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Original Article

Asymptomatic bacteriuria and antimicrobial susceptibility pattern of the isolates among pregnant women attending Dessie referral hospital, Northeast Ethiopia: A hospital-based cross-sectional study

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ABSTRACT

Objective: The aim of the current study was to find out the prevalence of asymptomatic bacteriuria, antimicrobial susceptibility pattern of the isolates and related risk factors among pregnant women.

Material and methods: A hospital-based cross-sectional study was carried out from February 2017 to May 2017 among asymptomatic pregnant mothers attending Dessie Referral Hospital, Northeast Ethiopia. About 10-15 mL of freshly voided midstream urine samples were collected from each study participants, and analyzed at Dessie regional research microbiology laboratory with conventional antibiotic susceptibility, and biochemical tests. Isolates were tested against commonly used antimicrobials using Kirby Bauer disc diffusion method. Data were analyzed by SPSS version 20 software and in all cases, p-values below 0.05 was considered as statistically significant.

Results: Overall, 358 pregnant women were included in the study with a mean age of 26.5±4.6 years (range, 19-43 yrs). The overall prevalence of asymptomatic bacteriuria was 56% (15.6%). Isolated microorganisms were mainly *Escherichia coli* and *Staphylococcus aureus* (for each, n=18; 31%). *Escherichia coli* and *Staphylococcus aureus* were resistant to ampicillin (66.7%), and penicillin (94.44%). The prevalence of multidrug- resistant isolates was 72.4%. History of catheterization [AOR=2.28, 95% CI=(1.03-5.06)] and anemia [AOR=4.98, 95% CI=(2.395-10.34) were statistically significant regarding the prevalence of asymptomatic bacteriuria.

Conclusion: The overall prevalence of asymptomatic bacteriuria among pregnant women in the study area was high. The presence of asymptomatic bacteriuria and their antibiotic susceptibility test results should be taken into consideration during the management of pregnant women who are visiting antenatal care clinic.

Keywords: Asymptomatic bacteriuria; drug susceptibility; Ethiopia; pregnant women.

Introduction

Bacteria identified from urine of patients with asymptomatic urinary tract infection (UTI) usually stem from the normal flora of the gut, vagina and per urethral region.[1] 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.[1,2]

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.[3] Nowadays, asymptomatic bacteriuria (ASB) is common in pregnancy.[2] Pregnancy is one of the factors which increase the risk of UTI partly, due to the combination of alterations

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in hormonal, anatomical, mechanical, physical factors and maternal immunity throughout pregnancy. This gives to major changes in the urinary tract, which has a reflective impact on the attainment of bacteriuria.[4] Additionally, progesterone slows down peristaltic movements of ureteric smooth muscle causing dilatation of ureters, which is more worsened due to pressure from the expanding uterus. All these features lead to urinary stasis, nonfunctional ureteric valves, and vesicoureteral reflux, which facilitate bacterial migration and ascending infection.[5]

A recent study showed that both Gram-negative and positive bacteria are predominantly responsible from ASB during pregnancy worldwide. The most commonly implicated bacteria responsible for ASB in pregnant women are *Escherichia coli, Proteus* spp., *Klebsiella spp., Pseudomonas spp., Enterococcus spp., Staphylococcus aureus,* and coagulase-negative *Staphylococci*.[6-10] *Escherichia coli* is the most predominant bacteria that cause asymptomatic UTI among pregnant women.[11,12] ASB due to *Streptococcus agalactiae* (group B Streptococcus) has been associated with adverse obstetric outcomes.[13] Group B Streptococcus (GBS) is recognized to colonize the female genitourinary tract and to be transmitted vertically to the neonate prior, during, or after birth.

