Addis Ababa University

College of Health sciences

School of Pharmacy

Department of Pharmacology and Clinical Pharmacy

Msc Thesis

Prevalence of Asymptomatic Bacteriuria, Antimicrobial Susceptibility Pattern of the Bacterial Isolates and Associated Risk Factors among Pregnant Women Attending Antenatal Care (ANC) Clinic of Assosa General Hospital, Benishangul Gumuz Region, Western Ethiopia

BY: Duresa Abu (BSC, Msc candidate)

Advisor - Prof. Tefera Abula

December, 2019

Addis Ababa University

School of Graduate studies

This is to certify that the thesis prepared by Duresa Abu entitled "**Prevalence of asymptomatic bacteriuria, antimicrobial susceptibility pattern of the bacterial isolates and associated risk factors among pregnant women attending antenatal care (ANC) clinic of Assosa General Hospital, Benishangul Gumuz Region, Western Ethiopia"** and submitted in partial fulfillment of the requirements for the degree of Master of science in pharmacology (clinical) complies with regulations of the university and meets the accepted standards with respect to originality and quality.

Signed by the Examining committee:

Internal Examiner:

Signature: _____date_____

External Examiner:

Signature: _____date_____

Advisor:

Signature: _____date_____

ACKNOWLEDMENT

I would like to express my gratitude to Addis Ababa University for the financial support and school of Pharmacy department of Pharmacology and Clinical Pharmacy for facilitating my MSc study. I would like also to thank Assosa University for sponsoring my education.

I would like to express my heartfelt gratitude to my advisor Prof. Tefera Abula for his constructive criticism and for the consistent guidance in the subsequent research activities.

I would also like to acknowledge ANC and Laboratory staff of Assosa General Hospital for their commitment in data collection. Finally, my sincere gratitude goes to the study participants for their willing participation.

TABLE OF CONTENTS

Contents

ABBREVIATIONS AND ACRONYMS

ABU: Asymptomatic Bacteriuria

AMR: Antimicrobial resistance

ANC: Antenatal Care

ASB: Asymptomatic Bacteriuria

AST: Antimicrobial Susceptibility Test

CFU: Colony Forming Unit

CoNS: Coagulase Negative Staphylococci

CI: Confidence Interval

CLED: CysteineLactose Electrolyte Deficient

CLSI: Clinical Laboratory Standard Institute

E. coli: Escherichia Coli

GBS: Group B Streptococcus

MDR: Multidrug resistance

MHA: Muller Hinton Agar

NCCLS: National Committee for Clinical Laboratory Standard

OR: Odds Ratio

RPM: Revolutions per Minute

UTI: Urinary Tract Infection

LIST OF FIGURES

Figure **Page**

LIST OF TABLES

Tables **Page**

ABSTRACT

Background: ASB is a common problem in pregnant women and about 40% of women with untreated asymptomatic bacteriuria during pregnancy develop pyelonephritis, which might lead to low birth weight, preterm, premature rupture of membranes and preterm labour. Therefore, this study aimed to assess the prevalence of asymptomatic bacteriuria, antimicrobial susceptibility pattern of the isolates and related risk factors among pregnant women attending antenatal care clinic of Assosa General Hospital, western Ethiopia.

Methods: A facility-based cross sectional study was conducted from January to February 2019. Data collection involved face to face interview and freshly voided midstream urine samples was collected from each study participants then urine culture and antimicrobial susceptibility tests was conducted. A total of 283 pregnant women were involved. Data was analyzed using SPSS statistical software version 20.0 and multivariate logistic regression analysis was used to determine the predictors and P-value.

Result: The overall prevalence of ASB among pregnant women in this study was 14.85%.E. coli was the most predominant isolate (50 %,) followed by K. pneumoniae (16.7%,), S. aureus (14.3%), coagulase negative staphylococci (CONS) (11.9%), and group B streptococci (GBS) (7.1%).Gram-negative bacteria were highly resistant for tetracycline (96.4%), ampicillin .Gram-positive bacteria were 100% sensitive for ceftazidime. In multivariate logistic regression, educational status [illiterate (AOR=14.7; 95%CI: 4.06-52.63), without formal education (AOR=9.8; 95%CI: 2.81-34.78)], gestational age [1st trimester (AOR=6.76; 95%CI: 1.81-25), 2nd trimester (AOR=6.9; 95%CI: 2.0-23.81)], history of UTI (AOR: 3.46; 95%CI: 1.48-8.1) and history of catheterization (AOR: 4.1; 95%CI:1.7-10.2) were significantly associated with asymptomatic bacteriuria.

Conclusion: Significant bacteriuria was observed in asymptomatic pregnant women. Therefore, routine laboratory diagnosis of ASB in pregnant women and providing appropriate treatment should be needed to reduce its complications. Increasing antibiotic resistance complicates empirical regimens and local resistance rates need to be taken into consideration when deciding on therapy.

Keywords: Asymptomatic Bacteriuria, Antimicrobial Susceptibility, Pregnant Women, Assosa General Hospital.

1. INTRODUCTION

1.1. Background

Urinary tract infections (UTIs) are relatively common problems during pregnancy. The physiologic changes related to pregnancy make healthy women susceptible to complications such as asymptomatic and symptomatic urinary tract infections. The combination of mechanical, hormonal and physiologic changes during pregnancy contributes to significant changes in the urinary tract, which has a profound impact on the acquisition and natural history of bacteriuria during pregnancy(1,2).

UTIs may arise more often in women than men because of the shortness of female urethra, and in a patient exposed to urinary catheters and/or bacteria on contaminated urological instruments, during sexual intercourse, and fluid which may enter into the genitourinary area without previous host colonization(3).Asymptomatic UTI occurs following the movement of bacteria by way of the urethra into the bladder, occasionally with the subsequent act of ascending to the kidney. Nowadays, asymptomatic bacteriuria (ASB) is common in pregnancy(4).

Asymptomatic bacteriuria (ASB) is defined as the presence of $10^5$and more colony forming units (CFU) per milliliter(mL) of urine in the absence of specific symptoms of acute UTIs (3,5).It is, however more likely to progress to symptomatic urinary tract infection during pregnancy because of the physiological changes associated with pregnancy(6).This may result Pregnant women are likely to develop acute pyelonephritis, postpartum UTI, hypertensive disease, anemia, prematurity, low birth weight babies and prenatal death if untreated(6,7).Pregnant women are at increased risk of asymptomatic bacteriuria due to mechanical factors, hormonal changes, urinary stasis and reflux of urine from bladder to ureters(8).In addition to physiologic changes, there are other conditions like low socioeconomic status, sickle trait, diabetes mellitus and grand multiparty that have been reported to be associated with two fold increase in the rate of bacteriuria(9). Therefore, screening for bacteriuria during pregnancy irrespective of whether patient is symptomatic or not is important in first care setting as early treatment can prevent subsequent complications(10,11).

1.1.1 Prevalence Asymptomatic Bacteriuria among Pregnant women

The prevalence of ASB ranges from 2% to 11% during pregnancy (12,13). This variation of prevalence from one country to other and among region of the same country due to differences exists in geographical location, social behavior of the population, the environment and study settings. As a result the incidence of ASB during pregnancy that was reported across a globe was varied.

Cross-sectional study done at two tertiary centers in Cairo, Egypt on Prevalence of undiagnosed asymptomatic bacteriuria and associated risk factors during pregnancy: showed that out of 170 pregnant women tested, prevalence was 10% (14). Moreover other studies done among pregnant women in South east Nigeria, Nairobi Kenya, Sulaimani city Iraq and Maharashtra India, showed that prevalence of 79.2%,21.5,42.9, and 23% respectively[15,16,17,18].

Even if no national study done on prevalence of ASB in Ethiopia, there was varied incidence of ASB was reported among pregnant women in different regions of the country. Study conducted on a total of 244 pregnant women with no sign and symptom of urinary tract infection, Hawassa Teaching and Referral Hospital showed that 18.8% were positive for asymptomatic bacteriuria (19). Other study done in Adigrat General Hospital, Northern Ethiopia shows Out of 259 pregnant women, the prevalence of asymptomatic bacteriuria was 21.2%)(20). While other studies done in Adama Central Ethiopia, Dessie Northwest Ethiopia, Dire Dawa Eastern Ethiopia and study conducted Northwest Ethiopia showed that 16.1%,15.6%,11% and 8.5%, prevalence respectively (21,22,23,24)

1.1.2 Etiologic agents of Asymptomatic Bacteriuria during Pregnancy

Gram-negative and positive bacteria are predominantly responsible from ASB during pregnancy worldwide [3]. Escherichia coli is found in 70– 90% of isolates that cause ASB. Other bacteria like Klebsiella, Proteus, Pseudomonas and Staphylococcus Saprophyticus also involved. Most of these pathogens exist naturally in the periurethral area and in the perianal area and their ascension through the urethral orifice can lead to UTI/ASB (2).

Cross-sectional study done in Cairo, Egypt showed that E. coli was the most predominant organism followed by Klebsiella; no other isolated organisms showed significant growth (14). Other cross-sectional study done in Ghana shows mostly isolated bacteria were Escherichia coli (62.5%) and Klebsiella pneumoniae (30.6%), also P. mirabilis and Gram-positive Enterococcus fecalis was isolated.[25].However study done India reports S. aureus (82.60%) was found to be the most common uropathogen isolated followed by Klebsiella spp. (13.04%) and Micrococci (4.35%)[8]. While other cross-sectional study done in Hawassa Teaching and Referral Hospital revealed total number of bacterial isolates was 51 of this bacterial isolates, (51%) were Gram-positive bacteria and the rest (49%) were Gram-negative bacteria. The predominant bacterial species were coagulase negative Staphylococcus (CoNs) (32.6%), E. coli (26.1%), S. auerus (13%), Enterobacter species (8.7%), and Klebsiella species (6.5%). CoNS and E. coli was responsible for (8.7%) of mixed infection(19).Other study done in Ethiopia also show deferent etiologic agents pattern, report in Adigrat General Hospital, Northern Ethiopia showed Gram negative bacteria, specifically Escherichia coli was the predominant isolates followed by Klebsiella species and Proteus mirabilis. In this study the Gram positive identified bacteria, Staphylococcus aureus was main isolate(20).

1.1.3 Pathogenesis and clinical presentation of Asymptomatic Bacteriuria during Pregnancy

In general, organisms gain entry into the urinary tract via three routes: the ascending, hematogenous (descending), and lymphatic pathways. The female urethra usually is colonized by bacteria which originate from the faecal flora. The short length of the female urethra and its proximity to the rectal area make colonization of the urethra likely UTIs are more common in females than in males because of the anatomic differences in location and length of the urethra tends to support the ascending route of infections as the primary acquisition route [4]. Pregnant women are at increased risk for UTIs which begins in week 6 and peaks during weeks 22 to 24, approximately 90 percent of pregnant women develop ureteral dilatation, which will remain until delivery (hydronephrosis of pregnancy).And also other factors like Increased bladder volume and decreased bladder tone and decreased ureteral tone, contribute to increased urinary stasis and ureterovesical reflux (26). Additionally, the physiologic increases in plasma volume during pregnancy decreases urine concentration up to 70% of pregnant women develop glycosuria, which encourages bacterial growth in the urine. Increase in urinary progestin's and estrogens

may lead to a decreased ability of the lower urinary tract to resist invading bacteria, this decreased ability may be caused by decreased ureteral tone or possibly by allowing some strains of bacteria to selectively grow. These factors may all contribute to the development of UTIs during pregnancy [8, 14].

1.1.4 Risk factors of Asymptomatic Bacteriuria during Pregnancy

The prevalence of bacteriuria in pregnancy is closely related to socioeconomic status [1].Study done by Turck et al. reported the prevalence of significant bacteriuria determined by a single catheterized urine at delivery to be 2% in non-indigent pregnant women of middle socioeconomic status compared to 6·5% of indigent patients(27). Several factors are also associated with the rapid increase in the prevalence of ASB among pregnant mothers. This factors are like history of UTIs, age, multiparty, lower level of education(28). Multi gravidity, advanced gestational age, sexual activity, poor sanitation, lack of general hygiene practice, disorders like diabetes mellitus and anemia in pregnancy and history of catheterization (29).

Cross-sectional study done, Egypt on pregnant women without signs or symptoms of urinary tract infection showed that regarding the relationship between ASB and the range of demographic and personal hygiene risk factors they found that ASB was predominant in participants with higher sexual activity: (65%) participants reported their sexual activity as greater than twice per week, and 11 of the 17 ASB cases were seen in this cohort (p=0.01). ASB was also significantly higher among participants who reported washing their genitals from back to front after defecation (88%, p=0.03 ;). There were no statistically significant differences between ASB and age, gestational age, parity, educational level, socio- economic level(14).But Other cross-sectional study done by conducted in a total of 244 pregnant women with no sign and symptom of urinary tract infection in Hawassa Teaching and Referral hospital show age of the mothers ,family income level (< 1000 ETB) and gestational period were found significantly associated with asymptomatic bacteriuria(19).Other study in Adigrat General Hospital, Northern Ethiopia found that age of the mothers (18–25 years old) with [AOR=8.5, 95% CI (2.2, 32.9), P value=0.001] family income level and gestational period (1st trimester with, [AOR=11.9, 95% CI (4.4, 32.4), P value=0.001] and (2nd trimester) with, [AOR; 5.6, 95% CI (2.0, 15.5%), P value=0.01] were significantly associated with asymptomatic bacteriuria.[20]. And also study

done Dessie referral hospital, Northeast Ethiopia was found that ASB was significantly associated with history of catheterization and hemoglobin level [22].

