UTI
- History of obstetric and Gynecologic surgery

3.7. Data collection Method and Laboratory investigation

3.7.1. Data collection procedure

A structured questionnaire designed for the collection of Clinical/ socio-demographic data. It demonstrate identification number of the patient, age, pregnancy (gestational age) and marital status, urinary signs and symptom, predisposing factor, and other related information. Culture and sensitivity results were also endorsed on the questioner. Four trained data collectors (nurses) were collect the data.

3.7.2. Laboratory investigation

3.7.2.1. Sample collection and transportation

In this study a total of 204 pregnant women were recruited and urine specimen collected from each participant within a period of November, 2017 to January, 2018. Of these four samples were excluded (1contaminated and 3 not refrigerated properly), while the rest were processed for culture and those positive culture test result further processed for antimicrobial susceptibility test.

From all study participants, ~10–20 mL of urine specimen was collected. All the specimens that were from pregnant women who had antenatal care, irrespective of age were included. The urine specimens were excluded from the study, when the specimen was stored out of refrigerator, contaminated as well as when the safe transport could not be ascertained.

Clean catch mid-stream urine specimen were collected by the pregnant women after explaining the technique of urine sample collection, which was through the following process:

- Thorough wash hands with water then dry.
- Labial separation with one hand.
- Clean with water Area around the urinary opening in back ward direction then dry thoroughly.
- With separating the labia void the first 20 to 30 ml in the toilet and then collect a sample of the remaining urine into a sterile universal utensil.
- Close the cap of urine bottle immediately considering not to touch either the edge of the bottle or inner side of the bottle cap

The bottle were labeled with unique client's ID number, date and collection time after that the collected samples processed microscopically and stored in refrigerator of central medical laboratory of HFSUH then send to the Department of Microbiology at Harari Health Regional Research and Regional Laboratory, Harar, Ethiopia, which is around 150 meter away from the study area, within two hour of collection. All urine samples were turned up and down gently to allow proper mixing of urine. Urine examinations were performed at laboratories that follow the standard procedures for culture. If there was any delay the specimens were refrigerated or voided

3.7.2.2. Sample Processing: Bacterial isolation and identification

This included macroscopic, and biochemical testing. Ones the urine samples were delivered to the laboratory immediately following collection they were screened for the presence of bacterial agents according to the standard procedures for the diagnosis of bacterial UTI.

The well mixed as well as non-centrifuged specimens were inoculated onto Cystine Lactose Electrolyte-Deficient (CLED) and MacConkey agar(with and without crystal violet, Titan, Biotech LTD, India) through a surface streak procedure using a standard wire loop. CLED was used because it gives consistent results and allows the growth of both gram negative and gram positive bacterial pathogens.

The plates were put in incubator at 37°C overnight(18-24hr) under completely aerobic conditions and those cultures that became negative at the end of 24 hrs incubations were further incubated for 48 hours. After 24 hours of incubation, the culture plates were examined macroscopically to evaluate the colony appearance, and size of the colonies. Then, the confirmed colonies was counted from CLED and multiplied by 1000 to determine the number of bacteria per ml (CFU/ml) of the Original urine specimen. Plates with pure growth, and colonies $\geq 10^5$ CFU/ml were further subjected for identification and sensitivity testing.

Cut off point of $\geq 10^5$CFU / ml was used to define UTI. The bacterial isolates were identified using standard biochemical tests. Gram-negative bacteria were identified by performing a series of biochemical tests, namely oxidase, indole, Simmons citrate agar(citrate utilization), lysine decarboxylation, lactose fermentation, gas and H_2S production as well as motility tests. Gram-positive bacteria were also identified based on their catalase test and coagulase tests. Then Antimicrobial susceptibility of isolated pathogens was tested to ensure that appropriate and adequate antibiotic provided.

Simmons Citrate

Klingor Iron Agar (KIA)

Sulphide Indole Motility (SIM)

Muller Hinton Agar

MacConkey

Fig 3: Samples of Prepared Media

3.7.2.3 Antimicrobial Susceptibility testing (AST)

Antibiotic susceptibility testing was done by using Kirby Bauer (disk diffusion) method on Muller Hinton agar. The suspension of bacterium was prepared by picking pure colony with a sterile wire loop, suspended and emulsified into a test tube containing 5 ml of nutrient saline then mixed gently until uniform suspension was formed. Standard inoculums were adjusted to 0.5 McFarland.

Using a sterile loop, sample of the standardized inoculums was taken and streaked on the entire surface of the dried Mueller–Hinton agar plate(Biomark, Laboratory , India), turning the plate at 60° angle between each streaking to ensure even distribution.

The following antimicrobial agents were used for susceptibility testing: augmentin, (AMC, 30µg), ampicillin (AMP,10µg), chloramphenicol (C,30µg), ciprofloxacin (CIP,5µg), norfloxaacine (NOR,10µg), trimethoprim+sulphamethazole (SXT,25µg,1.25/23.75µg), amikacin(AK,10µg), gentamicin (GEN,10µg), ceftriaxone (CRO,30µg), ceftazidine (CAZ,30µg), nalidixic acid (NA, 30µg), and nitrofurantoin (F, 300µg), were applied on the plates using forceps, and properly spaced to prevent any overlap. All the antimicrobials used for the study were Oxoid Ltd. Bashing store Hampaire, UK products.

The discs were placed at least 24 mm away from each other and 15 mm from the edge to avoid the overlapping of the zone of inhibition and pressed down to ensure complete contact with the agar surface. The plates were inverted upside down and incubated aerobically at 37 °C for 18 to 24 hours. The diameter of the zone of inhibition around each disc was measured to the nearest whole mm by using a digital caliper.

Then, the bacterial isolates were classified as sensitive (S), intermediate (I) or resistance (R) by comparing against the inhibition zone diameter of interpretative standards as indicated in the Clinical and Laboratory Standards Institute (CLSI) guideline.

Bacterial isolates resistant to three or more antimicrobials belong to different structural classes was classified as MDR (70). The reference strains used as control were E.*coli* (ATCC 25922), S. aureus (ATCC25923) and P. aeruginosa (ATTC 27853).