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.[6] Rates of antimicrobial resistance varies according to geographic locations and they are directly proportional to the use and misuse of antimicrobials. Antimicrobial therapy of a pregnant woman is a serious concern during pregnancy.[6]

Several factors are associated with the rapid increase in the prevalence of ASB among pregnant mothers. The factors such as history of UTIs,[14] age, low socioeconomic status, multiparity, lower level of education, multigravidity, advanced gestational age, sexual activity,[15] poor sanitation, lack of general hygiene practice,[16] disorders like diabetes mellitus and anemia in pregnancy[15] and history of catheterization. In the study area, little was known about the prevalence of ASB and antimicrobial susceptibility pattern among asymptomatic pregnant women. Therefore, in this study we aimed to assess the prevalence of ASB, antimicrobial susceptibility pattern of the isolated bacteria and related risk factors among pregnant women in Dessie Referral Hospital, Northeast Ethiopia.

Material and methods

Study design, period and area

Hospital-based cross-sectional study was carried out from February to May, 2017 at Dessie Referral Hospital, Eastern Ethiopia. The referral hospital is located in Dessie town with a distance of 400 km from Addis Ababa, the capital city of Ethiopia. The hospital is providing health services for more than 6 million people. This large number of people from the surrounding zones and nearby regions visits the hospital intended for different medical services. Every month the hospital is providing antenatal care for approximately 330-420 pregnant women, every year 4000-5000 pregnant women are visiting antenatal care unit.

Study participants

All pregnant women who came for antenatal check-up at Dessie Referral Hospital without any sign and symptom of UTI but willing to participate in the study were enrolled. A total of 358 study participants were selected during the study period using systematic random sampling method.

Those women with a history of urolithiasis, urological surgery, urogenital fistula and active bleeding and those who are currently on antimicrobials or had taken antimicrobials within two weeks were excluded from the study.

Collection of sociodemographic and clinical data

After taking written informed consent of the patients, sociodemographic and clinical data of the study participants were collected by trained midwives through face-to-face interviews using coded, structured and pre-tested questionnaires.

Collection of urine samples

Urine specimens were collected from each pregnant woman who were instructed by midwives about collection of mid-stream urine to reduce the chance of contamination. About 10 to 15 mL of mid-stream urine samples were collected from every pregnant woman in a sterile screw-capped, wide-mouth container. It was then delivered to Dessie regional microbiology research laboratory and processed within 1-2 hours for analysis.

Bacterial culture and identification

Urine specimens obtained from the pregnant women were directly inoculated on cystine lactose electrolyte deficient agar (CLED) (Oxoid, Ltd, England) media using calibrated inoculating wire loop (0.001 mL). Culture plates were incubated in the aerobic environment at 37^{0}C for 24 hrs. After incubation, all suspected colonies were sub-cultured on to MacConkey agar (Oxoid, England), Mannitol salt agar (MSA) (Oxoid, England) and 5% sheep blood agar (Oxoid, England) for further identification.

In the present study, cut-off values of conventional semi-quantitative evaluation (S-QBC) for significant bacteriuria were determined as 10^3 cfu/mL and 10^5 cfu/ml for GBS, and other bacteria, respectively. Lower threshold of $\geq 10^3$ S-QBC would be suitable for diagnosis of GBS-induced UTI as described by Tan et al.[17]. The colonies of isolates were recognized at their species level using colony characteristics, gram-staining technique and by the biochemical pattern folloing standard procedures. Most Gram-negative bacteria were identified using indole test, lysine decarboxylase, H_2S and gas production in triple sugar agar, citrate utilization, urease and motility tests. The Gram-positive bacteria were identified using catalase and coagulase tests, for the identification of GBS, pyrrolidonyl arylamidase test (PYR), CAMP test and bacitracin and trimethoprim-sulfamethoxazole tests were used.

Antimicrobial susceptibility testing

Antimicrobial susceptibility tests were carried out by Kirby-Bauer disk diffusion technique on Muller-Hinton agar medium and for GBS 5% sheep blood was added (Oxoid Basingstoke, UK) as explained in Clinical Laboratory Standard Institute (CLSI) guidelines and interpreted accordingly.[18] About 3-5 selected colonies of bacteria were taken from a pure culture and transferred to 5 mL sterile nutrient broth containing tube and mixed smoothly until a homogenous mixture was formed and incubated at 37°C until the turbidity of the mixture became attuned to 0.5 McFarland standard. A sterile cotton applicator stick was used to distribute the bacteria consistently over the whole surface of Mueller-Hinton agar. The inoculated culture plates were left at room temperature until dried for 3-5 minutes and discs impregnated with 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), nitrofurantoin (300 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) were used for the identification of bacteria isolates. The culture plates were then incubated at temperature of 37°C for 24 hours. The diameters of inhibition zones around the discs were measured by ruler and the isolates were classified as susceptible, intermediate and resistant based on the standardized CLSI criteria.[18]