1.1.5 Diagnosis of Asymptomatic Bacteriuria during Pregnancy

Screening of pregnant women for ASB at first prenatal checkup helps us to analyze the associated factors and prevents its effects on pregnancy(1)**.** Quantitative urine culture, which was initially described in the 1950s, enabled the identification of asymptomatic bacteriuria for the first time(30). Quantitative urine culture is the gold standard for diagnosis of ASB (14,30). A key aspect in the diagnosis of both symptomatic and asymptomatic urinary tract infections is differentiating contamination from true bacteriuria. The original criterion for diagnosing asymptomatic bacteriuria was > 10^5cfu/mL of a single uropathogen on two consecutive clean catch samples, with a 95% probability that the woman has true bacteriuria or the detection of > 10^5cfu/mL in a single voided midstream urine is accepted as a more practical and adequate alternative, although there is only an 80% probability the woman has true bacteriuria(14,31,32).

1.1.6 Treatment of Asymptomatic Bacteriuria during Pregnancy

Treatment of asymptomatic bacteriuria has been shown to reduce the rate of pyelonephritis in pregnancy and therefore screening for and treatment of asymptomatic bacteriuria has become a standard of obstetrical care(32). Screening for asymptomatic bacteriuria became standard obstetric care, and most antenatal guidelines today include routine screening for asymptomatic bacteriuria. The United States Preventive Services Task Force strongly recommends screening and treatment, and similar recommendations are included in guidelines from Infectious Diseases Society of America, the National Institute for Clinical Excellence, the European Association of Urology, the Canadian Task Force on Preventive Care, and most recently from the Scottish Intercollegiate Guidelines Network.[33-38]. Also Standard Treatment Guidelines in Ethiopia also recommend screening and treatment of ASB.

Clinical trials done during the subsequent 15 years repeatedly showed that pregnant women with untreated asymptomatic bacteriuria had a 20–30% risk of developing pyelonephritis in later pregnancy, this risk was reduced by 80% when asymptomatic bacteriuria was identified early in the course of the pregnancy and treated with antimicrobials(30). On the basis of consistent and compelling observations, screening for asymptomatic bacteriuria in early pregnancy and treatment of positive women to prevent pyelonephritis became a standard practice in high-

income countries (30,39). Unfortunately, universal screening is not practiced worldwide, especially in developing countries where the costs of standard plate cultures are prohibitive to limited health care budgets and because they also may lack adequate laboratory facil- ities or trained microbiologists or both. A Cochrane review showed that treatment with antibiotics could effectively reduce the incidence of pyelonephritis from 21% in untreated women to 5% in treated women (risk ratio [RR] 0·23, 95% CI 0·13–0·41).Similar positive effects were reported for birth weight less than 2500 g (8·5% in treated women vs. 13% in untreated women; RR 0·66, 95% CI 0·49–0·89) and for preterm delivery (defined as a gestational age <38 weeks). Therapy should consist of an agent administered for 7 days that has a relatively low adverse effect potential and is safe for the mother and baby. The administration of a sulfonamide, amoxicillin, amoxicillin/clavulanate, cephalexin, or nitrofurantoin is effective in 70% to 80%of patients. Tetracycline's should be avoided because of teratogenic effects(40). Appropriate management of UTI in pregnant women can avoid or reduce associated complications such as preterm labour, sepsis and pyelonephritis(41,42).However, screening and treatment of pregnant women for asymptomatic bacteriuria never became standard ANC follow-up practice in Ethiopia.

1.1.7 Antimicrobial susceptibility pattern of Bacteriuria isolated from ASB pregnant woman

There is no clear consensus in the literature on the choice of antibiotic, and as a result practice is more likely guided by national patterns of practice and local resistance patterns than evidence from clinical trials(32).At the sometime Antimicrobial resistance in bacteriuria is increasing worldwide and some bacteria are virulent and capable of acquiring multidrug resistance to antimicrobials. Rates of antimicrobial resistance vary according to geographic locations and they are directly proportional to the use and misuse of antimicrobials. Du to this Antimicrobial therapy of a pregnant woman is a serious concern during pregnancy. Deferent studies show deferent resistance pattern.

Cross-sectional study done, Egypt showed that nitrofurantoin, imipenem and amikacin demonstrated 100% sensitivity. A range of other antibiotics showed good sensitivity including norfloxacin and ceftazidime; however, 88% of the urinary isolates were resistant to cephalexin(14).Other Cross-sectional study done in ethiopia in Hawassa Teaching and Referral

Hospital. Showed susceptibility of norfloxacin (64.7%), gentamicin (47.1%), cefotaxime (43.15%), penicillin (30.8%), trimethoprim-sulphamethoxazole (25.5%), vancomycin (23.5%), and ampicillin (17.3%) and multi-drug resistance was observed in all isolated bacteria[19]. but study done in Adigrat General Hospital, Northern Ethiopia showed all Gram negative isolates were found 100% resistan to Ampicllin. Moreover, all Gram positive isolates were found sensitive to Vancomycin at 100%(20).Other study done in Dessie referral hospital shows the majority of the gram-negative bacterial isolates were sensitive to nitrofurantoin (95.2%), norfloxacin (85.7%), ciprofloxacin (80.95%) and ceftriaxone (80.95%), amikacin (76.2%), ceftazidime (71.4%), gentamycin (66.7%) and trimethoprim-sulfamethoxazole (57.1%). and tetracy- cline (57.1%). However, most Gram-negative bacteria were resistance to ampicillin (66.6%), amoxicillin- clavulanic acid (; 62%), and cefotaxime (47.6%), followed by trimethoprim-sulfamethoxazole (42.9%), and tetracycline (; 42.9%). most Gram- positive bacteria sensitive to nitrofurantoin (n=33; 94.3%), ciprofloxacin and norfloxacin (for each, n=26; 74.3%), chloramphenicol (n=24; 64.7%), and followed by clindamy cin (n=23; 62.2%). Staphylococcus[22].

1.2 Statement of the problem

Urinary tract infections (UTIs) are the most commonly occurring bacterial infections and account for 8 million patient visits annually. Approximately 1 in 3 females will have had a urinary tract infection by age 24 years. Due to several anatomical and hormonal changes, pregnant women are more susceptible to develop UTIs) (6,8,41).Asymptomatic bacteriuria is one of the major risk factors for the development of UTIs during pregnancy which accounts for about 70% of the cases. If untreated, it causes about 40% cystitis and 30% pyelonephritis which might lead to delivery of premature or low-birth-weight infants, intrauterine growth retardation, preterm labor, intrauterine fetal death, and increased prenatal mortality and morbidity(7,40).As result the American College of Obstetricians and Gynecologists guideline, screening for ASB is recommended in all pregnant women (43).

ASB is common problem among pregnant women and it has been reported That prevalence of ASB ranges from 2% to 11% during pregnancy (12,13). The variation of prevalence from one country to other and among region of the same country due to differences exists in geographical location, social behavior of the population, the environment and study settings. As a result the incidence of ASB during pregnancy that was reported across a globe was varied reports in Nigeria, Kenya, Iraq and India, showed that prevalence of 79.2%,21.5,42.9, and 23% respectively[15,16,17,18].By screening for and aggressively treating pregnant women with asymptomatic bacteriuria, it is possible to significantly decrease the annual incidence of pyelonephritis during pregnancy.

In randomized controlled trials, treatment of pregnant women with asymptomatic bacteriuria has been shown to decrease the incidence of preterm birth and low birth weight infants(44).Recently, antimicrobial resistance in bacteriuria is increasing worldwide and some bacteria are virulent and capable of acquiring multidrug resistance to antimicrobials. For example, Escherichia coli is Gram-negative bacteria which can generate large-spectrum of beta-lactam enzymes making them resistant to most beta-lactam antibiotics(45).Results of antibiotic susceptibility pattern also showed that there is a vast difference in susceptibility pattern of uropathogens (8,10,46,47), these results indicate that susceptibility pattern varies from hospital-to-hospital, population-to-population and country-to-country and signifies the importance of study of susceptibility pattern.

However, there was lack of data on the prevalence of ASB and antimicrobial susceptibility of the bacterial isolates among pregnant women in Benishangul Gumuz Region particularly in this study area. Therefore, this study was aimed to assess the prevalence of asymptomatic bacteriuria, antimicrobial susceptibility pattern of the bacterial isolates and related risk factors among pregnant women attending antenatal care (ANC) clinic of Assosa General Hospital, Western Ethiopia.

1.3 Significance of the study

Asymptomatic bacteriuria was reported to be a major risk factor for development of a urinary tract infection during pregnancy which results in serious medical and obstetrical complications (48).Up to 40% of pregnant women with asymptomatic bacteriuria will develop an acute kidney infection such as pyelonephritis. Approximately 50% of these will have premature labour. Untreated asymptomatic bacteriuria in pregnancy often will lead to adverse maternal and fetal outcomes; adverse maternal outcomes that may occur include symptomatic cystitis, pyelonephritis and preterm labour and delivery. In pregnancy pyelonephritis may lead to septicemia, chronic pyelonephritis, loss of renal function and respiratory distress syndrome, prematurity, low birth weight and perinatal mortality are possible adverse fetal outcomes(13,49).

This is particularly important for Ethiopian's high birth rate of 4.20 births per woman nearly double that seen in Western Europe or the USA. However, in most developing countries including Ethiopia screening for ASB in pregnancy is not considered as an essential part of antenatal care. Little is also known regarding the epidemiology of asymptomatic bacteriuria in pregnant women in Ethiopia. And also Antimicrobials are widely used empirically, especially in the developing world, like Ethiopia. The impact of antimicrobial overuse on the anti- microbial susceptibility of human pathogens impairs the effectiveness of current and future antimicrobial agents and may led to emergence of antibiotics resistant (41).However in Ethiopia, particularly in the study area there is miss of recent data on both antibiotic susceptibility patterns and prevalence of ASB and its associated factors is not known in study area. Also antibiotic susceptibility patterns vary according to regional and geographical location and changes through time. So this study contributes some information on Risk factor and their antibiotic susceptibility in study area which is helpful, in health-intervention programs designed for pregnant women, to recommend prescribing antibiotics for successful treatment of ASB and minimizing its complications and emergence of resistance in the community. Furthermore, this study will be used as base line data for further studies.

2. Objectives

2.1. General objective

To assess the prevalence of asymptomatic bacteriuria, antimicrobial susceptibility pattern of the bacterial isolates and associated risk factors among pregnant women attending antenatal care (ANC) clinicof Assosa General Hospital, Benishangul Gumuz region, Western Ethiopia.

2.2. Specific objectives

- To determine the prevalence of asymptomatic bacteriuria among pregnant women attending ANC clinic of Assosa General Hospital, Western Ethiopia.
- To determine bacteria isolated from pregnant women with asymptomatic bacteriuria attending ANC clinic of Assosa General Hospital, Western Ethiopia.
- To determine the antimicrobial susceptibility pattern of the bacterial isolates from pregnant women with asymptomatic bacteriuria attending ANC clinic of Assosa Genera l Hospital, Western Ethiopia
- To identify risk factors associated with asymptomatic bacteriuria among pregnant women attending ANC clinic ofAssosa General Hospital, Western Ethiopia.

3. Materials andmethods

3.1. Study area and period

This study was conducted at Assosa General Hospital from January to February, 2019. Assosa general hospital is one of the two general hospitals found in Benishangul Gumuz Regional State (BGRS). The hospital is found in Assosa town and the townis 670 km away from the capital city of Ethiopia, Addis Ababa in Western part of the country. As a part of the Assosa zone, Assosaworeda is bordered by Kurumuk and Homesha in the north, by Menge in the northeast, by OdaBuldigilu in the east, by Bambasi in the southeast, by Mao-Komo special woreda in the south and by Sudan in the west. The woreda has one general hospital, 3 health centers and 27 health stations or health posts. The 2007 national census reported a total population for this woreda of 104,147, of whom 52,968 were men and 51,179 were women; 24,214 or 23.25% of its population were urban dwellers (Census 2007. Benishangul Gumuz Region Archived 2012). Assosa General Hospital has 22 OPDs and ANC OPD is one of the 22 OPDs that give services on average for 700 pregnant women per month. The hospital provides service for about 150,000 patients per year. The total population of Assosa general hospital catchment area is about 750,000 populations (from hospital record).