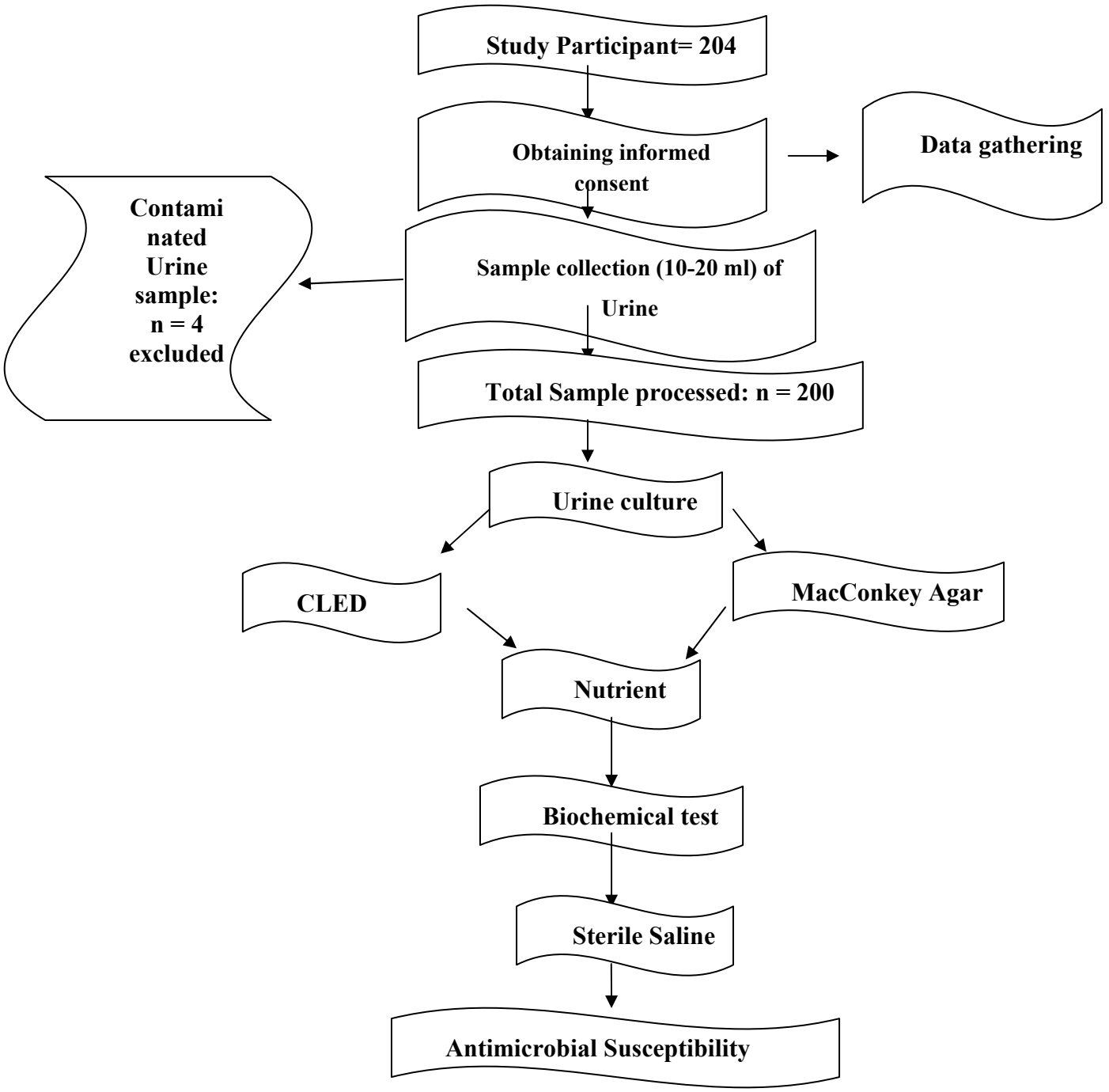


Fig 4: Data Collection and Sample processing Flow Chart

3.8. Data quality control

Prior to data collection the data collectors were trained for half a day by the researcher on how to go for data collection. Supervision was made by researcher.

Before the actual data was collected, pretest was done on 5% of sample size from where data is not collected to check the consistency and reliability. These helps familiarize data collectors to the instrument and to make necessary correction as necessary.

Some of the questionnaires were modified based on the result of pretest. Proper instruction was given for the participant before the survey as to the importance of the study and the data were collected under close supervision. The data quality controlled before collection through pre-testing; during and after collection through direct observation .The questionnaires were reviewed for completeness, accuracy, and consistency by supervisors and by principal investigator.

Prior to the actual work, training was given for the data collectors on an interview and urine sample collection instruction for half day, practical refreshment training for medical laboratory health professionals on urine culture, how to clean, sterilize and reusable laboratory materials for laboratory attendants by the investigator.

Participants were oriented on how to collect self-midstream urine samples by trained data collectors. The specimens were stored in the refrigerator of HFSUH central medical laboratory with controlled temperature and transported to the Hrari Health research center and regional Laboratory within 2-4 hr of collection in ice box and immediately processed under supervision of Medical Microbiologist. The culture media's were checked daily to observe if crack, contamination and decolarization formed during culture process.

3.9. Data processing and Analysis

The Collected data were checked for completeness, coded, entered and cleaned using Epi-Data version 3.1 and was exported and analyzed using SPSS version 20 software. Descriptive statistics such as frequency, percentage and cross tabulation were used to present the findings in the form of graph and table.

To measure association between dependent and independent variables, crude odd ratio (COR) and adjusted odd ratio (AOR) with 95% confidence interval (CI) was calculated.
All independent variables with a p- value less than or equal to 0.25 in the bivariate analysis were included in the multivariate logistic regression model to identify variables which were associated independently. P-value < 0.05 was considered statistically significant

3.10. Ethical considerations

Before starting the study the proposal was reviewed and approved by Ethical review board of AAU college of Health Sciences, School of Pharmacy and communicated to the Hiwot Fana Specialized University Hospital and the Harari Health Research center and Regional Laboratory to obtain permission and facilitation of the study by a formal letter from AAU college of health sciences, school of pharmacy .

Participation in this study was entirely voluntary. Written informed consent from participants was taken only if they agree to participate in the study. Information such as sample collection procedure, potential risk and benefit of the study was explained to the study participants during the data collection. There was no any direct payment for participating in this study and those participants who have tested positive for a UTI, their culture as well as antibiotic susceptibility test result were given to participants who came to the research center to take their result for appropriate treatment and management.
Any information obtained from the participants was kept confidential and the specimens collected from them were used only for an intended study purpose. No reference was made in oral or written reports that could link participants in the study.
All processed samples, antimicrobial disks, culture media and non-reusable laboratory materials were disinfected, sterilized and disposed in an environmental friendly manner.

3.11. Operational Definition

Urinary tract infection (UTI) /**significant bacteriuria**: A culture that grew $\geq 10^5$colony-forming unit (CFU/mL) in single voided midstream urine

Symptomatic UTI: referred to patients whose urine is yielding positive cultures ($\geq 10^5$CFU/ml) and who have symptoms referable to the urinary tract.

Asymptomatic bacteriuria: significant growth of pathogen ($\geq 10^5$ bacteria/ml) in the absence of clinical manifestation (38).

Mid-stream urine specimen: - a specimen obtained from the middle part of urine flow: Clean catch urine specimen.

Multiple Drug Resistance: is operationally defined as non-susceptibility to at least one agent in three or more antimicrobial categories.

History of UTI: is any history of infection pertaining to the urinary tract diagnosed by a physician.

Previous antibiotic use: patients who had received antibiotic therapy before 15 days of the 1st ANC follow up of study period.

4. Results

4.1. Socio-demographic, obstetrics and clinical characteristics of study participant

The study participants were within the age ranges of 18–44 years with the mean age of 26.36 years, in which the majority lie within the age group of 23-27 years. More than 89% of the study subjects lived in urban area. Moreover, 61(30.5%) had educational level of secondary cycle (9-12grade), 185 (92.5 %) married and 61(30.5%) were worked as employee.

Their obstetric data showed that 79% had gravidity of 1-3 times. Among study participants, 27% had previous history of UTI, 6.5% undergone obstetric and gynecologic surgery and 4% reported prior use of indwelling catheter (table 1).

Table 1: Sociodemographic, obstetric and clinical variables of pregnant women attending at ANC clinic of HFSUH, Harar, Eastern Ethiopia, from November, 2017- January 2018.