Statistical analysis

All relevant data were entered and analyzed with IBM Statistical Package for the Social Sciences (IBM SPSS Statistics; Armonk, NY, USA) software version 20 statistical package. Data were summarized using cross tab and frequency tables. Bivariate and multivariate logistic regression models were applied to check for statistically significant association between the dependent and independent variables. The p-value below 0.05 was considered as statistically significant.

Results

Socio-demographic characteristics

A total of 358 pregnant mothers without signs and symptoms of UTI were included in this study; the mean age of culture positive pregnant women was 26.49±4.623 years (range 19-43 years). The majority of study participants 301 (84%) were urban residents, 205 (57%) attended high school and above, and more than half of the study participants (n=201 56%) were housewives (Table 1).

Prevalence of asymptomatic bacteriuria

Of the 358 study participates, 56 (15.6%) had significant bacteriuria. Fifty-eight cases of bacteriuria were identified based on the microbiological analysis of total urine culture samples. Among cases of significant bacteriuria, two urine cultures (3.6%) showed mixed growth, while 54 (96.4%) of them demonstrated single bacterial growth. Gram-positive isolates were more prevalent (n=37/58: 63.8%) than Gram-negative bacteria (n=21/58; 36.2%). The most commonly isolated bacteria were *S. aureus* (n=18; 31%) and *E. coli* (n=18; 31%), followed by Coagulase- Negative Staphylococcus (CoNS) (n=17; 29.3%), *K. pneumonia* (n=2: 3.4%) and GBS (n=2; 3.4%) and *Enterobacter* species (n=1; 1.7%) (Table 2).

Antimicrobial susceptibility patterns of gram-negative bacterial isolates

The rates of susceptibility for gram-negative isolates ranged from 33.3-95.2%. The majority of the gram-negative bacterial isolates were sensitive to nitrofurantoin (n=20; 95.2%), norfloxacin (n=18; 85.7%), ciprofloxacin (n=17; 80.95%) and ceftriaxone (n=17; 80.95%), amikacin (n=16; 76.2%), ceftazidime (n=15; 71.4%), gentamycin (n=14; 66.7%) and trimethoprim-sulfamethoxazole (n=12; 57.1%). and tetracycline (n=12; 57.1%). However, most Gram-negative bacteria were resistance to ampicillin (n=14; 66.6%), amoxicillin-clavulanic acid (n=13; 62%), and cefotaxime (n=10; 47.6%), followed by trimethoprim-sulfamethoxazole (n=9; 42.9%), and tetracycline (n=9; 42.9%). Among gram-negative bacteria, the most important isolate was *E. coli* (n=18; 85.7%) and 31.03% of all isolates among gram-negatives showed high level of sensitivity to nitrofurantoin (n=17; 94.4%), norfloxacin, amikacin, ciprofloxacin and ceftriaxone (for each, n=15; 83.3%). All *K. pneumonia* isolates were 100% sensitive to nitrofurantoin and norfloxacillin. All isolates of *Enterobacter aerogenes* were resistance to trimethoprim-sulphamethoxa-

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Table 1. Socio-demographic characteristics

	Asymptomatic bacteriuria			
	Positive No (%)	Negative No (%)	Total No (%)	p
Age, years				
15-24	17 (13.9)	105 (86.0)	122 (34.1)	
25-34	34 (16.6)	171 (83.4)	205 (57.3)	0.523
35-44	5 (16.1)	26 (83.9)	31 (8.7)	0.575
Occupation				
Farmer	3 (14.3)	18 (85.7)	21 (5.9)	0.356
Housewife	43 (21.4)	158 (78.6)	201 (56.1)	0.002
Student	0 (0)	11 (100.0)	11 (3.1)	0.999
Employee	10 (8.0)	115 (92.0)	125 (34.9)	
Residence				
Urban	50 (16.6)	251 (83.4)	301 (84.1)	
Rural	6 (10.5)	51 (89.5)	57 (15.9)	0.251
Educational status				
Illiterate	10 (20.8)	38 (79.2)	48 (13.4)	0.148
Literate	4 (25.0)	12 (75.0)	16 (4.5)	0.161
Primary school	15 (16.9)	74 (83.1)	89 (24.9)	0.316
Secondary school	15 (14.6)	88 (85.4)	103 (28.8)	0.554
Higher education	12 (11.8)	90 (88.2)	102 (28.5)	