Fig 1. Map of the study area

3.2. Study design

A facility-based cross sectional study was conducted amongpregnant women attending antenatal clinic (ANC) of Assosa General Hospital, Benishangul Gumuz Region, Western, Ethiopia.

3.3. Population

3.3.1. Source population

All pregnant women attending ANC clinic of Assosa General Hospital for ANC services

3.3.2. Study population

All pregnant women attending ANC clinic of Assosa General Hospital without any signs and symptoms of UTIs and willing to participate in the study were the study population.

3.4. Inclusion and exclusion criteria

3.4.1. Inclusion criteria

All pregnant women who attend ANC clinic of Assosa General Hospital for ANC services and without any sign and symptom of UTI were included in study.

3.4.2. Exclusion criteria

- Pregnant women with history of antibiotic therapy in previous two weeks ·
- Pregnant women who were critically sick and unable to answer the questionnaire.

3.5. Sample size determination

The sample size was determined using statistical formula for single population proportion with the following assumptions: 95% confidence interval; degree of precession (5%) and 21% (p=0.21) prevalence of ASB among pregnant women which was taken from study done in Adigrat, Northern Ethiopia (20).

$$n = \frac{(Z\alpha/2)^2 P (1-P)}{d^2}$$

Where:

n= sample required

Z= 95% confidence interval (1.96)

D= margin of error (5%)

P= prevalence rate (21% or 0.21).

Then $n_o = \frac{(1.96)^2 (0.21*0.79)}{(0.05)^2} = 257$

By considering 10% non-response rate, the total sample size was 257+26 =**283**.

3.6. Sampling technique

All pregnant women attending the ANC clinic of Assosa General Hospital for ANC services and without signs and symptoms of UTIs were included consecutively as study subjects.

3.7. Variables of the study

3.7.1. Dependent variables

Asymptomatic bacteriuria

3.7.2. Independent variables

- Socio-demographic characteristics (age, ethnicity, religion, residence, occupation, marital status, monthly income, educational status)
- Associated risk factors (gestational age, parity, water source, washing genitalia, direction of washing genitalia, history of catheterization, history of UTI, history of preeclampsia, history of diabetes, history of obstetrics and gynecology surgery).

3.8. Data collection method and laboratory investigation

3.8.1. Socio-demographic and clinical data collection

After taking written informed consent from the pregnant women, socio- demographic data (age, religion, residence, occupation, marital status, monthly income), clinical and risk-related data (history of UTI ,gestational age, parity, water source, washing genitalia, direction of washing genitalia, history of catheterization, history of preeclampsia, history of diabetes, history of obstetrics and gynecology surgery)of the study participants was collected by trained midwives using pre-tested structured questionnaires.

3.8.2. Collection of urine samples

About 5 mL of freshly voided midstream urine samples were collected from each study participant susing a sterile screw-capped, wide-mouth container and the urine samples were transported to Assosa Regional Laboratory and processed within one hours of collection and specimens that were not processed within one hours of collection were refrigerated at 4 °C until it was processed.

3.8.3. Bacterial culture and identification

Well-mixed and uncentrifuged urine specimens obtained from the pregnant women was directly inoculated on cystine lactose electrolyte deficient agar (CLED) (Oxoid, Ltd, England) media by streak plate method using calibrated inoculating wire loop (0.001 mL). Culture plates were incubated in the aerobic environment at 37 ^{0}C for 24-48 hrs and following overnight incubation plates were checked for growth. All plates with 10^5 and more bacterial colonies per milliliter (ml) of urine were sub-cultured on to MacConkey agar (Oxoid, England), and 5% sheep blood agar (Oxoid, England) for further identification. Bacterial isolates were identified as per the standard bacteriological procedure using colony characteristics, gram-staining, and series of biochemical tests (50).All procedures were done under microbiology team support. Most Gram-negative bacteria was identified using the following biochemical tests such asindole test, lysine decarboxylase, H_2S and gas production in triple sugar agar, citrate utilization, urease and motility tests while the Gram-positive bacteria were identified using catalase, coagulase, pyrrolidonyl arylamidase test (PYR), CAMP, bacitracin and trimethoprim-sulfamethoxazole tests.

3.8.3. Antimicrobial susceptibility testing

Antimicrobial susceptibility test was carried out by Kirby- Bauer disk diffusion technique on Muller-Hinton agar medium and the diameter of zone of inhibition was interpreted according toClinical Laboratory Standard Institute (CLSI) guidelines (50).About 3-5 pure bacterial colonies were suspended in normal saline and mixed smoothly until 0.5 McFarland standard was reached. By using sterile swab, the prepared standard suspension was evenly swabbed onto the surface of Muller-Hinton agar and the inoculated plates were stored at room temperature for 3-5minutes to allow the medium to absorb the moisture from the inoculum and will be dried by placing the plates in incubators at 35-36.5^{o}C. The antibiotic discs were placed at equal distance to thedried Muller-Hinton agarmedia containing the inoculated bacteria and was incubated at 37^{o}C for 18-

24hrs and the diameter of zone of inhibition around the disc was measured and interpreted according to CLSI (50).For both Gram-positive and Gram-negative bacteria the following antibiotic discs were tested: ampicillin (10 μg), amoxicillin-clavulanic acid (20/10 μg), ciprofloxacin (300 μg), gentamicin (10 μg), ceftriaxone (30 μg), cefotaxime (30 μg), tetracycline (5 μg), ceftazidime (30 μg), amikacin (30 μg), norfloxacin (10 μg), trimethoprim-sulfamethoxazole (1.25/23.75 μg), clindamycin (2 μg), erythromycin (15 μg), penicillin (30 μg), chloramphenicol (30 μg), ciprofloxacin (300 μg) and vancomycin (30 μg)**.**

3.9. Data quality control

A detailed quality assurance procedure was used to keep the quality of data. To avoid language barrier and ambiguities, the questionnaire was first translated to the local language and 5% of the questionnaire was pre-tested. Training was given to data collectors to minimize technical errors and to maintain the quality of data. The collected data were checked for completeness at the end of each day of data collection. Standard operating procedures ((SOPs) were strictly followed during all aspects of laboratory procedure including sample collection, sample inoculation, culturing, biochemical tests, and antimicrobial susceptibility testing. The culture media was tested for sterility and performance. The American Type Culture Collection (ATCC) reference strains such as Escherichia coli (ATCC-25922), Staphylococcus aureus (ATCC-25923), and Pseudomonas aeruginosa (ATCC-27853) were used as quality control parameters during culture and antimicrobial suscep tibility testes. All the standard strains were obtained from the Ethiopian Public Health Institute.

3.10. Data processing and analysis

Data was initially entered and cleaned using Epi-data version 3.1 and exported to SPSS version 20.0 for analysis. Statistical analyses was performed using SPSS windows version 20 statistical package and it was summarized and presented by frequency tables and summary statistics presented by graphs, tables and other summery measures. Descriptive statistics were done to indicate the frequency of the variables and multiple logistic regression analysis was used to determine the predictors of asymptomatic bacteriuria. The 95% CI used to show the accuracy of data analysis. P value < 0.05 was considered as statistically significant.

3.11. Ethical consideration

The study was ethically approved by Ethical review board of Addis Ababa UniversityCollege of Health Sciences, School of pharmacy (ERB). Official permission was obtained from Benishangul Gumuz Region Health Bureau and from Assosa General Hospital administrative bodies. During data collection, each study participant was informed about the purpose of the study and written informed consent obtained from the pregnant mothers. Anyone who was not willing to participate in the study was excluded from the study. Any information concerning the study participants kept confidential and the specimen collected from the study participants wasonly analyzed for the intended purposes. Pregnant women who had significant bacteriuria received appropriate treatment according to the national guideline.

3.12. Operational Definitions

Asymptomatic UTI (ASB): It is the presence of significant bacteria ($\geq 10^5$cfu/ml) in a patient without signs or symptoms of UTI.

Midstream urine: A specimen obtained from the middle part of urine flow.

Multidrug resistance: is antimicrobial resistance shown by a species of microorganism to three or more antibiotics of different classes.

3.13. Dissemination of the finding

The finding of this study will be presented to Addis Ababa University, College of Health Sciences School of Pharmacy and department of Pharmacy and Clinical pharmacy. The finding will be disseminated to Benishangul Gumuz Region and Assosa General Hospital. The finding will be also presented to different governmental and non-governmental organizations. Finally, the finding will be published on reputable journals.

4. Results

4.1. Socio-demographic characteristics of the study participants

A total of 283 pregnant mothers without signs and symptoms of UTI were included in this study. The mean age of the study participants was 24.5 years with standard deviations (SD) of 4.5 (ranged 17–37 years), and 59.7% of them aged between 15 and 24 years. About 12.4% (n=35) of the study participants were illiterate while 25.4% (n=72) attended primary school and 34.3% (n=97) attended secondary school and above. Regarding place of residence and marital status, 85.2% (n=241) and 96.85 (n=274) of the study participants were urban dwellers and were married, respectively.Concerning monthly income, about 54.8% (n=185) have monthly income greater than 1999 Ethiopian birr (Table 1)

Table 1.Socio-demographic characteristics of the pregnant women attending antenatal care (ANC) clinic of Assosa General Hospital, Benishangul Gumuz Region, western Ethiopia, from January to February, 2019 (n=283).

Characteristics	Frequency (n=283)	Percentage (%)
Age		
15-24	169	59.7
25-34	97	34.3
35-44	17	6
Residence		
Urbane	241	85.2
Rural	42	14.8
Marital status		
Single	9	3.2
Married	274	96.8
Religion		
Orthodox	147	51.9
Muslim	86	30.4
Protestant	41	14.5
[1]Other	9	3.2

Marital status		
Single	9	3.2
Married	274	96.8
Educational status		
Illiterate	35	12.4
Read and write	29	10.2
Primary school	98	34.6
secondary school and above	121	42.8
Family monthly income (birr)		
<500	62	21.9
500-1999	66	23.3
> 1999	155	54.8

1, Wakefeta, Gova wittenace,

4.2. Clinical, reproductive health and hygiene related characteristics of the study participants

Among the total study participants (n=283), about 50.5% (n=) had previous history of UTI. With regard to previous history of catheterization and surgery, 10.6% (n=30) of the study participants had history of catheterization while 4.9% (n=14) had previous history of obstetric and gynecological surgery. About 2.1%(n=6) and 5.3% (n=15) of the study participants had previous history of diabetic mellitus and history of preeclampsia, respectively. Based on their parity, 19.8 % (n=56),43.5 % (n=123) and 36.7% (n=104) of the study participants were nulliparous, primiparous and multiparous, respectively. Regarding gestational age, 41% (n=116) were in the 2nd trimester. All of the study participants (100%; n=283) wash their genital after toilet; out of which 87.6% of them use Tape water source for washing their genital, and about 7.1% of the study participants wash their genital back-to-front direction (table 2).

Table 2.Clinical, reproductive health and hygiene related characteristics of the pregnant women attending antenatal care (ANC) clinic of Assosa General Hospital, Benishangul Gumuz Region, western Ethiopia, from January to February, 2019 (n=283)

Characteristics	frequency (n=283)	Percentage (%)
Gestational age		
First trimester	73	25.8
Second trimester	116	41
Third trimester	94	33.2
Parity		
Nullipara	56	19.8
Primipara	123	43.5
Multipara	104	36.7
History of UTI		
Yes	143	50.5
No	140	49.5
History of catheterization		
Yes	30	10.6
No	253	89.4
History of DM		
Yes	6	2.1
No	277	97.9
History of obstetric and gynecological Surgery		
Yes	14	4.9
No	269	95.1
History of preeclampsia		
Yes	15	5.3
No	268	94.7
Washing Habit of genitals		
Yes	283	100
No	0	0
Water Source for washing genitals		
river water	9	3.2
Tape water	248	87.6
Well water	26	9.2
Direction of washing genitals		

Back to front	20	7.1
Front to back	263	92.9

Abbreviation: DM: diabetes mellitus, UTI: urinary tract infection

4.3. Prevalence of asymptomatic bacteriuria among pregnant women

The prevalence of ASB among pregnant women in this study was 14.85% (n=42/283).The prevalence of ASB significantly decrease with increasing educational status as pregnant women without any kind of education and without formal education had significantly higher prevalence of ASB than their counter parts (x^2=26.05; p=0.001); 37.1% and 31%, respectively. Pregnant women in 2ndtrimester and 1st trimester had significantly higher prevalence of ASB than those in 3rd trimester (x^2=12.56; p=0.002); 20.7% vs. 19.2% vs. 4.6%, respectively. With respect to clinical parameters, pregnant women with previous history of UTI (x^2=10.69; p=0.001) and catheterization (x^2=16.81; p=0.001) had significantly higher prevalence of ASB than their counter parts; 21.7% vs 7.9% for previous history of UTI and 40% vs 11.9% for history of catheterization.(Table 3).