Patient characteristics	Total Participant (n=200)	
	Frequency (n)	Percentage (%)
Age (in year)		
18-22	52	26
23- 27	72	36
28-32	48	24
33-37	15	7.5
38-42	12	6
≥43	3	0.5
Residence		
Rural	22	11
Urban	178	89
Educational Status		
Illiterate	28	14
Read & write	33	16.5
Primary cycle(1-8)	46	23
Secondary cycle(9-12)	61	30.5
Higher education(> 12)	32	16
Marital Status		
Married	185	92.5
Divorced	10	5.0
Widowed	5	2.5
Gravidity		
1 – 3	158	79.0
4 – 6	32	16.0
7 – 9	10	5.0
Parity		
Nullipara	85	42.5
Primipara(one)	50	25.0
Multipara	65	32.5
Gestational age		
1st trimester	34	17
2nd trimester	92	46
3rd trimester	74	37
History of obstetric and Gynecologic surgery		
Yes	13	6.5
No	187	93.5
History of catheterization		
Yes	8	4
No	192	96

Table 1 continued

History of UTI		
Yes	54	27
No	146	73
Current symptom of UTI		
Symptomatic	62	31
Asymptomatic	138	69
Diabetes Mellitus		
Yes	8	4
No	192	96

Abbreviation: DM, Diabetes mellitus, HFSUH, Hiwot Fana Specialized University Hospital, UTI, Urinary tract infection,

4.2. Prevalence of UTI vs. Socio-demographic, Obstetric and Clinical variables of pregnant women

Among 200 urine samples investigated, 31 of them grow bacteria in culture with significant bacterial growth were given with overall prevalence of 15.5%.

The distributions of the infection on the basis of age revealed the higher rate, 45.2% followed by 32.5% was observed within the age group of 23-27 years and 28-32 years respectively. Whereas lower rate of UTI recorded among the age category of ≥ 43 and 33- 37 years with rate of 3.2 % and 0% consecutively. The prevalence rate for the groups was found to be varied one with the other (P> 0.05).

Among the study participants with significant bacteriuria, 27/31(87%) live in urban area. Those study subjects, who had history of catheterization, prior Obstetric and Gynecologic surgery, and previous history of UTI showed that, 4/8(50%), 5/13(38.5%), and 19/54(35.2%) prevalence of UTI respectively. Out of the 200 midstream urine samples processed, 13/62(20.9%) and 18/138(13%) had shown significant bacteriuria among symptomatic and asymptomatic participants respectively. The overall prevalence of UTI vs. different study variable depicted in table 2.

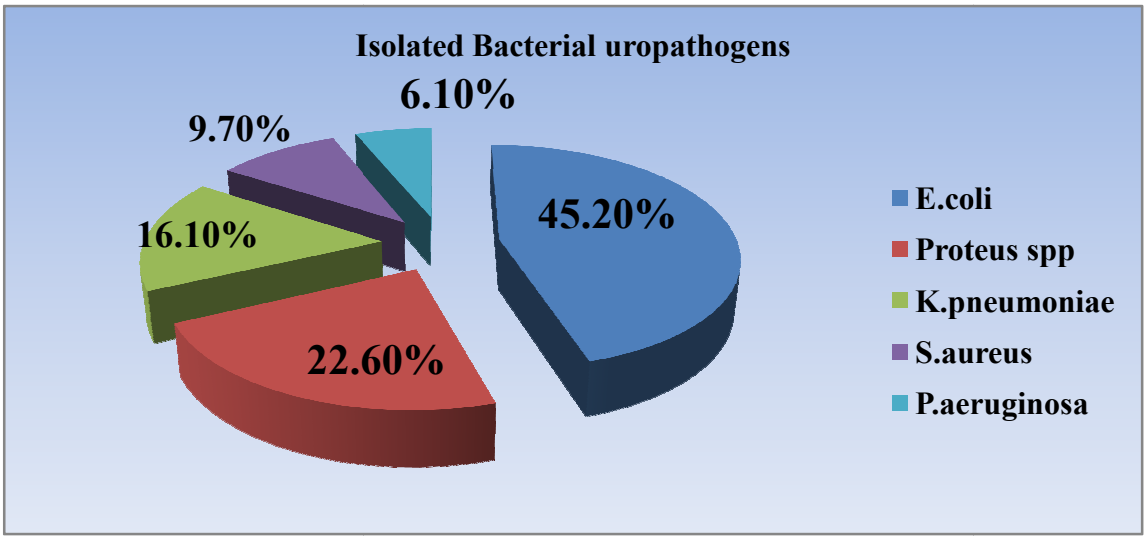
Table 2: Prevalence of UTI vs. Sociodemographic, Obstetric and Clinical variables of pregnant women attending ANC clinic of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia, from November 2017- January 2018.

Variables	Bacteriuria		
	Significant Bacteriuria, n (%)	No-Significant Bacteriuria, n (%)	Total (n)
Age (in year)			
18-22	4(12.9)	48(28.4	52
23- 27	14(45.2	58(34.3	72
28-32	10(32.3	38(22.5	48
33-37	2(6.4)	13(7.7)	15
38 - 42	0(0)	12(7.1)	12
≥ 43	1(3.2)	0(0)	1
Total	31	169	200
Residence			
Rural	4(13)	18(10.7)	178
Urban	27(87)	151(89.3)	22
Educational Status			
Illiterate	5(16)	23(13.6)	28
Read & write	10(32.2)	23(13.6)	33
Primary cycle(1-8)	7(22.6)	39(23)	46
Secondary cycle(9-12)	7(22.6)	54(31.9)	61
Higher education(> 12)	2(6.6)	30(17.6)	32
Marital Status			
Married	30(96.8)	155(91.7)	185
Divorced	1(3.2)	9(5.3)	10
Widowed	0(0)	5(3)	5
Gravidity			
1 – 3	30(96.8)	128(75. 7	158
4 – 6	1(3.2)	31(18.3)	32
7 – 9	0(0)	10(6)	10
Parity			
Nullipara	12(38.7)	73(43.2)	85
Primipara(one)	11(35.5)	39(23.1)	50
Multipara	8(25.8)	57(33.7)	65
Gestational age			
1st trimester	5(16.1)	29(17.2)	34
2nd trimester	16(51.6	76(44.9)	92
3rd trimester	10(32.3)	64(37.9)	74

Table 2. Continued	Bacteriuria		
Variables	**Significant Bacteriuria,n(%)**	**No-Significant Bacteriuria, n(%)**	**Total (n)**
History of obstetric & Gynecologic surgery			
Yes	5(16.1)	8(4.7)	13
No	26(83.9)	161(95.3)	187
History of catheterization			
Yes	4(12.9)	4(2.4)	8
No	27(87.1)	165(97.6)	192
History of UTI			
Yes	19(61.3)	35(20.7)	54
No	12(38.7	134(79.3)	146
Current symptom of UTI			
Symptomatic	13(41.9	49(29)	62
Asymptomatic	18(58.1)	120(71)	138
Diabetes Mellitus			
No	28(90.3)	164(97)	192
Yes	3(9.7)	5(3)	8

4.3. Isolated Bacterial uropathogens

In the current study, out of the total mid stream urine sample culture test, a total of (n=31) bacteria were isolated, with five different species; of this majority of them were Gram negative organisms 28(90.3%) than Gram positive 3(9.7%). E.*coli* was the most commonly isolated bacteria 14(45.2%) followed by Proteus *spp* 7(22.6%), k.*pneumoniae* 5(16.1%), S.*aureus* 3(9.7%), and P.*aeruginosa* 2(6.4%).



Abbreviations: E.*coli*, Escherichia coli; P.*aeruginosa*, Pseudomonas *aeruginosa*; S.*aureus*: Staphylococcus *aureus*, k.*pneumoniae*: Klebsiella *pneumoniae*

Figure 5: Isolated bacterial uropathogens among pregnant women with UTI attending at Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia, from November 2017- January, 2018.