zole and ampicillin, amikacin and gentamycin (n=1; 100%); whereas fully sensitive to ciprofloxacillin, nitrofurantoin, amoxicillin-clavulanic acid, ceftriaxone, ceftazidime, and cefotaxime (Table 3).

Antimicrobial susceptibility patterns of gram-positive bacterial isolates

The greater number of gram-positives was non-susceptible to the majority of the antimicrobials tested when compared with gram negatives. As described in Table 4, 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 clindamycin (n=23; 62.2%). *Staphylococcus aureus* was the predominant isolates among gram-positives (n=18; 48.6% of gram-positive isolates, 31% of all isolates) non-susceptible to most of the antimicrobials tested. Isolates of CoNS showed also high-level non-susceptibility to penicillin (n=15; 88.33%), trimethoprim-sulfamethoxazole (n=12; 70.56%) and tetracycline (n=9; 52.94%); whereas most isolates of CoNS were sensitive to nitrofurantoin (94.1%), norfloxacin (76.5%) and ciprofloxacin (70.6%). Additionally, *S. agalactiae* was 100% sensitive to erythromycin, penicillin, ceftriaxone, vancomycin and ampicillin; whereas one isolate of GBS was non-susceptible to clindamycin, chloramphenicol, and tetracycline (Table 4).

Table 2. Asymptomatic bacterial isolates retrieved from pregnant women

Bacterial isolates	Patient no. (%)
Single bacterial infection	
S. aureus	17 (30.35)
E. coli	17 (30.35)
CoNS	15 (26.80)
Enterobacter aerogenes	1 (1.80)
K. pneumoniae	2 (3.60)
S. agalactiae	2 (3.60)
Mixed bacterial infection	
CoNS and *S. aureus*	1 (1.80)
CoNS and *E. coli*	1 (1.80)
Total patients	56 (100)

CoNS: Coagulase-Negative Staphylococcus

Multidrug resistance patterns of bacterial isolates

Among the overall isolates (n=58), multidrug resistance was recorded for 42 (72.4%) isolates. Fifteen (71%) gram-negative and 27 (73%) Gram-positive bacteria were non-susceptible to at least one antimicrobial agent in three or more antimicrobial categories (Table 5).

Factors associated with the prevalence of asymptomatic bacteriuria

In the present study, a bivariate analysis showed that educational status, average family income, parity, history of catheterization, history of UTI, and anemia were statistically significant association with the prevalence of ASB among pregnant women. In a multivariate analysis, the occurrence of ASB was associated with history of catheterization and hemoglobin level of <11 mg/dL. Pregnant women who had history of previous catheteriza-

Table 3. Antimicrobial susceptible patterns of Gram-negative bacterial isolates retrieved from asymptomatic pregnant women