Table 3. Prevalence of asymptomatic bacteriuriain relation to clinical, reproductive health and hygiene related characteristics of the pregnant women attending antenatal care (ANC) clinic of Assosa General Hospital, Benishangul Gumuz Region, western Ethiopia, from January to February, 2019 (n=283)

Characters	Asymptomatic bacteriuria		Total No	Chi-square value	p-value
	Positive No(n=42)	Negative No(n=241)			
Age					
15-24	23(13.6)	146(86.4)	169		
25-34	18(18.5)	79(81.5)	97	2.34	0.310
35-44	1(5.8)	16(94.2)	17		
Residence					
Urban	39(16.2)	202(83.8)	241	2.31	0.128
Rural	3(7.1)	39(92.9)	42		
Educational status					
Illiterate	13(37.1)	22(62.9)	35		
Read and write	9(31)	20(69)	29	26.05	0.001
Primary	11(11.2)	87(88.8)	98		
Higher > 12	9(7.4)	112(92.6)	121		
Family monthly income (birr)					
<500	15(24.2)	47(75.8)	62		
500-1999	8(12.1)	58(87.9)	66	5.49	0.064
> 1999	19(12.3)	136(87.7)	155		
Gestational age					
First trimester	14(19.2)	59(80.8)	73		
Second trimester	24(20.7)	92(79.3)	116	12.56	0.02
Third trimester	4(4.6)	90(95.7)	94		
Parity					
Nullipara	6(10.7)	50(89.2)	56		
Primipara	16(13)	107(87)	123	2.67	0.264
Multipara	20(19.2)	84(80.8)	104		
History of UTI					
Yes	31(21.7)	112(85.3)	143	10.692	0.001
No	11(7.9)	129(92.1)	140		

History of catheterization					
Yes	12(40)	18(60)	30	16.80	0.001
No	30(11.9)	223(88.1)	253		
History of DM					
Yes	1(16.7)	5(83.3)	6	0.02	0.899
No	41(17.4)	236(82.6)	277		
History of obstetric and gynecological Surgery					
Yes	3(21.4)	11(78.6)	14	0.51	0.477
No	39(14.5)	230(85.5)	269		
History of preeclampsia					
Yes	3(20)	12(80)	15	0.334	0.564
No	39(14.5)	229(85.4)	268		
Washing of genital during toilet	42(14.8)	241(85.2)	283		
Yes	0()	0()	0		
No					
Water source for washing genital					
Pipe	1(11.1)	8(88.9)	9		
Well	37(15)	211(85)	248	0.07	0.948
River	4(15.4)	22(84.6)	26		
Direction of washing genital					
Back to front	5(25)	15(75)	20	1.757	0.185
Front to back	37(14)	226(86)	263		

Abbreviation: DM: diabetes mellitus, UTI: urinary tract infection

4.4. Bacterial uropathogens isolated from pregnant women with ASB

In this study, a total of 283 midstream urine sample from pregnant women without sign and symptoms of UTI were cultured for isolation, identification and antimicrobial susceptibility of bacterial uropathogens. Among these cultured urine samples, a total of 42 bacteria (14.8%) were isolated (colony forming unit $>10^5$/ml of urine), out of which gram-negative bacteria accounted for 66.7% (n=28) while gram-positive bacteria accounted for 33.3% (n=14) of the isolates. Five different species of bacteria were isolated: E. coli was the most predominant isolate (50%, n=21) followed by K. pneumoniae (16.7%, n=7), S. aureus (14.3%, n=6), coagulase negative

staphylococci (CONS) (11.9%, n=5), and group B streptococci (GBS) (7.1%, n=3). Among the isolated gram-negative bacteria, E. coli was the most common bacteria isolate (75%) followed by K. pneumoniae (25%). Similarly, S. aureus was the most commonly isolated gram-positive bacteria (42.9%) followed by CONS (35.7%), and group B streptococci (GBS) (21.4%)(Fig 2).

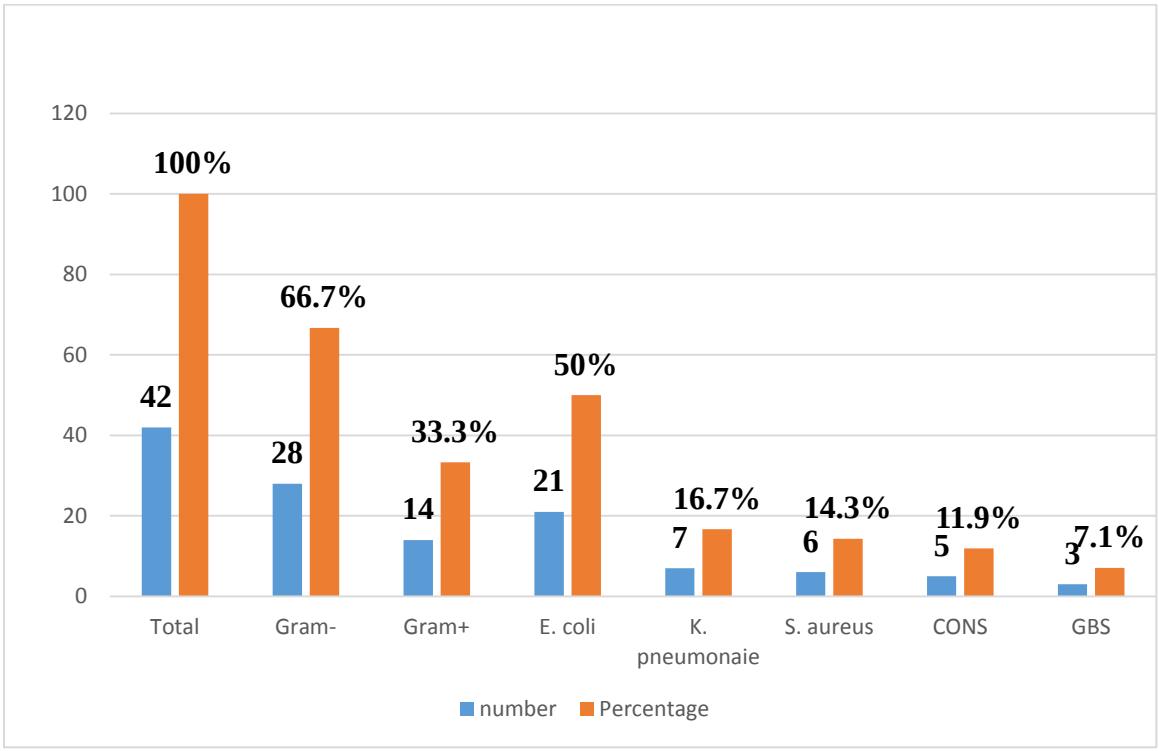

Fig 2. Frequency of bacterial uropathogens isolated from pregnant women without sign and symptoms of UTI attending ANC clinic of Assosa General Hospital, BenishangulGumuz Region, Western Ethiopia, from January to February, 2019 (n=283)

4.5. Antimicrobial susceptibility pattern of isolated bacterial uropathogens

4.5.1. Antimicrobial susceptible patterns of Gram-negative bacterial isolates

Gram-negative bacteria were highly resistant for tetracycline (96.4%), ampicillin (92.9%), trimethoprim-sulfamethoxazole (82.1%), amoxicillin- clavulanic acid (75%), nalidixic acid (60.7%) and gentamycin (57.1%) while were susceptible for tobramycin, amikacin and ciprofloxacin, 85.7%, 75% and 57.1% respectively. Gram-negative isolates were also 35.7%, 35.7%, 14.3%, and 3.6% resistant for ceftriaxone, cefotaxime, ceftazidme, and meropenem, respectively. All K. pneumoniae isolates (100%) were resistant for tetracycline, ampicillin and

trimethoprim-sulfamethoxazole while all isolates (100%) were susceptible for ceftazidime and meropenem. About 71.4% of K. pneumoniae isolates were resistant for nalidixic acid, ciprofloxacin, gentamycin, amoxicillin- clavulanic acid and cefotaxime while 57.1% were resistant for ceftriaxone, tobramycin and amikacin. Similarly, E. coli isolates were highly resistant for tetracycline (95.2%), ampicillin (90.5%), trimethoprim-sulfamethoxazole (76.2%), augmentin (76.2%), nalidixic acid (57%) and gentamycin (52.4%) while were 100%, 85.7% and 66.6%susceptible for tobramycin, amikacin, and ciprofloxacin, respectively. Resistant rates of E. coli for ceftriaxone, cefotaxime, ceftazidime and meropenem were 28.6%, 23.8%, 19%, and 4%, respectively (Table 4).

Bacterial isolates (no.)		Antimicrobial agents tested												
		TER	NA	CIP	SMT	GEN	AMK	TOB	AMP	AMX-C	CEF	CTX	CAZ	MER
E. coli (n=21)	S	1 4.8	9 42.9	14 66.6	5 23.8	10 47.6	18 85.7	21 100	2 9.5	5 23.8	15 71.4	16 76.2	17 81	20 95.2
	R	20 95.2	12 57.1	7 33.4	16 76.2	11 52.4	3 14.3	0 0	19 90.5	16 76.2	6 28.6	5 23.8	4 19	1 4.8
K. pneumonia(7)	S	0 0	2 28.6	2 28.6	0 0	2 28.6	3 42.9	3 42.9	0 0	2 28.6	3 42.9	2 28.6	7 100	7 100
	R	7 100	5 71.4	5 71.4	7 100	5 71.4	4 57.1	4 57.1	7 100	5 71.4	4 57.1	5 71.4	0 0	0 0
Total (n=28)	S	1 3.6	11 39.3	16 57.1	5 17.9	12 42.9	21 75	24 85.7	2 7.1	7 25	18 64.3	18 64.3	24 85.7	27 96.4
	R	27 96.4	17 60.7	12 42.9	23 82.1	16 57.1	7 25	4 14.3	26 92.9	21 75	10 35.7	10 35.7	4 14.3	1 3.6

S: susceptible; R: resistant; CPR: ciprofloxacin; TER: tetracycline; STX: trimethoprim-sulfamethoxazole; CEF: ceftriaxone; AMP: aampicillin; Amox-clav: amoxicillin-clavulanic acid; CAZ: ceftazidime; GEN: gentamycin; AMK: amikacin; MER: meropenem;NA: nalidixicacid;COF: cefotaxime

Table 4. Antimicrobial susceptibility pattern of gram-negative bacteria isolated from the urine of pregnant women without sign and symptoms of UTI attending ANC clinic of Assosa General Hospital, BenishangulGumuz Region, Western Ethiopia, from January to February 2019 (n=28)

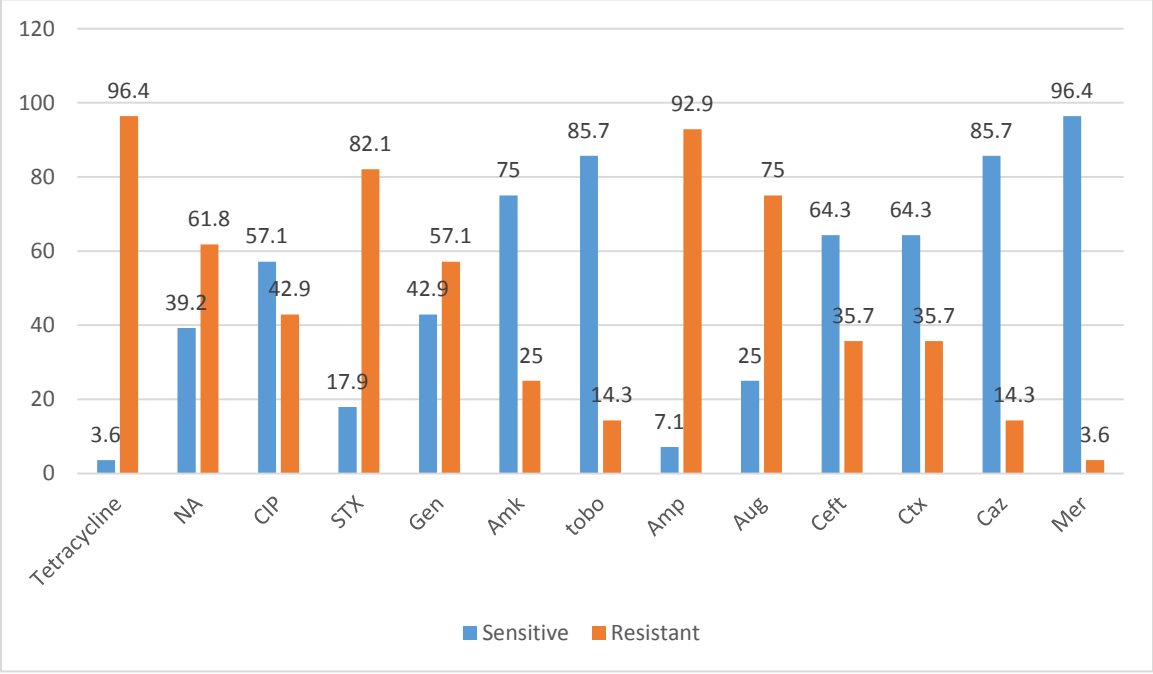

Fig 3.Overall antimicrobial susceptibility pattern of gram-negative bacterial isolated from pregnant women attending ANC clinic of Assosa General Hospital, Benishangul Gumuz Region, Western Ethiopia, from January to February 2019 (n=28)

4.5.2. Antimicrobial susceptibility patterns of Gram-positive bacterial isolates

Gram-positive bacteria were highly resistant for tetracycline (100%), trimethoprim-sulfamethoxazole (78.6%), penicillin (71.4%), amoxicillin- clavulanic acid (75%) and nalidixic acid (57.1%) while were 100% sensitive for ceftazidime. Gram-positive isolates were 7.1%, 7.1%, 14.3%, 21.4%, 29.6%, 35.7%, and 35.7% resistant for vancomycin, clindamycin, tobramycin, chloramphenicol, norfloxacillin, ciprofloxacin and erythromycin, respectively.S. aureusisolatesshowed high rate of resistant for tetracycline (100%),trimethoprim-sulfamethoxazole (83.3%), penicillin (83.3%) and nalidixic acid (50%), however, were 100% sensitive for clindamycin, tobramycin and ceftazidime. (Table 5).