4.4. Antimicrobial susceptibility pattern of isolated bacterial uropathogens

4.4.1. Gram negative isolates

According to current finding, Gram negative bacterial uropathogens were sensitive to amikacin (96.4%), nitrofurantoin (89.3%), gentamicin (82.2%), chloramphenicol 71.5% and Highest rate of resistance were also observed to ampicilline (60.7%), augmentin (53.6%), cotrimoxazole (50%) and nalixidic acid (46.4%).

With regard to specific isolated Gram negative bacteria , Escherichia coli were highly sensitive to amikacin (100%), gentamcin (92.3%), nitrofurantoin (85.7%) and 71.4% to each of ceftriaxone, ceftazidine, chloramphenicol, norfloxacine, and ciprofloxacin, while high resistance rate observed to ampicillin 50%, 42.9% to each of augmentin and cotrimoxazole,
Proteus *spp* showed that highest sensitivity of 100% to amikacine and nitrofurantoin, while 71.4% to gentamicine as well as 57.1% to each of norfloxacillin, ciprofloxacin, and chloramphenicol. However, 71.4% resistance observed to each of cotrimoxazole and nalixidic acid as well as 57.1% to each of augmentin, ampicilline and ceftazidime.
Antimicrobial sensitivity of K.*pneumonia*e exhibited that there were highest rate of sensitivity 100% to each of amikacine, chloramphenicol and nitrofurantoin, However highest rate of resistance observed for ampicilline (80%), augmentin (60%). In last P.*aeruginosa* showed that highest rate of sensitivity 100% to ceftriaxone, while 100% resistance to each of augmentin and ampicilline.
Results of antimicrobial susceptibility pattern of the isolated Gram negative bacteria was presented in table 3**.**

Table 3: Antimicrobial susceptibility pattern of Gram negative bacteria isolated from the urine of pregnant women at ANC clinic of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia from November, 2017 to January 2018.

Isolated Bacteria	Total No	Pattern	Antimicrobial agent tested											
			AMC n (%)	AMP n (%)	NOR n (%)	CIP n (%)	CN n (%)	AK n (%)	CRO n (%)	CAZ n (%)	SXT n (%)	C n (%)	NA n (%)	F n (%)
E.coli	**14**	S	8(57.1	7(50)	10(71.4)	10(71.4	13(92.3	14(100	10(71.4	10(71.4	6(42.9	10(71.4	6(42.9	12(85.7
		I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(7.1)	1(7.13	2(14.2	2(14.3)	3(21.5	2(14.3)
		R	6(42.9	7(50)	4(28.6)	4(28.6)	1(7.7)	0(0)	3(21.5)	(21.5	6(42.9	2(14,3)	5(3.6)	0(0)
Proteus spp	**7**	S	1(14.3	2(28.6	4(57.1)	4(57.1)	5(71.4)	7(100)	3(42.9)	3(42.90	1(14.3	4(57.1)	1(14.3	7(100)
		I	2(28.6	1(14.3	1(14.3)	1(14.3)	2(28.6)	0(0)	1(14.2)	(0)	1(14.3	0(0)	1(14.3	0(0)
		R	4(57.1	4(57.1	2(28.6)	2(28.6)	0(0)	0(0)	3(42.9)	4(57.1	5(71.4	3(42.9)	5(71.4	0(0)
K.pneumoniae	**5**	S	1(20)	1(20)	3(60)	3(60)	4(80)	5(100)	3(60)	3(60)	3(60)	5(100)	1(20)	5(100)
		I	1(20)	0(0)	0(0)	1(20)	0(0)	0(0)	0(0)	0(0)	1(20)	0(0)	2(40)	0(0)
		R	3(60	4(80)	2(40)	1(20)	1(20)	0(0)	2(40)	2(40)	1(20)	0(0)	2(40)	0(0)
P.aeruginosa	**2**	S	0(0)	0(0)	1(50)	1(50)	1(50)	1(50)	2(100)	1(50)	1(50)	1(50)	0(0)	1(50
		I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(50)	0(0)
		R	2(100)	2(100	1(50)	1(50)	1(50)	1(50)	0(0)	1(50)	1(50)	1(50)	1(50)	1(50)
Total	**28**	S	10(35.7	10(35.7	18(64.3)	18(64.3	**23(82.2**	**27(96.4**	18(64.3	17(60.7	10(35.7	20(71.5	8(28.6	**25(89.3**
		I	3(10.7	1(3.6)	1(3.6)	2(7.1)	2(7.1)	0(0)	2(7.1)	1(3.6)	4(14.3	2(7.1)	7(25)	2(7.1)
		R	**15(53.6**	**17(60.7**	**9(32.1)**	**8(28.6)**	**3(10.7)**	**1(3.6)**	**8(28.6)**	**10(35.7**	**14(50)**	**6(21.4)**	**13(46.4**	**1(3.6)**

Abbreviation: AMC: Amoxacillin-clavulinate**, AMP:** Ampicillin**, NOR:** Norfloxacine, **CIP:** Ciprofloxacin **CN:** Gentamicine **AK:** Amikacin **CRO:** ceftriaxone, **CAZ:** Ceftazidime **SXT:** Cotrimoxazole **C:** Chloramphenicol **NA:** Nalixidic acid **F:** Nitrofurantoin

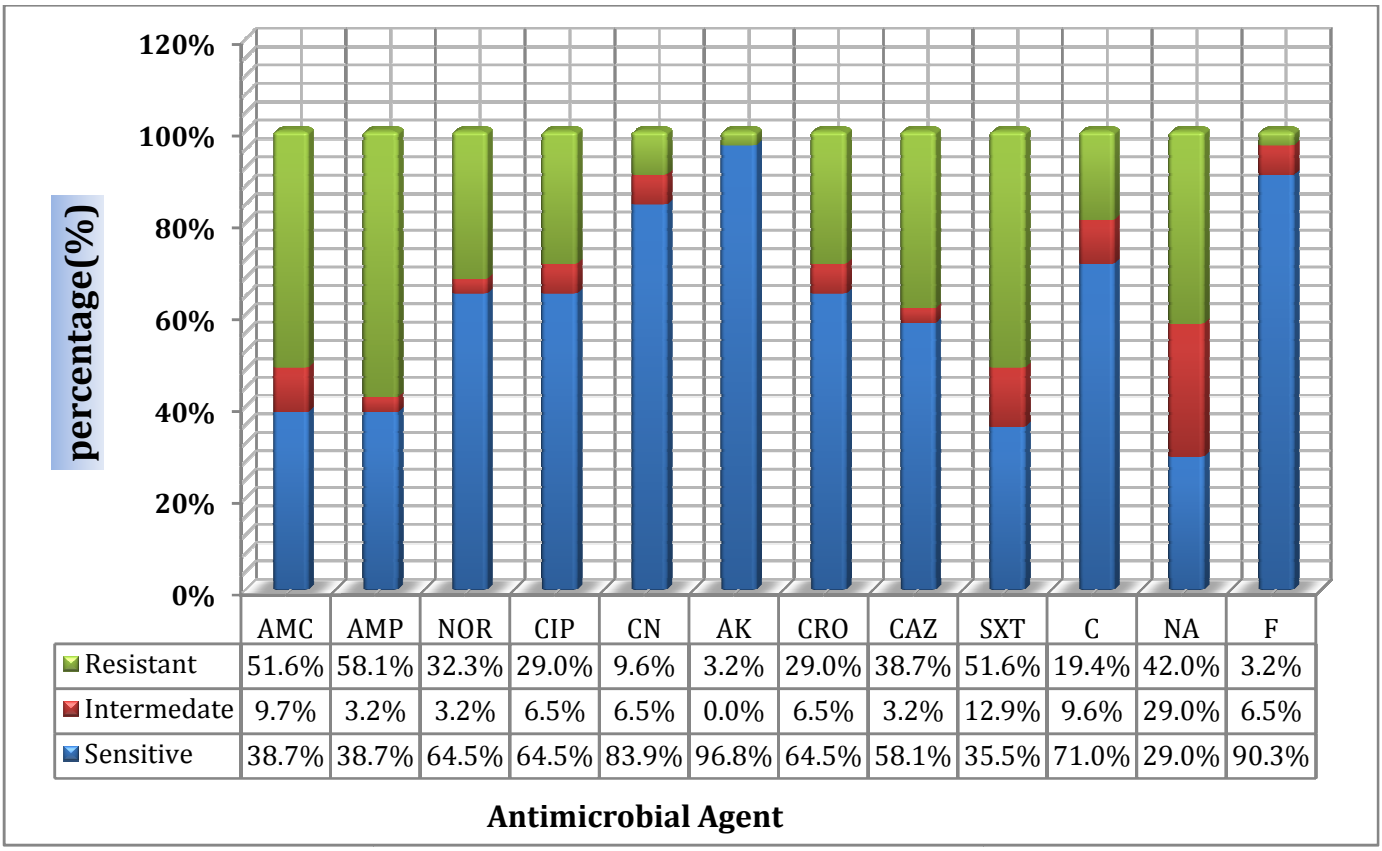
4.4.2. Gram positive isolates

The only Gram positive isolate was S.*aureus*, which showed that highest rate of sensitivity 100% to each of nitrofurantoin, gentamicine and amikacine, while 66.7% resistance to each of ceftazidime and cotrimoxazole.

Table 4: Antimicrobial susceptibility pattern of S, *aureus* isolated from the urine of pregnant women at ANC clinic of HFSUH, Harar, Eastern Ethiopia from November, 2017 to January 2018.

Isolated Bacteria	Total No	Pattern	Antimicrobial agent tested											
			AMC n (%)	AMP n (%)	NOR n (%)	CIP n(%)	CN n(%)	AK n(%)	CRO n(%)	CAZ n(%)	SXT n(%)	C n(%)	NA n(%)	F n(%)
		S	2(66.7)	2(66.7	2(66.7	2(66.7	**3(100**	**3(100)**	2(66.7)	1(33.3)	1(33.3)	2(66.7	1(33.3)	**3(100)**
S.aureus	**3**	**I**	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(33.3	2(66.7)	0(0)
		R	1(33.3)	1(33.3	1(33.3	1(0)	0(0)	0(0)	1(33.3)	**2(66.6)**	**2(66.7)**	0(0)	0(0)	0(0)

Abbreviation: AMC: Amoxacillin-clavulinate**, AMP:** Ampicillin **, NOR:** Norfloxacine, **CIP:** Ciprofloxacin **CN:** Gentamicine **AK:** Amikacin **CRO :** ceftriaxone **CAZ:** Ceftazidime **SXT:** Cotrimoxazole **C:** Chloramphenicol **NA:** Nalixidic acid **F:** Nitrofurantoin



	AMC	AMP	NOR	CIP	CN	AK	CRO	CAZ	SXT	C	NA	F
Resistant	51.6%	58.1%	32.3%	29.0%	9.6%	3.2%	29.0%	38.7%	51.6%	19.4%	42.0%	3.2%
Intermedate	9.7%	3.2%	3.2%	6.5%	6.5%	0.0%	6.5%	3.2%	12.9%	9.6%	29.0%	6.5%
Sensitive	38.7%	38.7%	64.5%	64.5%	83.9%	96.8%	64.5%	58.1%	35.5%	71.0%	29.0%	90.3%

Figure 6. Overall Susceptibility pattern of tested Antimicrobial agent

Abbreviation: AMC: amoxacillin-clavulinate**, AMP:** ampicillin **, NOR:** norfloxacine, **CIP:** ciprofloxacin **CN:** gentamicine **AK:** amikacin **CRO :** ceftriaxone **CAZ:** ceftazidime **SXT:** cotrimoxazole **C:** chloramphenicol **NA:** nalixidic acid **F:** nitrofurantoin

4.4.3. Multiple drug resistance patterns of bacterial uropathogens

Among the total isolates (n = 31) multi drug resistance (MDR = resistance in ≥3 drugs group) were recorded in 16 (51.6 %) of all bacterial uropathogens. 15(53.6%) isolates of Gram negative bacteria and 1(33.3 %) of S.*aureus* showed resistance for three or more drugs. In general, MDR features presented in (**Figure 7).**

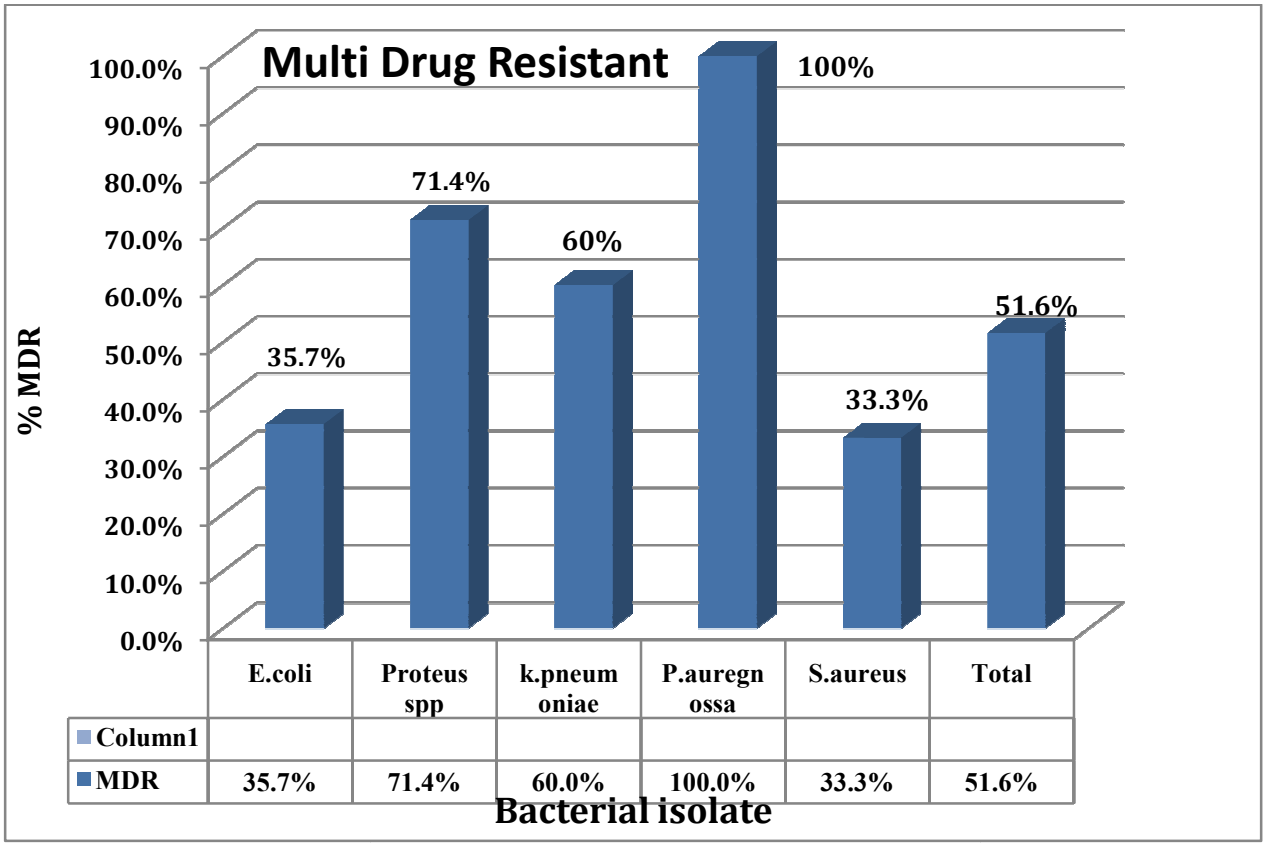


Figure 7: Multidrug resistance (MDR) pattern of isolated bacterial uropathogens among pregnant women at HFSUH, Harar, Eastern Ethiopia, from November, 2017 to January, 2018