Table 5. Antimicrobial susceptibility pattern of gram-positive bacteria isolated from the urine of pregnant women without sign and symptoms of UTI attending ANC clinic of Assosa General Hospital, Benishangul Gumuz Region, Western Ethiopia, from January to February 2019 (n=14)

Bacterial isolates (no.)	Antimicrobial agents tested											
		CLI	ERY	CAF	PE	CAZ	NA	TOB	CIP	STX	NOR	VAN	TET
S. aureus(6)	S	6 (100)	4 (66.7)	5 (83.3)	1 (16.7)	6 (100)	3 (50)	6 (100)	4 (66.7)	1 (16.7)	5 (83.3)	5 (83.3)	0 (0)
	R	0 (0)	2 (33.3)	1 (16.7)	5 (83.3)	0 (0)	3 (50)	0 (0)	2 (33.3)	5 (83.3)	1 (16.7)	1 (16.7)	6 (100)
CoNS (5)	S	4 (80)	3 (60)	4 (80)	2 (40)	5 (100)	2 (40)	4 (80)	3 (60)	1 (20)	3 (60)	5 (100)	0 (0)
	R	1 (20)	2 (40)	1 (20)	3 (60)	0 (0)	3 (60)	1 (20)	2 (40)	4 (80)	2 (40)	0 (0)	5 (100)
GBS(3)	S	3 (100)	2 (66.7)	2 (66.7)	1 (33.3)	3 (100)	1 (33.3)	2 (66.7)	2 (66.7)	1 (33.3)	2 (66.7)	3 (100)	0 (0)

	R	0 (0)	1 (33.3)	1 (33.3)	2 (66.7)	0 (0)	2 (66.7)	1 (33.3)	1 (33.3)	2 (66.7)	1 (33.3)	0 (0)	3 (100)
TOTAL(14)	S	13 (92.9)	9 (64.3)	11 (78.6)	4 (28.6)	14 (100)	6 (42.9)	12 (85.7)	9 (64.3)	3 (21.4)	10 (71.4)	13 (92.9)	0 (0)
	R	1 (7.1)	5 (35.7)	3 (21.4)	10 (71.4)	0 (0)	8 (57.1)	2 (14.3)	5 (35.7)	11 (78.6)	4 (29.6)	1 (7.1)	14 (100)

CLN: clindamycin; ERY: erythromycin; CAF: Chloramphenicol; Pen: penicillin; CAZ: ceftazidime; CPR: ciprofloxacin; TET: tetracycline; STX: trimethoprim-sulfamethoxazole; NOR: norfloxaci; VAN: vancomycin;

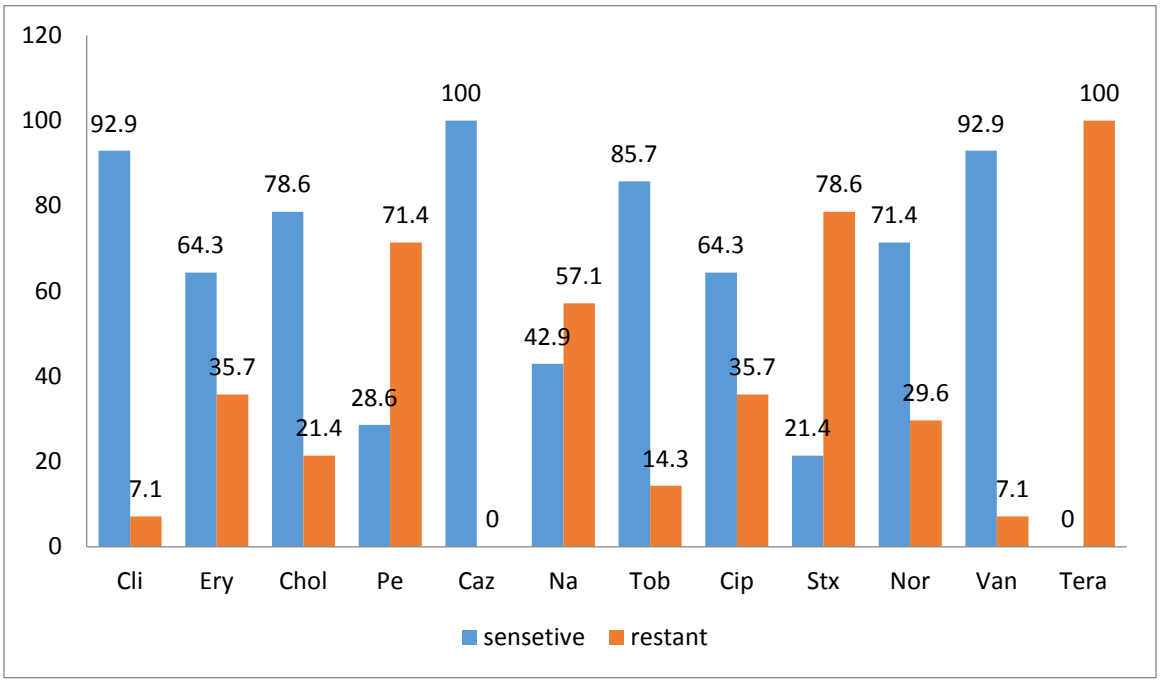

Fig 4. Overall antimicrobial susceptibility pattern of gram-positive bacterial isolated from pregnant women attending ANC clinic of Assosa General Hospital, Benishangul Gumuz Region, Western Ethiopia, from January to February 2019 (n=14)

4.5.3. Multidrug resistance patterns of bacterial isolates

Among the total isolates (n=42) multi-drug resistance (MDR= resistance to three or more antibiotics of different classes) were recorded in 76.2% (n=32/42). About 52.3% (n=22/42) of gram-negative bacteria isolates showed MDR, out of which 16.7% (n=7/42) of K. pneumonia isolates and 35.7% (n=15/42) of E. coli isolates showed MDR. Regarding gram-positive isolates, 24% (n=10/42) of the isolates were MDR, out of which 12% (n=5/42), 7.1% (n=3/42) and 5% (n=2/42) of S. aureus, CoNS, and GBS isolates showed MDR, respectively. (Table 6)

Table 6. Multidrug resistance (MDR) pattern of the isolated bacterial uropathogens among pregnant women attending ANC clinic of Assosa General Hospital, BenishangulGumuz Region, Western Ethiopia, from January to February 2019 (n=42)

	Antimicrobial pattern						
Bacterial isolate	Total (%)	R0	R1	R2	R3	R4	R5
Gram negative	**28** **66.7**	**1** **3.6**	**2** **7.1**	**3** **10.7**	**7** **25**	**6** **21.4**	**9** **32.1**
Escherichia coli	21 75	1 4.8	2 9.5	3 14.3	5 23.8	4 19	6 28.5
K. pneumonia	7 25	0 0	0 0	0 0	2 28.6	2 28.6	3 42.8
Gram positive	**14** **33.3**	**0** **0**	**3** **21.4**	**1** **7.1**	**0** **0**	**3** **21.4**	**7** **50**
Staphylococcus aureus	6 42.8	0 0	1 16.7	0 0	0 0	1 16.7	4 66.7
C0NS	5 35.7	0 0	1 20	1 20	0 0	1 20	2 40
GBS	3 21.4	0 0	1 33.3	0 0	0 0	1 33.3	1 33.3
TOTAL	**42** **100**	**1** **2.4**	**5** **11.9**	**4** **9.5**	**7** **16.7**	**9** **21.4**	**16** **38**
R0: no resistance; R1: resistence to one; R2: resistance to two; R3: resistance to three; R4: resistance to four; R5: resistance to five antibiotics							

4.6. Factors associated with the prevalence of asymptomatic bacteriuria among pregnant women

In multivariate logistic regression, educational status [illiterate (AOR=14.7; 95%CI: 4.06-52.63), without formal education (AOR=9.8; 95%CI: 2.81-34.78)], gestational age [1st trimester (AOR=6.76; 95%CI: 1.81-25), 2nd trimester (AOR=6.9; 95%CI: 2.0-23.81)], history of UTI (AOR: 3.46; 95%CI: 1.48-8.1) and history of catheterization (AOR: 4.1; 95%CI:1.7-10.2) were

significantly associated with asymptomatic bacteriuria among pregnant women. However, the other variables included in this study were not associated with asymptomatic bacteriuria (p>0.05).

Table 7. Factors associated with asymptomatic bacteriuria among pregnant women attending antenatal care (ANC) clinic of Assosa General Hospital, Benishangul Gumuz Region, western Ethiopia, from January to February, 2019 (n=283)

Variables						
	Positive No (%)	Negative No (%)	COR (95%CI)	p	AOR (95%CI)	P
Age						
15-24	23(13.6)	146(86.4)	2.52 (0.32-20)	0.381		
25-34	18(18.5)	79(81.5)	3.65 (0.45-29.41)	0.224		
35-44	1(5.8)	16(94.2)	Ref (1)			
Residence						
Urban	39(16.2)	202(83.8)	2.51 (0.74-8.55)	0.140	3.93 (4.06-52.6)	
Rural	3(7.1)	39(92.9)	Ref (1)		Ref (1)	
Educational status						
Illiterate	13(37.1)	22(62.9)	7.35 (2.8-19.23)	0.001	14.7(4.06-52.63)	0.001
Without formal education	9(31)	20(69)	5.59 (1.98-15.87)	0.001	9.8(2.81-34.48)	0.001
Primary	11(11.2)	87(88.8)	1.57 (0.62-3.97)	0.337	1.97(0.71-5.46)	
Higher > 12	9(7.4)	112(92.6)	Ref (1)			
Marital status						
Single	1 (11.1)	8 (88.9)	Ref (1)			
Married	41 (15)	233 (85)	1.41 (0.17-11.56)			
Family monthly income (birr)						
<500	15(24.2)	47(75.8)	2.28 (1.07-4.85)	0.032	1.23(0.44-3.49)	
500-1999	8(12.1)	58(87.9)	0.99 (0.41-2.38)	0.997	0.84(0.29-2.38)	
> 1999	19(12.3)	136(87.7)	Ref (1)			
Gestational age						
First trimester	14(19.2)	59(80.8)	5.35 (1.67-16.95)	0.005	6.76 (1.81-25)	0.040
Second trimester	24(20.7)	92(79.3)	5.88 (1.96-17.54)	0.002	6.9 (2.0-23.81)	0.042
Third trimester	4(4.6)	90(95.7)	Ref (1)		Ref (1)	

Parity						
Nullipara	6 (10.7)	50 (89.3)	Ref (1)			
Primipara	16 (13)	107 (87)	1.2 (0.46-3.37)	0.665	1.32 (0.38-4.58)	
Multipara	20 (19.2)	84 (70.8)	1.98 (0.75-5.26)	0.169	1.83 (0.54-6.21)	
History of UTI						
Yes	31(21.7)	112(85.3)	3.25 (1.56-6.76)	0.002	3.46 (1.48-8.1)	0.004
No	11(7.9)	129(92.4)	Ref (1)		Ref (1)	
History of catheterization						
Yes	18(30)	42(70)	3.36 (1.77-7.14)	0.001	4.11 (1.66-10.16)	0.002
no	24(10.8)	199(89.2)	Ref (1)		Ref (1)	
History of DM						
Yes	1	5	1.15 (0.13-10.11)	0.899		
No	41	236	Ref (1)			
History of obstetric and gynecological Surgery						
Yes	11(19.2)	46(80.7)	1.5(0.7-3.21)			
No	31(13.7)	195(86.3)	Ref(1)			
History of preeclampsia						
Yes	3(20)	12(80)	1.47 (0.4-5.44)	0.566		
No	39(14.5)	229(85.4)	Ref (1)			
Washing of genital during toilet						
Yes	42	241				
No	0	0				
Water source for washing genital						
River	1(11.1)	8(88.9)	Ref (1)			
Tape water	37(15)	211(85)	1.4 (0.17-11.5)	0.75		
Well	4(15.4)	226(84.6)	1.45 (0.14-1.52)	0.75		
Direction of washing genital						
Back to front	5(25)	15(75)	2.04 (0.7-5.94)	0.193	1.10 (0.23-5.10)	
Front to back	37(14)	226(86)	Ref (1)		Ref (1)	

5. DISCUSSION

In this study, the prevalence of asymptomatic bacteriuria(ASB) among pregnant women attending antenatal clinic of Assosa General Hospital was 14.8% which is comparable with studies done in Adama Central Ethiopia (16.1%), Dessie Northwest Ethiopia(15.6%) and with study done in India(13.8%)[21,22,51]. However, our finding was relatively lower than studies done in Adigrat Northern Ethiopia (21.2%) [20], Hawassa Southern Ethiopia (18.8%) [19], Ambo Central Ethiopia(17.8%) [52] studies done in Southeast Nigeria(79.2%) [15], Nairobi Kenya(21.5%) [16], Sulaimani city Iraq 42.9%) [17] And Maharashtra India(23%)[18]; but was higher than studies done in Dire Dawa Eastern Ethiopia (11%)[**23**],Baher Dare Northwest Ethiopia (8.5%)[24], Ghana (7.3%) [53], Tanzania (8.9%) [54], Egypt (10%) [14], Kashmir (6.1%) [55] Iran (11.5%) [56], Manipal, India(8.4%) [57] and Ajman, United Arab Emirates(11.7%) [58]. The possible explanation for this variation of might be differences in geographical location, socio-demographic characteristics of the study participants, socio-economic and socio-cultural characteristics of the study participants, level of education, methods of detecting ASB, and differences in habit of keeping personal hygiene.