Antibiogram showed that, of all isolates (74.2%) of bacteria were found to be resistant to one or more of the commonly used antimicrobial agents. Observed multiple drug resistance (MDR) were 22.6%, 12.9% and 16.1% for three, four and five drug group respectively. Only 8 (25.8%) of bacterial isolates were susceptible to all antibiotics. Overall MDR pattern present in table 5.

Table 5: Multidrug resistance (MDR) pattern of isolated bacterial uropathogens among pregnant women at attending at ANC clinic of HFSUH, Harar, Eastern Ethiopia, from November, 2017 to January, 2018

Bacterial isolate	**Total**	**Multiple Antimicrobial Resistances (%)**							
		Ro	**R1**	**R2**	**R3**	**R4**	**R5**	**R6**	**R7**
E.*coli*	14	5(35.7)	4(28.6)	0	2(14.3	1(7.1)	2(14.3)	0	0
Proteus *spp*	7	1(14.2)	1(14.3)	0	1(14.3	2(28.6)	2(28.6)	0	0
K.*pneumoniae*	5	1(20)	1(20)	0	3(60)	0	0	0	0
P.*aerugniosa*	2	0	0	0	1(50)	0	1(50)	0	0
S,*aureus*	3	1(33.3)	1(33.3)	0	0	**1(33.3)**	0	0	0
Total	31	**8(25.8)**	7(22.6)	0	**7(22.6**	**4(12.9)**	**5(16.1)**	0	0

R_0: susceptible to all antimicrobials tested; R_1, R_2, R_3, R_4, R_5, R_6, R_7: Resistance to one, two, three, four, five, six and seven antimicrobials group, respectively

4.5. Factors associated with UTI

In this study Bivariate and Multivariate logistic regression was performed to check whether there was an association between the existence of significant bacteriuria and associated risk factor. And all independent variables with a p- value less than or equal to 0.25 in the Bivariate analysis were included in the multivariate logistic regression model to identify variables which were associated independently, and the result presented in table 6**.**

The Bivariate logistic regression analysis revealed that there was no significant relationship between UTI and participant age group, residential area, educational level, marital status, Gravidity, parity, gestational age. ($P > 0.05$)

The proportion of UTI that was recorded among study participants with prior history of obstetric surgery and catheterization were 16.1% and 12.9% respectively. Bivariate logistic regression result for them showed that there was a statistically significant association between prior use of indwelling catheter and UTI (COR: 6.111, 95% CI: 1.442, 25.907) as well as having previous history of obstetric and Gynecologic surgery and UTI (COR: 3.870, 95% CI: 1.175, 12.743). , However, the Odds of infection was not significant for prior history of Obstetric surgery after adjustment of other associated risk factors (AOR: 2.877, 95% CI: 0.704 , 11.755) but significant association was observed with prior history of catheterization after adjustment of other associated risk factors (AOR: 5.348, 95% CI: 0.984 ,29.075).

In this study higher incidence of UTI was observed among participants with previous history of UTI (61.3%). There was statistical significant association between a prior history of UTI and occurrence of UTI (COR: 6.062, 95% CI: 2.689, 13.666). The Odds of infection was also significant after adjustment of other associated risk factors (AOR: 5.624, 95% CI: 2.385, 13.261). Indeed, the association between the varies independent variables and the growth of bacteria in their urine were measured. Of these only those having prior history of Obstetric and Gynecologic surgery ($P = 0.027$), catheterization ($P = 0.014$) and having previous history of UTI ($P= 0.000$) were found to be crudely significantly associated with growth of bacteriuria. Following multivariate analysis two of them and additional other covariate (DM) become significantly associated; with having prior history catheterization ($p = 0.046$), previous history of UTI ($P=0.000$) and having history of DM (0.027).

Table 6: Binary logistic regression for predictors associated factor towards bacteriuria among pregnant women attending ANC clinic of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia from November, 2017 – January, 2018.

Variables	Bacteriuria		Bivariate analysis		Multivariate analysis	
	Yes , n (%)	No- , n (%)	COR 95% CI	P- value	AOR 95% CI	P- value
Age (in year)						
18-22	4(12.9)	48(28.4	**I**			
23- 27	14(45.2	58(34.3	1.247 [0.491- 7.914]	0.648		
28-32	10(32.3	38(22.5	3.222 [0.849 -12.229]	0.146		
33-37	2(6.4)	13(7.7)	1.137 [0.172 - 7.503]	0.764		
38 - 42	0(0)	12(7.1)	0.690 [0.066 - 7.250]	0.845		
≥ 43	1(3.2	0(0)	4.833 [0.332 - 70.399]	0.349		
Residence						
Rural	4(13)	18(10.7)	I			
Urban	27(87)	151(89.3)	0.805 [0.253 - 2.562]	0.713		
Educational Status						
Illiterate	5(16)	23(13.6)	I			
Read & write	10(32.2)	23(13.6)	3.250 [0.783 - 13.482]	0.104		
Primary cycle(1-8)	7(22.6)	39(23)	0.788[0.202 - 3.073]	0.731		
Secondary (9-12	7(22.6)	54(31.9)	0.291[0.072 - 1.177]	0.083		
Higher education(> 12	2(6.6)	30(17.6)	0.212 [0.042 1.070]	0.060		
Marital Status						
Married	30(96.8)	155(91.7)	I			
Divorced	1(3.2)	9(5.3)	0.574 [0.070 - 4.700]	0.605		
Widowed	0(0)	5(3)	0.000 [0.000]	0.999		
Gravidity						
1 – 3	30(96.8)	128(75. 7	I			
4 – 6	1(3.2)	31(18.3)	0.138 [0.018 -1.049]	0.056		
7 – 9	0(0)	10(6)	0.000 [0.000] .	0.999		
Parity						
Nullipara	12(38.7)	73(43.2)	I			
Primipara	11(35.5)	39(23.1)	1.716 [0.694 - 4.245]	0.243	1.301 [0.465 -3.642]	0.617
Multipara	8(25.8)	57(33.7)	0.854[0.327 -2.228]	0.747	0.591 [0.193 -1.809]	0.357

Table 6: continued Variables	Bacteriuria		Bivariate analysis			Multivariate analysis	
	Yes , n(%)	No- , n(%)	COR 95% CI 95% CI	P- value	AOR 95% CI		P- value
Gestational age							
1st trimester	5(16.1)	29(17.2)	I				
2nd trimester	16(51.6)	76(44.9)	1.221 [0.410 - 3.637]	0.720			
3rd trimester	10(32.3)	64(37.9)	0.906 [0.284 - 2.890]	0.868			
Diabetes Mellitus							
No	28(90.3)	164(97)	I				
Yes	3(9.7)	5(3)	3.514 [0.795 - 15.537]	0.097	7.040[1.243 - 39.862]		**0.027****
History of obstetric & Gynecologic surgery							
No	26(83.9)	161(95.3)	I				
Yes	5(16.1)	8(4.7)	3.870[1.175 - 12.743]	**0.026****	2.877[0.704 - 11.755]		0.141
History of catheterization							
No	27(87.1)	165(97.6)	I				
Yes	4(12.9)	4(2.4)	6.111[1.442 - 25.907]	**0.014****	5.348[0.984 -29.075]		**0.046***
History of UTI							
No	12(38.7	134(79.3)	I	**0.000****	5.624[2.385 - 13.261]		**0.000*****
Yes	19(61.3)	35(20.7)	6.062 [2.689 - 13.666]				
Current symptom of UTI							
Asymptomatic	18(58.1)	120(71)	I				
Symptomatic	13(41.9)	49(29)	1.769 [0.805 - 3.885]	0.156			

Where: I- reference group

5. Discussion

The current study revealed an overall prevalence of UTI, 15.5%. This is comparable with prevalence of UTI reported among pregnant from a study done in Tanzania (15.5%), Khartoum Sudan (14%), and with a report in Dire Dewa, Eastern Ethiopia (14%) (19, 20 and 24). However, it was relatively higher than from other regions of Ethiopia, such as 11.6 % from Addis Ababa, 10.4% from Gondar and 9.5% from Bahir Dar (21 -23). In contrast it was lower than a report 75% from Niger and 20% from Saudi Arabia (16, 18). The difference in the standard of personal hygiene and education, sample size and social habits might be the possible reason for the variation.

The prevalence of UTI among symptomatic and asymptomatic pregnant women in this study was 21% and 13% respectively. The occurrence of UTI case among symptomatic was in line with the previous study done in Addis Ababa and Dire Dewa Ethiopia 20% and 17% respectively (23, 24). Moreover it also in agreement with a study done in Tanzania, 17.9% (19). But, it was slightly higher than the study conducted else where in the world like; Makka, Saudi Arabia (12%), Gondar University Hospital, Gondar Ethiopia (10.2%), (16, 21). The variation might be due to difference in study setting (primary health care or hospital), screening test used (Urine dipstick, microscopy or culture) or it might be due to involvement of small number of pregnant with clinical manifestation of UTI case. As mentioned above the incidence of Asymptomatic UTI case in this study was 13%. This result was in agreement with a study conducted from abroad, India, Sudan and Tanzania were 11.6%, 14.7% and 13% respectively (17,19 and 20) .Moreover, comparable finding also reported from Dire Dewa, Ethiopia, 11% (24). However, the finding was relatively higher than the study performed in 9% Gondar, Ethiopia and 8% from Makka, Saudi Arabia (16, 21). The main problem with asymptomatic bacteriuria in pregnancy is that the patients are asymptomatic and unless they are screened it can remain discreet leading on to grave complications for both the mother and the fetus therefore periodic examination is needed.

This study revealed a total of 31 bacterial uropathogens. Of these, majorities of them were Gram negative organisms 28(90.3%) than Gram positive 3(9.7%). The current finding is in line with the studies reported from Tertiary Care Hospital in Indian (91.3%) and (8.7%) for Gram negative and Gram positive pathogens respectively (71).

Moreover, majority of studies reported in Ethiopia and else where was in line with this study, in which Gram negative bacteria as the most common UTI associated pathogens with a rate of 67.5% from Gondar,73.1% from Dire Dewa, Ethiopia, 75% from Kenyatta National hospital, Kenya, (21,24,42). This could be due to the existence of unique structure in gram-negative bacteria which foster their attachment to the uroepithelial cells, multiplication and tissue invasion resulting in invasive infection during gestation period (20).

Among isolated pathogens, E.*coli* was the most frequent pathogens with overall rate of 14(45.2%) followed by Proteus *spp* 7(22.6%) and K.*pneumoniae* 5(16.1%). Comparable finding was also reported regarding predominance of E.*coli* with varies studies performed else ware, with a rate of 50% from Afikpo Ebony state ,42.7% from Chandanaish, Bangladesh**,** 42.4% from Khartoum, Sudan**,** and 41.5 % from Yemen**,** (20, 72 - 74). and in Ethiopia it was in line with a study conducted in Bahir Dar , Gondar and Tikur Anbessa Specialized Hospital, Addis Ababa with 47.5%, 45.7%, and 44% respectively (21 - 23).The predominance of E.*coli* in this and other studies is attributed to the fact that it's a commensal of the bowel, this owed to the fact that commensals of the intestine are more involved in the UTI due to its proximity to genito-urinary area anatomically (75). Not only that E. *coli* is also considered uropathogenic due to a number of virulence factors (the P-fimbria and S-fimbria adhesions) specific for colonization and invasion of the urinary epithelium (76). But, contradict with a study from Minna in Niger state in which Klebsiella *spp* showed the highest frequency of Occurrence (39.1%), (18). The possible explanation for the difference in the type of bacterial uropathogens isolates might be due to endemicity of the isolate in the hospital, climatic and geographic variation of the study sites.

Antimicrobial resistance among uropathogens to the commonly used antibiotics become increasing that make clinicians with very few choices of drugs for the treatment of UTI. In the present study, the overall antimicrobial susceptibility patterns of Gram negative isolates have shown that sensitive to amikacin (96.4%), nitrofurantoin (89.3%), gentamycin (82.2%), chloramphenicol 71.5%. highest rate of resistance was observed to ampicillin (60.7%), augmentin (53.6%), cotrimoxazole (50%) and nalixidic acid (46.4%).

The highest sensitivity pattern for aforementioned drug might be due to the drug less likely prescribed or rarely purchased without prescription in the study area. However, high rate of resistance might be due to earlier frequent exposure of the isolate to the above listed drug, the drugs might be used for empiric therapy most of their time or the drugs might be used irrationally which foster the occurrence of drug resistance.

The current study revealed that amikacin, nitrofurantoin, gentamicin, chloramphenicol were relatively effective antibiotics (>70%) against isolated Gram negative pathogens. On the other hand ampicillin, augmentin and cotrimoxazole which are commonly used antibiotics were poorly effective against majority of isolated Gram negative pathogens with resistance rate of 60.7%, 53.6% and 50% respectively.

In the current study, E. *coli* was highly sensitive to amikacin (100%), gentamicin(92.3%), nitrofurantoin (85.7%) and 71.4% to each of ceftriaxone, ceftazidine, chloramphenicol, Norfloxacine, and ciprofloxacin. This is in consistent with a study report in Dire Dewa, Ethiopia, in which E. *coli* demonstrated high level of sensitivity to gentamicin (100%), chloramphenicol (77.8%), ciprofloxacin (88.9%). However, In contrast with a study done in kanchipuram, India, in which there was lower rate of sensitivity of isolate to amikacin (40%), nitrofurantoin (40%). This variation might be due to existence of resistant strain of E.*coli* or could be due to the prior antibiotic usage and self-medication.