In this study, gram- negative bacteria (66.7%) were more prevalent than gram- positive bacteria (33.4%) which are consistent with other studies done in Adigrat Northern Ethiopia (64.1%) [21]. and studies done in Nairobi Kenya (78.8%) [16], central region of Iran (69.6%) [56] and Bengal India(62.3%) [59]. This might be due to the fact that most uropathogenic bacteria in pregnant women are gram negative that usually originate from the bowel and ascend to the upper urinary tract due to the close proximity of female urethra to the anal area. In addition, during pregnancy difficulties in cleaning genital area during defecation might result in contamination of female urinary tract with fecal bacteria (mostly gram-negative). Gram-negative bacteria have also a unique structure (pilus adhesions) which help the bacteria to attach to the uroepithelium lining and prevent them from urinary lavage which facilitate bacterial multiplication and invasion of upper urinary tract [60].However, our finding is in contrary to studies done in Dessie Northeast Ethiopia [22], Hawassa Southern Ethiopia [19], and studies done in Maharashtra, India [18] and which reported the predominance of gram-positive bacteria over gram-negative bacteria among pregnant women with ASB. The possible explanation for this discrepancy might be due

to differences in environmental conditions such as temperature and humidity between these different study areas and differences in the level of antimicrobial usage by patients among these different study sites, all of which could affect the distribution of bacteria in different countries and among different regions in the same country.

Regarding bacterial species, E. coli (50%) was the predominant bacterial isolates observed in this study followed by K. pneumonia (16.7%), S. aureus (14.3%), CoNS (11.9%) and GBS (7.1%). The predominance of E. coli in our study is consistent with studies done in Adigrat Northern Ethiopia [20], Bahir Dar Northwest Ethiopia [24], Hawassa Southern Ethiopia [19] and studies done in Ghana [53], Egypt [14] and India [59].The acquired ability of E. coli to produce a number of virulence factors that facilitate colonization and invasion of the urinary epithelium might be one possible explanation for the predominance of E. coli in pregnant women with ASB [61]. Since E. coli is the most common fecal flora, and poor hygienic practices due to abdominal distension and other physiologic changes during pregnancy makes it easier for E. coli to travel up the urethra to the kidney room the perianal areas causing significant bacteriuria during pregnancy [62]. In addition, increased relaxation of ureteric smooth muscles due to hormonal changes combined with increased pressure from enlarged uterus during pregnancy results in urinary stasis which creates a suitable environment for the growth and multiplication of E. coli [26].

The result of this study showed that women's educational status, gestational age, history of UTI and history of catheterization were significantly associated with ASB among pregnant women (P value < 0.05). Although the prevalence of ASB was higher among pregnant women aged 15–24 years (13.6%) and those aged 25–34 years (18.5%) than pregnant women aged 35-44 years (5.8%), the association was not statistically significant in multivariate logistic regression ($p>0.05$). Though our finding indicated that pregnant women of all age groups are at risk of developing ASB, the finding also highlighted that young aged pregnant women (15-34 years) are relatively at higher risk of developing ASB than old aged pregnant women (>34 years) which might be due to minor urethral trauma in younger women resulting from early and intensive sexual intercourse can provide an opportunity for the transfer of uropathogenic bacteria from the perineum into the bladder [63]. Similar studies done in Adigrat Northern Ethiopia [20], Dir Dawa Eastern Ethiopia [23], Nigeria [15], Kota [64], kanpur, India [65], and Maharashtra, India [18] also showed that young aged pregnant women are at higher risk of developing ASB than old

aged pregnant women. However, studies done in Adama Central Ethiopia [21],Hawassa Southern Ethiopia[19], Ashanti Region, Ghana[25] ,Ajman, UAE[58] showed that old aged pregnant women were at higher risk of acquiring ASB than young aged pregnant women. The possible explanation for these differences might be differences in socio-economic characteristics of the pregnant women, differences in the level of education among the pregnant women and differences in risk behaviors of the pregnant women in these different study areas.

In this study, pregnant women who were illiterate and without formal education were fifteen times [AOR=14.7, 95%CI=4.06-52.63] and ten times [AOR=9.8, 95%CI=2.81-34.48] more likely to develop ASB than pregnant women with secondary education and above, respectively. This could be due to the fact that education will improve awareness and knowledge of keeping personal hygiene during pregnancy which ultimately reduce the possible contamination and infection of urinary tract from the fecal flora and risk of developing UTI. Our finding was in agreement with study done in Dire Dawa Eastern Ethiopia [23], Kota [64], Central Iran [56], but was in contrary to studies done Dessie Northeast Ethiopia [22], Bahir Dar Northwest Ethiopia [24], and studies done in Cairo Egypt [14].which report education level has no deferenace on ASB.

Similarly, the prevalence of ASB in this study was significantly associated with gestational age as pregnant women in 1sttrimester [AOR=6.76, p=0.040, 95% CI (1.81, 25)] and 2nd trimester [AOR; 6.9, p=0.042, 95% CI (2.0, 23.81)] were seven times more likely to have ASB than those pregnant women in 3rd trimester. This finding is in line with studies done in Adigrat Northern Ethiopia [20], Adama Central Ethiopia [21], Nigeria [66] and Ghana [67,25].This might be due to the fact that ASB/UTI during pregnancy begins within 6 weeks of gestation and peaks during 22–24 weeks of pregnancy due to hormone-induced urethral dilation, increased bladder volume and decreased bladder tone along with decreased urethral tone, all of which results in urinary stasis that creates conducive environment for the multiplication and growth of bacterial uropathogens with subsequent development of significant bacteriuria during early and mid-pregnancy [68].In line with our finding, screening and treatment of ASB in pregnant women by culturing the urine sample of pregnant women during 12-16 weeks of gestation is recommended to reduce the risk of pyelonephritis, preterm labor and low-birth weight infants [69].

The prevalence of ASB among pregnant women in this study was also significantly associated with previous history of UTI as pregnant women with history of UTI were three times more likely to develop ASB than their counterparts (AOR=3.46; 95%CI= 1.48-8.1). Our finding is in line with studies done in Dire Dawa Eastern Ethiopia [23], Ambo Western Ethiopia [52], Karnataka, India[51], central region of Iran[56],and Iraq [17]. The possible explanation for the association of ASB with previous history of UTI in pregnant women could be the presence of antimicrobial resistant bacterial strains from previous episodes of UTI with subsequent multiplication and growth of the resistant strains that results in development of bacteriuria particularly during alterations in immune status such as pregnancy. However, our finding was in contrary to studies done in Dessie Northeast Ethiopia [22] and Tanzania [54].The possible explanation for this difference might be differences in the risk behaviors of the pregnant women in these different study areas.

The finding of our study also showed that pregnant women with previous history of catheterization were four times more likely to develop ASB than pregnant women without history of catheterization [AOR=4.11, 95%CI=1.66-10.16; P=0.002]. The association between history of catheterization and increased risk of developing ASB in pregnant women might be explained by the fact that catheterization can induce urethral mucosa injury that provides an opportunity for transfer of uropathogenic bacteria from urethral and perianal area to upper urinary tract. In addition, contaminated catheters during frequent catheterization can also act as a source of bacteria for the infection of urinary tract that eventually results in development of ASB. Our finding is consistent with studies done in Dessie Northeast Ethiopia [22].However, our finding is in contrary to studies done in Tanzania [56].

Regarding the antimicrobial susceptibility pattern of bacterial uropathogens, the finding of our study showed that bacterial uropathogens isolated from pregnant women with asymptomatic UTI develop resistant to commonly used antimicrobial agents. In this study, Most of the Gram-negative bacterial isolates were sensitive to meropenem (96.4 %), ceftazidm (85.7 %), tobramycin (85.7 %), amikacin(75%), ceftriaxone (64.3), cefotaxime (64.3%), ciprofloxacin (57.1%) while were highly resistant for tetracycline (96.4%), ampicillin (92.9%), trimethoprim-sulfamethoxazole (82.1%), augmentin (75%), nalidixic acid (60.7%) and gentamycin (57.1%). Our finding is in line with studies done in Dessie Northeast Ethiopia [22], Baghdad, Iraq [17], and Kanpur, India[65]. Which show that most of the Gram-negative isolates were sensitive to

ceftazidm, ceftriaxone, cefotaxime, amikacin, tobramycin and ciprofloxacin and resistant to tetracycline and amoxicillin. However, our finding is in contrary to studies done in Kashmir [55], and Adigrat Northern Ethiopia [20]. Which show that most of the Gram-negative isolates were sensitive trimethoprim-sulfamethoxazole augmentin, nalidixic acid and gentamycin. The easy accessibility of the commonly prescribed antimicrobials over-the counter combined with the misuse of the antibiotics by both patients and clinicians due to lack of facilities and trained personnel for urine culture in most health facilities in Ethiopia and frequent use of common antimicrobial agents by peoples without prescription or medical supervision might be responsible for the observed high prevalence of antimicrobial resistance to commonly used antibiotics such as augmentin, nalidixic acid, gentamycin, trimethoprim-sulfamethoxazole and ciprofloxacin with increasing trends for developing resistance to β-lactamase inhibitors such as cephalosporins (ceftriaxone, cefotaxime, ceftazidime). In addition, indiscriminate use of antibiotics can kill the periurethral flora that can create an opportunity for the growth and multiplication of resistant bacterial uropathogens and exchange of resistant genes among gram-negative bacterial uropathogens mainly E. coli and others [25, 70].

Concerning the antimicrobial susceptibility of specific Gram-negative bacterial isolates, the finding of this study showed that E. coli, which was the predominant Gram-negative isolate, showed high rate of resistance to tetracycline (95.2%), ampicillin (90.5%), trimethoprim-sulfamethoxazole (76.2%), nalidixic acid (57%) and gentamycin (52.4%) while were 100%, 85.7% and 66.6% sensitive for tobramycin, amikacin, and ciprofloxacin, respectively. About 76.2%, 28.6%, 23.8%, and 19% of E. coli isolates were resistant for β- lactamase inhibitors such as augumentin, ceftriaxone, cefotaxime, and ceftazidime, respectively. Relatively similar resistant rates of E. coli isolates to gentamycin, ceftriaxone, cefotaxime and ceftazidime is reported from studies done in Ambo town, Central Ethiopia[52], Dessie Northeast Ethiopia[22]. However, lower resistant rates of E. coli for augumentin, ceftriaxone, cefotaxime, and ceftazidime are reported from studies done in Bengal, India [59], but relatively higher resistance rates for augumentin, ceftriaxone, cefotaxime, and ceftazidime are reported from studies done in Ghana [25]. The possible explanation for differences in resistance rates of E. coli to these antimicrobial agents might be differences in the misuse or indiscriminate use of the antibiotics among the study areas. Increased resistance of E. coli to β-lactamase inhibitors combined with the emergence of extended spectrum β-lactamase (ESBL) inhibitors (meropenem) resistant E.

coli isolates (4%) in this study area is a worrying situation that needs continuous monitoring and surveillance of antimicrobial resistance of E. coli mainly in highly vulnerable groups such as pregnant women. Similarly, K. pneumoniae isolates were 100% resistance to tetracycline, ampicillin and trimethoprim-sulfamethoxazole; however, (100%) sensitive for ceftazidime and meropenem. This might be due to the fact that ceftazidime and meropenem are offered in injection form and their unavailability in tablet form might minimize their misuse or indiscriminate use in the community.