While in this study higher resistance of E.*coli* observed to ampicillin (50%) and 42.9% for both augmenti and cotrimoxazole. This is in line with a study report from various region of Ethiopia, in which E.coli showed higher rate of resistance to ampicilline, Gondar (100%), and Dire Dewa (77.8%). Moreover 50% resistance to ampicilline, in contrast 100% sensitivity observed to Augmentin, from Kenyatta National Hospital, Nairobi, Kenya (42).

In the current study K.*pneumoniae* exhibited highest rate of sensitivity 100% to each of amikacine, chloramphenicol and nitrofurantoin. This is in agreement with report from India Nairobi Kenya and Gondar, Ethiopia, in which this isolate showed that 100% sensitivity to nitrofurantoin, amikacin and chloramphenicol, respectively(17,42,58) . However in contrast with study report from Dire Dewa, Ethiopia, in which K.*pneumoniae* exhibited lower rate of sensitivity to chloramphenicol (33.3%) and 100% resistance to nitrofurantoin (24).

The possible explanation for this variation might be due, existence of resistance strain microorganism or use of such drug inappropriately.

The other isolated Gram negative bacteria were P.*auregnossa.* This isolate showed that high level of sensitivity 100% to ceftriaxone, moderate level 50% to Ciprofloxacin, while 100% resistance to each of augmentin and ampicilline. This is in agreement with report from Dire Dewa, Ethiopia (24), in which P.*auregnossa* demonstrated moderate level of sensitivity, 75% to both ceftriaxone and ciprofloxacin. But, high rate of resistance to ampicillin 100%.

The only Gram positive bacterial pathogen isolated in this study was S.*aureus*. This study found that S.aureus is highly sensitive to amikacin, gentamicin and nitrofurantoin each having 100%. And moderate level of sensitivity 66.7% observed to each of chloramphenicol and ciprofloxacin. This was comparable with the finding from Gondar, Ethiopia, in which S.aureus showed sensitivity of 50% and 75% for chloramphenicol and ciprofloxacin respectively (66).

In the current study, multidrug resistance (MDR = resistance in ≥3 drugs group) were recorded in 16 (51.6 %) of isolated bacterial uropathogens. This is relatively lower than previous study performed in different regions of Ethiopia, 100%, 95% and 74% MDR report from Dire Dewa, Gondar, and Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia respectively. This indicates that MDR was found to be very high to the commonly used antibiotics. Variations in the overall prevalence of MDR among these study settings might be due to inappropriate antibiotic use, inappropriate prescription for empiric therapies and lack of appropriate infection control strategies. It could also be due to the use of drugs for other non-human purposes such as in raising livestock and animal muscle growing activities, which may foster rate of resistance to available antibiotics (77).

In this study, high proportion of UTI was recorded among the age group of 23 - 27 years (45.2%). This is in agreement with previous studies conducted in Gondar, Ethiopia in which high rate of UTI, 12.5% observed among the age group of (26 – 30years) (67).

Moreover, a study conducted in south eastern Nigeria revealed high proportion of UTI within this age group with incidence of 61.5% (75). However, high proportion of UTI was reported among the age group of (40 – 49 years) 100% from study done in Minna, Niger state.

This might be due to women in this age group are more sexually active which might predispose them to UTI, while those in later group the higher proportion of UTI were associated with aging and decline in immune status of patients.

In the current study difference was not observed between individual residence, marital status, Occupation, parity, number of pregnancy, education with bacteriuria. This was in line with studies in Tanzania and Sudan (19, 20). Moreover similar finding obtained from study done in Gondar, Ethiopia. But, in contrast parity have been previously observed as risk factor of UTI among pregnant women (78). However, some published report reveals, impact of parity on UTI is loosely described.

The current study showed that, highly significant proportion of UTI was recorded among those study subjects with prior history of UTI, 27% than those without history of UTI. The multivariate logistic regression analysis of current study showed that, having prior history of UTI is predictor variable for the occurrence of UTI (AOR: 5.624, 95% CI: 2.385, 13.261) with P- vale = **0.000.** This finding is similar with report from other regions of Ethiopia like Gondar, (p-value= 0.001), (21), from Dire Dewa (p-value= 0.006), (24). Moreover, it also in line with a study performed in Pakistan (79). The probable explanation for higher rate of UTI among patients with prior history of UTI, is due to the presence of resistant strains, prior use of inappropriate treatment or irrational use of prescribed antimicrobial (may not follow full regimen) among subjects with history of UTI may predispose them for recurrency of the infection .

But, this was in contrast with studies in Nairobi, Kenya (42). This had shown that there was no difference in the occurrence of UTI among pregnant women with and without prior history of UTI. The possible explanation for this might be due to effective treatment for the earlier UTI episodes without any resistant strains of the study community

The current study showed that, those study subjects with prior history of catheterization founds significant high rate of UTI than those who had no of them (AOR: 5.348, 95% CI: 0.984, 29.075) (P = 0.046). This finding had an agreement with report from Korea (80).

Moreover, the current study finding on prior indwelling catheter use was in line with report by Getachew Ferede and his friends (2012), Gondar, Ethiopia (65), and another study done by Agersew and his friends in Gondar, Ethiopia (21).

The probable reason for this finding might be due to frequent and longer exposure to catheter use or it might be due to improper insertion of catheter may facilitate urethral injury and bacterial spread. Therefore proper method of catheter insertion and use is required to decrease the risk of infection among catheterized.

Limitation of the study

- This study didn't undertake urinalysis; diagnosis was only based on clinical manifestation and culture result.
- The study didn't consider the type of Antibiotic in which the participant used during their earlier one.
- Only bacterial pathogens were addressed.

6. Conclusion

In conclusion the current study show that, the overall prevalence of UTI was high, 15.5%, in which there was comparable rate of the infection among symptomatic and asymptomatic pregnant women in the study area. The majority of isolated bacterial uropathogens were gram-negative bacteria, and E.*coli* was the most frequent isolate followed by Proteus *spp*, K.*pnemoniae*, S.*aureus*, and P. *aeruginosa*. amikacin, nitrofurantoin and gentamicin were relatively effective antibiotics, however, high level of resistance developed to ampicillin, augmentin and cotrimoxazole from all isolated bacterial uropathogens, and Majority of the bacterial isolates had multiple drug resistant features. Having prior obstetric surgery, catheterization and prior history of UTI are the factors significantly associated with the occurrence of UTI. Therefore, the current findings indicate, threats of UTI as a serious public health problem in pregnancy within the study area and the need for constant follow up of susceptibility of specific pathogens in different populations to commonly use anti-microbial which will significantly assist clinicians in the rational choice of antibiotic to prevent indiscriminate use of antimicrobial agent.

7. Recommendations

Based on the finding of the current study;

- Health professional working at ANC clinics of Hiwot Fana Specialized University Hospital to give health education on different means for prevention of UTI and good environmental sanitation habit particularly during pregnancy: periodic screening should also be carried out for asymptomatic UTI among pregnant. Proper use of prescribed antibiotic by the user (patients).
- Hiwot Fana Specialized University Hospital to establish well equipped bacteriology laboratory in order to identify pathogens that cause UTI and their antimicrobial susceptibility pattern for selection of preferable antibiotic.
- Clinicians should consider culture and antimicrobial susceptibility tests before prescribing antibiotics in order to minimize emergence of drug- resistant strain in the community.
- Based on our findings, currently Nitrofurantoin could be considered as choice of empirical therapy in area where sample culture not available since it is safer than gentamicin and amikacin.
- Nationwide antimicrobial surveillance to make the right recommendation of alternative antibiotics with strict compliance to antibiotic use in order to minimize the emergence and spread of antimicrobial resistant bacteria uropathogens.

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