The finding of our study also showed that Gram-positive bacterial isolates were highly resistant for tetracycline (100%), trimethoprim-sulfamethoxazole (78.6%), penicillin (71.4%), augmentin (75%) and nalidixic acid (57.1%). Relatively similar resistance rates of Gram-positive isolates for these antibiotics are also reported from studies done in, Gondar Northwest Ethiopia [70], and India [59] which might be due to the indiscriminate and misuse of the antibiotics for empirical therapy. In this study, most of Gram-positive bacteria isolates were sensitive for ceftazidime (100%), vancomycin (92.9%,), clindamycin (92.9%), tobramycin(85.7%),chloramphenicol (78.6%), norfloxacillin (70.4%), ciprofloxacin(64.3%) and erythromycin (64.3%). Relatively similar susceptibility rate of Gram-positive isolate to most of these antimicrobial agents are reported from studies done in Adama Central Ethiopia [21].which might be due to the relative inaccessibility of these antibiotics over the counter.

Regarding the antimicrobial susceptibility of specific Gram-positive isolates, the finding of this study showed that S. aureus showed high rate of resistance for tetracycline (100%), trimethoprim-sulfamethoxazole (83.3%), penicillin (83.3%) and nalidixic acid (50%), however, 83.7% sensitive for chloramphenicol, norfloxacillin, vancomycinand 100% sensitive for clindamycin, tobramycin and ceftazidime. This low level of resistance observed for these drugs might be related to the relative inaccessibility.Hence, these drugs can be considered as alternative options in the empirical treatment of ASB.

An irrational and unnecessary use of antibacterial agents can result in the emergence of bacterial strains that exhibit multidrug resistance [71]. In this study, multi drug resistance (MDR = resistance in $\geq$ 3 drugs) was seen in 76.2 % of the isolated bacterial uropathogens. Our finding is higher than studies done in Dessie Northeast Ethiopia (72.4%) [22], Tikur Anbessa Specialized Hospital Addis Ababa (74%) [72]. The high prevalence of MDR reported in this study might be

due to the unrestricted availability and high rate of use of prescribed drugs. It could also be related to the rapid spread of resistant bacteria and high misuse of antimicrobial drugs such as self-medication, unnecessary use, failure to adhere to standard treatment guideline, lack of appropriate infection prevention strategies and inadequate or absence of antimicrobial drug resistance surveillance program.

Although, this study is the first study that assessed the prevalence of ASB and the antimicrobial susceptibility pattern of the isolates among pregnant women in Benishangul Gumuz Region and in current study area, the study was not without limitations. The cross sectional nature of the study which makes testing of an association difficult is one of the main limitations of the study. Due to final constraints, we were unable to determine the antimicrobial susceptibility of some important antimicrobial agents such as nitrofurantoin and fosfomycin

6. CONCLUSION

The study revealed an overall high prevalence (14.8%) of ASB among pregnant women. The prevalence of ASB among pregnant women was significantly associated with educational status, gestational age, history UTI and previous history of catheterization. E. coli was the most predominant bacterial isolate followed by K. pneumoniae, S. aureus, CONS and GBS. A large number of the bacterial isolates were resistant to the commonly used antimicrobial drugs (tetracycline, ampicillin, trimethoprim-sulfamethoxazole and augmentin) but were sensitive to ceftazidime, clindamycin, cefotaxime and meropenem. The prevalence of MDR bacterial isolates among pregnant women with ASB in this study area was high. Therefore, routine laboratory diagnosis of ASB in pregnant women and providing appropriate treatment should be needed to reduce its complications. In addition, since antibiotic resistance complicates empirical regimens, local resistance rates need to be taken into consideration when deciding on therapy.

7. RECOMMENDATION

Based on the finding of this study, the following recommendations were suggested:

- Infection prevention strategy such us utilizing of sterile catheter should be continuously applied and promoted
- All pregnant women should be regular screened for asymptomatic bacteriuria and should be treated using appropriate treatment regimens based on their susceptibility pattern.
- Continuous surveillance of antimicrobial resistance pattern of bacterial uropathogens among pregnant women should be regularly performed and rational use of antibiotics should be encouraged to prevent the emergence of MDR strains.
- Assosa General Hospital should establish well equipped bacteriology laboratory in order to identify pathogens that cause ASB among pregnant women and their antimicrobial susceptibility pattern for selection of preferable antibiotic
- Tetracyclines, ampicillin, trimethoprim-sulfamethoxazole and augmentin should not be used for the treatment of bacteriuria in this study area
- Cephalosporins can be used for effective treatment of bacteriuria among pregnant women in this study area.

REFERENCE

1. Annierajaratn, Nehmaria, Homas.S. Diagnosis of asymptomatic bacteriuria and associated risk factors among pregnant women in mangalore. Karnataka, India. Journal of Clinical and Diagnostic Research. 2014,-8(9):23-25

2. S. Worku,Derbie,Alemneh Sinishaw,Adem, and F. Biadglegne. Prevalence of bacteriuria and antimicrobial susceptibility patterns among diabetic and nondiabetic patients attending at Debre Tabor Hospital, Northwest Ethiopia. International Journal of Microbiology. 2017,8.

3. Ali,Gizachew. M. Asymptomatic bacteriuria and antimicrobial susceptibility pattern of the isolates among pregnant women attending dessie referral hospital , Northeast Ethiopia : a hospital-based cross-sectional study. Turk J Urol 2018;44(3):251–60.

4. Beyene.G, Tsegaye.W. Bacterial in urinary tract infection and antibiotic susceptibility pattern in Jimma university specialized Hospital,Southwest ethiopia. Ethiop J Health Sci.2011;21(2) :141–6.

5. South Australian Maternal, Neonatal & Gynaecology Community of practiceurologic; Clinics of North America. 2017;1-10

6. Dr.Habiba.I,Abdullahi.Symptomatic bacteriuria among pregnant women attending antenatal: evaluation of screening test. IOSR Journal Of Pharmacy.2015;5(8):41-47

7. RJ. Girishbabu,R. Srikrishna,S.T Ramesh.Asymptomatic bacteriuria in pregnancy.

International Journal of Biological & Medical Research.2011;2(3):740-742

8. Jojan J, Davane.M, Patil CD, Nagoba B. Asymptomatic bacteriuria in pregnant women from rural area of latur district of maharashtra India.Journal of Krishna Institute of Medical Sciences University 2017;6(3):48–54.

9. Mathur A, Mummigatti K, Ranganathan R, Sreedharan J. Asymptomatic bacteriuria in pregnant women : a hospital based study.Gulf medical journal.2012;1:17–21.

10. Bayati AH, Ghaib AH, Nasraldeen N, Hamalaw SA, Hamid ZA. Asymptomatic bacteriuria among pregnant women in sulaimani city. G.J.B.B.2016;5(3):327–30.

11. Mwei MK. Asymptomatic bacteriuria among pregnant women attending antenatal clinic at

kilimanjaro christian medical centre in northern tanzania. Clin. Pract 2018;15:917–22.

12. Pulcini,C.Tebano, Gianpiero.M, Nico,T.Selective reporting of antibiotic susceptibility test results in European countries: an ESCMID cross-sectional survey. International Journal of Antimicrobial Agents. 2017;49(2) 162-166

13. Courage S, Bscn.RN. Recommendations on screening for asymptomatic bacteriuria in pregnancy. Cmaj 2018;190(27):823–30.

14. Elzayat MA,Barnett-Vanes A, Farag M, Dabour E, Cheng F. Prevalence of undiagnosed asymptomatic bacteriuria and associated risk factors during pregnancy : a cross-sectional study at two tertiary centres in cairo , egypt. BMJ. 2017;1–7.

15.KC.Ekwedigwe,Sunday-Adeoye1,Eliboh,Isikhuemen,Uro-Chukwu, EzeonuB. et.al. prevalence and antimicrobial susceptibility of asymptomatic bacteriuria among women with pelvic organ prolapse in abakaliki, south-east nigeria. bmc women's health.2018;18(53) 2-5

16 Adelaide,Ogutu A & Gideon K, Christine B, Samuel K. college prevalence aetiology and antibiotic sensitivity profile of asymptomatic bacteriuria isolates from pregnant women in selected antenatal clinic from nairobi, kenya the pan african medical journal. 2017;26:41

17. Ali Hattem Bayati, Avan Hussain Ghaib, Narmeen Nasraldeen, Soran Amin Hamalaw & Zainab A. Hamid Asymptomatic bacteriuria among pregnant women in sulaimani city. g.j.b.b.2016: 5 (3)327-330

18. Jyoti J, Milind Davane, Chandrakala Dawle,Basavraj Nagob. asymptomatic bacteriuria in pregnant women from rural area of latur district of maharashtra, india journal of Clinical and Diagnostic Research.2017; 6:3

19. Tadesse E, Teshome M, Merid Y, Kibret B, Shimelis T. Asymptomatic urinary tract infection among pregnant women attending the antenatal clinic of hawassa referral hospital , southern Ethiopia. BMC Research Notes. 2014;7:155

20. Tadesse S, Kahsay T, Adhanom G, Kahsu G, Legese H, Aderajew G. Prevalence , antimicrobial susceptibility profile and predictors of asymptomatic bacteriuria among pregnant women in adigrat general hospital , northern ethiopia. Bmc res notes . 2018;1–6.

21. Abdul Kairun Nisha, Alemayehu Edossa Etana and Hailemichael Tesso. prevalence of

asymptomatic bacteriuria during pregnancy in adama city, ethiopia international journal of microbiology and immunology research. 2015;3(5), 058-063

22. Ismail Ebrie Ali, Teklay Gebrecherkos, Mucheye Gizachew,Martha Alemayehu Menberu, asymptomatic bacteriuria and antimicrobial susceptibility pattern of the isolates among pregnant women attending dessie referral hospital, northeast ethiopia: a hospital-based cross-sectional study, turk j urol 2018; 44(3): 251-60

23. Rizvi M, Khan F, Shukla I, Malik A, Shaheen. Rising prevalence of antimicrobial resistance in urinary tract infections during pregnancy: necessity for exploring newer treatment options. J lab phys 2011; 3(2):98-103.

24. Tazebew Demilie1 , getenet beyene2 , selabat melaku3 , wondewosen tsegaye* 2 urinary bacterial profile and antibiotic susceptibility pattern among pregnant women in north west ethiopia ethiop j health sci. Vol. 22, no. 2 july 2012

25. Acheampong, Desmond O.Afoakwah, Michael K. Boye, Evaluation of Diagnostic Methods and Antimicrobial Susceptibility Pattern of Asymptomatic Bacteriuria Among Pregnant Women in Ashanti Region, Ghana, ournal of Exploratory Research in Pharmacology2018 vol. 3 | 78–84

26. Nicolle le, bradley s, colgan r, rice jc, schaeffer a, hooton tm. Infectious diseases society of america guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults.Clinical Infectious Diseases 2005;643–54.

27. Chand, Anita E Sharma, Anita Sharma, Saurabh prevalence of asymptomatic bacteriuria in pregnant women attending antenatal clinics of gmc, kota gjra - global journal for research analysis,2018;(4):83–5.

28. Curtiss n, duckett j. Urinary tract infection in obstetrics and gynaecology. Obstetrics, Gynaecology and Reproductive Medicine, 2017;27(9):261–5. Available from: http://dx.doi.org/10.1016/j.ogrm.2017.06.006

29. Kang c, kim j, park dw, kim b, ha u, lee s, et al. Clinical practice guidelines for the antibiotic treatment of community-acquired urinary tract infections.Infection &

Chemotherapy, 2018;50(1):67–100.

30. Nicolle LE. Management of asymptomatic bacteriuria in pregnant women. Lancet infect dis 2015;3099(15):10–1.

31. Abduljabbar A, Aljanaby J, Abduljabbar I, Aljanaby J. Antimicrobial sensitivity pattern of pathogenic bacteria isolated from older women with asymptomatic bacteriuria . Biomedical Research,2018;29(12):2597–601.

32. Schnarr J. Asymptomatic bacteriuria and symptomatic urinary. European Journal of Clinical Investigation 2008;38:50–7.

33. US Preventive Services Task Force (USPSTF). Screening for asymptomatic bacteriuria: recommendation statement. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ), 2004.

34. Nicolle LE, Bradley S, Colgan R et al. Infectious diseases society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis 2005; 40: 643–654.

35. National Collaborating Centre for Women's and Children's Health. Clinical Guideline 6. Antenatal Care. Routine care for the healthy pregnant woman. London: National Institute for Clinical Excellence,2003.

36. Naber KG, Bergman B, Bishop MC et al. EAU guidelines for the management of urinary and male genital tract infections. Urinary Tract Infection (UTI) Working Group of the Health Care Office (HCO) of the European Association of Urology (EAU). Eur Urol 2001; 40: 576–588

37. Nicolle LE. Screening for asymptomatic bacteriuria in pregnancy. In Canadian guide to clinical preventive health care. Ottawa: Health Canada, 1994, p100–106

38. Scottish Intercollegiate Guidelines Network. Management of suspected bacterial urinary tract infection in adults. A national clinical guideline. Edinburgh: Scottish Intercollegiate Guidelines Network, July 2006.

39. School of Chemical and Biotechnology, sastra University, India.Urinary tract infection :

an overview of the infection and the associated risk factors. Journal of Microbiology & Experimentation 2014;1(2):1–15.

40. Sunil S, Nair AA, Sharifi S, Thomas TS. A review on urinary tract infection in pregnancy. International Journal of Pharma Research & Review.2018;7:1–6.

41. Mageto, Vincent Mogaka Gatwiri, Mathenge Scholastica Njoroge, wachukahospital r. Uropathogens antibiotic resistance patterns among type 2 diabetic patients in kisii teaching and referral hospital, kenya. Pan African Medical Journal 2018;8688:1–5.

42. Larsen B, Monif . Understanding the bacterial flora of the female genital tract. Clinical Infectious Diseases, 2001;4198:69–77.

43. Wondimeneh Y, Muluye D, Alemu A, Atinafu A, Yitayew G, Gebrecherkos T, et al. Urinary tract infection among obstetric fistula patients at gondar university hospital , northwest ethiopia.BMC Women's Health 2014;2–7.

44. Tract U, during I,Delzell JE, Lefevre ML. Urinary tract infections during pregnancy. 2016;1–5.

45. Gebrecherkos T, Gizachew M, Alemayehu M. Asymptomatic bacteriuria and antimicrobial susceptibility pattern of the isolates among pregnant women attending dessie referral hospital , northeast asymptomatic bacteriuria and antimicrobial susceptibility pattern of the isolates among pregnant women attending dessie referral hospital , northeast ethiopia : a hospital-based cross-sectional study. Turk J Urol 2018; 44(3): 251-60

46. Turpin, CA Minkah, Bridget Danso, KA Frimpong, Eh. Asymptomatic bacteriuria in pregnant women at- tending antenatal clinic at komfo anokye teach- Ghana medical journal. 2007;41(1):26–9.

47. Beetz R, Westenfelder M. antimicrobial agents antimicrobial therapy of urinary tract infections in children ☪. Int j antimicrob agents . 2018;38(2011):42–50.

48. Rukweza JM-, Haruzivishe C, Gidiri FM. Asymptomatic bacteriuria in pregnancy : a concept analysis.Journal of Microbiology Research and Reviews 2017;4(1):2–11.

49. Mukherjee K, Golia S, CV. Bhattacharjee D, Chakroborti G. A study on asymptomatic bacteriuria in pregnancy : prevalence , etiology and comparison of screening methods. Nternational Journal of Research in Medical Sciences 2014;2(3):1085–91.

50 Clinical Laboratory Standard Institute.Performance standards for antimicrobial susceptibility testing clsi supplement . Wayne: clinical and laboratory standards institute; 2016. P. 256

51. Annie Rajaratnam, Neha Maria Baby, Thomas .S. Kuruvilla, Santhosh Machado. diagnosis of asymptomatic bacteriuria and associated risk factors among pregnant women in mangalore, karnataka, india journal of clinical and diagnostic research. 2014 sep, vol-8(9): oc23-oc25

52. Yonas Alem Gessese, Dereje leta Damessa, Mebratenesh Mengistu Amare, Yonas Hailesilassie Bahta, Assalif Demisew Shifera, Fikreslasie Samuel Tasew et.al. urinary pathogenic bacterial profile, antibiogram of isolates and associated risk factors among pregnant women in ambo town, central ethiopia: a cross-sectional study antimicrobial resistance and infection control (2017) 6:132

53. C.A. Turpin, Bridget Minkah, K.A. Danso, and E.H. Frimpong. asymptomatic bacteriuria in pregnant women at- tending antenatal clinic at komfo anokye teach- ing hospital, kumasi, ghana ghana medical journal.2007;41:1

54. Moses kyania mwei1 bariki mchome1 beatrice john2 and eusebious maro asymptomatic bacteriuria among pregnant women attending antenatal clinic at kilimanjaro christian medical centre in northern tanzania 917 clin. Pract. 2018;15(6): 917-922

55. Shamweel Ahmad, Shehla Shakooh, Sajad Ahmad Salati, Abdul Muniem prevalence of asymptomatic bacteriuria among pregnant women in kashmir sri lanka journal of obstetrics and gynaecology 2011; 33: 158-162

56. Aliasghar Farazia, Mansooreh Jabbariasl B. a asymptomatic bacteriuria in pregnancy in the central region of iran: frequency, risk factors, and causative organisms clinical epidemiology and global health, 2018;.09; 009

57. Avivar awasthi A, Prashanth Adiga B. sugandhi rao prevalence of asymptomatic bacteriuria and sterile pyuria in pregnant women attending antenatal clinic in a tertiary care center in karnataka: a pilot study clinical epidemiology and global health.2013;1:44-49

58. Anuj Mathu,Kasturi Mummigatti,Ramesh Ranganathan, Jayadevan. asymptomatic bacteriuria in pregnant women: a hospital based study Ajman, UAE,GULF MEDICAL JOURNAL, 2012;1(1):17-21

59. Kheya Mukherjee, Saroj Golia, Vasudha, Babita, Debojyoti Bhattacharjee, Goutam Chakroborti. a study on asymptomatic bacteriuria in pregnancy: prevalence, etiology and comparison of screening methods Bengal, India international journal of research in medical sciences. 2014;(2)3:1087

60. J. Schnarr and F. asymptomatic bacteriuria and symptomatic urinary tract infections in pregnancy european journal of clinical investigation.2009;38: 51

61. Lavigne JP, Boutet-Dubois, Laouini, Combescure, Bouziges, Mares, and Sotto. Virulence potential of e. Coli strains causing asymptomatic bacteriuria during pregnancy. J clinmicrobiol.2011;49(11):3950–3

62. Ramos NL, Sekikubo M, Dzung DT, Kosnopfel C, Kironde F, Mirembe F, Brauner A. Uropathogenic E. Coli isolates from pregnant women in different countries. J clinmicrobiol. 2012;50(11):3569–74

63. Jalali M, Shamsi M, Roozbehani N, et al. Prevalence of urinary tract infection and some factors affected in pregnant women in Iran Karaj City. Middle East J Sci Res 2014;20:781–5

64. Dr.Anita E. Chand, dr. Anita sharma, dr. Saurabh Sharm. prevalence of asymptomatic bacteriuria in pregnant women attending antenatal clinics of gmc, kota - global journal for research.2018;7(4):2277 – 8160

65. Ujatha R, Nawan M. Prevalence of asymptomatic bacteriuria and its antibacterial susceptibility pattern among pregnant women attending the antenatal clinic at kanpur, India. J Clin Diagn Res. 2014;8(4):01–3.

66. Kehinde AO, Adedapo KS, Aimaikhu CO, Odukogbe AA, Olayemi O, Salko B. Significant bacteriuria among asymptomatic antenatal clinic attendees in ibadan, nigeria. Trop med health 2011; 3(3):73-76

67. Boye A, Siakwa P, Boampong J, Koffuor G, Ephraim R, Amoateng P, et al. Asymptomatic urinary tract infections in pregnant women attending antenatal clinic in cape coast, ghana. j med res 2012; 1(6):74-83

68. Judith Musona- Rukweza1 et al Asymptomatic Bacteriuria in Pregnancy: A Concept analysis journal of Microbiology Research and Reviews.2017:4(1),1-11

69. Guidelines of the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC). Enferm Infecc Microbiol Clin.2016;11:005.

70 Alemu A. et al. Bacterial profile and drug susceptibility pattern of urinary tract infection in pregnant women at university of gondar teaching hospital, northwest ethiopia. Bmc res notes. 2012;5:197

71. Wolday D, Erge W.bacterial in urinary tract infection and antibiotic susceptibility pattern in jimma university specialized hospital , southwest ethiopia ethiop med j , 1997, 35, 127–135

72 Assefa A, Asrat D, Woldeamanuel Y, G/Hiwot Y, Abdella A, Melesse T. Bacterial profile and drug susceptibility pattern of urinary tract infection in pregnant women at Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia. Ethiop Med J 2008;46:227-35

ANNEX I- Informed consent

My name is DURESA ABU, and I am post graduate student AAU. I am conducting a research to To assess the prevalence of asymptomatic bacteriuria, antimicrobial susceptibility pattern of the isolates and related risk factors. Your participation in this study is entirely voluntary. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose to participate, what is expected from everyone is to respond some question on socio demographic and socioeconomic aspects which take about ten minutes and give 5 ml urine samples which collected using a sterile screw-capped, wide-mouth container. Your participation will help us To assess the prevalence of asymptomatic bacteriuria, antimicrobial susceptibility pattern of the isolates and related risk factors this will benefit society and future generations. If you are positive for asymptomatic bacteriuria, opportunities for management will be arranged. We will not share the identity of participants in the study with anyone. The information that we collect from this study will be kept confidential. Any information collected about you will have a number on it instead of your name. Only the study team members will know what your number is, and we will lock that information up. We will share the knowledge that we get from this study with you before it is made available to the public. Confidential information will not be shared. Afterwards, we will publish the results and make them available so that other interested people may learn from our study.

Part II. Certificate of consent

I have been invited to participate in a study on prevalence of asymptomatic bacteriuria, antimicrobial susceptibility pattern of the isolates and related risk factors.

I have read the above information, or it has been read to me. I have had the opportunity to ask questions, and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate in this study.

name of participant:

Signature of participant: _____

Date: _____

dd/mmm/yyyy

Witness' signature: A witness' signature and the participant's thumbprint are required only if the patient is illiterate. In this case, a literate witness must sign. If possible, this person should be selected by the participant and should have no connection with the study team.

I have witnessed the accurate reading of the consent form to the potential participant, who has had the opportunity to ask questions. I confirm that the participant has given consent freely.

name of witness: and thumbprint of participant:

Signature of witness: _____

Date: _____

dd/mmm/yyyy

Investigator's signature:

I have accurately read or witnessed the accurate reading of the consent form to the potential participant, who has had the opportunity to ask questions. I confirm that the participant has given consent freely.

name of investigator:

Signature of investigator: _____

Date: _____

dd/mmm/yyyy

A copy of this informed consent form has been provided to the participant. _____ (initials of the principal investigator or assistant).

ANNEX –II. QUESTIONNAIR

Section - I - Socio-demographic characteristics and associated risk factors

ID No:_____ Card No:_____

no	Questions	Responses/coding categories
1	How old are you?	_____years
2	Where did you come from?	Urban Rural
3	What is your ethnicity?	Amhara Gurage Oromo Berta Shinasha if other specify
4	What is your religion?	Orthodox Catholic Muslim Protestant If other specify
5	What is your current Marital status?	Single Married Divorced Widowed

6	What is your Educational status	Illiterate Read and write Primary Secondary school and above
7	What is your Family monthly income (birr)	≤ 500 1001-1500 1501-2000 > 2000
8	What is your Gestational age	First trimester Second trimester Third trimester
9	Where is your Water Source	Spring water Tap water Others
10	DO you Wash you r genitals after toilet	Yes No
11	Which Direction you wash your genitals	Back to front Front to back
12	You have any History of catheterization	Yes No
13	How many times you changing your underwear (week)	1. 1–3 times 2. >3 times
15	Number of Parity	Grand multipara Multiparous Primigravida
16	Do you have any History of previous UTI	Yes No
17	Do you have History Pre-eclampsia before	Yes No
19	Do you have History of diabetes before	1. Yes 2. no
20	Do you have History of obstetrics and gynecology surgery	1. Yes 2. no

Section-II: Laboratory questionnaire

ID No: _____ Card No: _____

1. Urine culture result:
   1.1. Colony number: _____
   1.2. Bacterial species: _____
2. Antimicrobial susceptibility pattern result:

Antimicrobial agent	Antimicrobial susceptibility result
2.1. Penicillin	
2.2. Ampicillin	
2.3. Tetracyclin ampicillin	
2.4 Amox-clavulanic acid	
2.5 Ciprofloxacin	
2.6 Gentamicin	
2.7 Ceftriaxone	
2.8 Cefotaxime	
2.9 Tetracycline	
2.10 Ceftazidime	
2.11 Amikacin	
2.12 Norfloxacin	
2.13 Nalidixicacid	
2.13 Trimethoprim-sulfamethoxazole	
2.14 Clindamycin	
2.15 Erythromycin	
2.16 Penicillin	
2.17 Chloramphenicol	
2.18 Ciprofloxacin and	
2.19 Vancomycin	