Bacterial isolates (no.)		Antimicrobial agents tested											
		CPR	Tet	STX	Nit	Nor	Cefr	Aug	Cefo	Cefz	Amp	Amk	Get
E. coli (18)	S	15 (83.3)	10 (55.6)	12 (66.7)	17 (94.4)	15 (83.3)	15 (83.3)	7 (38.9)	10 (55.6)	14 (77.6)	6 (33.3)	15 (83.3)	13 (72.2)
	NS	3 (16.7)	8 (44.4)	6 (33.3)	1 (5.6)	3 (16.7)	3 (16.7)	11 (61.0)	8 (44.4)	4 (22.2)	12 (66.6)	3 (16.7)	5 (27.8)
E. aerogenes (1)	S	1 (100.0)	1 (100.0)	0 (0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	0 (0)	0 (0)	0 (0)
	NS	0 (0)	0 (0)	1 (100.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100.0)	1 (100.0)	1 (100.0)
K. pneumonia (2)	S	1 (50.0)	1 (50.0)	0 (0)	2 (100.0)	2 (100.0)	1 (50.0)	0 (0)	0 (0)	0 (0)	1 (50.0)	1 (50.0)	1 (50.0)
	NS	1 (50.0)	1 (50.0)	2 (100.0)	0 (0)	0 (0)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	1 (50.0)	1 (50.0)	1 (50.5)
Total (n=21)	S	17 (80.9)	12 (57.1)	12 (57.1)	20 (95.2)	18 (85.7)	17 (80.95)	8 (38.0)	11 (52.4)	15 (71.4)	7 (33.3)	16 (76.2)	14 (66.7)
	NS	4 (19.0)	9 (42.9)	9 (42.9)	1 (4.8)	3 (14.3)	5 (19.1)	13 (62.0)	10 (47.6)	6 (28.5)	14 (66.6)	5 (23.8)	7 (33.3)

S: sensitive; NS: non-susceptible; CPR: ciprofloxacin; Tet: tetracycline; STX: trimethoprim-sulfamethoxazole; Nit: nitrofurantoin; Nor: norfloxacin; Cef: ceftriaxone; Am: aampicillin; Aug: amoxicillin-clavulanic acid; Cefz: ceftazidime; Get: gentamycin; Amk: amikacin; Cfo: cefotaxime

tion was 2.28 times more likely to develop ASB as compared to those who did not have history of catheterization [AOR=2.28, 95% CI=(1.03, 5.06)] and pregnant women who had haemoglobin level of <11 g/dL was 4.98 times more likely to develop ASB as compared to those whose haemoglobin level was >11 g/dL [AOR=4.98, 95% CI=(2.395-10.34) (Table 6).

Discussion

Asymptomatic bacteriuria deserves special consideration during pregnancy due to the absence of symptoms and associated adverse effects on maternal and fetal outcomes.[19] In this study, the total prevalence of ASB was 15.6% which is in agreement with prior studies done in Hawassa, Ethiopia (18.8%),[11] and in Adama city, Ethiopia (16.1%).[7] However, our prevalence rates are lower than the prevalence reported from Nigeria (22.5%),[20] and Iraq (42.9%).[21] The variation might be justified by the reality that differences exist in geographical location, social behavior of the population, the environment, the model of educational status, and study settings (primary care, community-based, or in hospitals). The finding of our study is higher than the studies done in Northwest Ethiopia (8.5%),[22] Central Ethiopia (Addis Ababa) (10.6%),[23] Tanzania (4.1%),[24] and Eritrea (10.5%).[25] The possible explanation for this disparity might be related to variations in the study population, time of study period and sample size of study participants.

In this study, 96.4% of the urine cultures showed single bacterial growth. This finding is in agreement with the study conducted in Hawassa (89.1%)[11] and Adama (93.3%),[7] Ethiopia. In addition, gram-positive bacterial isolates were more prevalent (63.8%) than gram-negative isolates (36.2%) which is consistent with other studies carried out in Hawassa, Ethiopia where gram-positive and gram-negative isolates were reported in 51, and 49% of bacteria cultures,[11] and gram-positive and Gram-negative bacteria were indicated in 64, and 36% of the cultures in Dhule, India.[10] Most Gram-positive bacteria survived commensally. It has been well recognized that the isolates have been shifting with the environmental conditions such as (temperature, humidity), resistance patterns and antimicrobial usage. In addition, due to patient condition, sexual activity, medical history of the patient, and genital hygiene practice reason could be as a result of poor genital hygiene practices by pregnant women who may find it difficult to clean their anus properly after defecating or clean their genital area after passing urine.[16]

The result of the present study showed that the prevalence of *E. coli* was 31.04%. This finding is comparable with those reported in Adama, Ethiopia (37.3%),[7] and Nigeria (37.8%).[9] In pregnant women, progesterone relaxes ureteric smooth muscle which causes dilatation of ureters which additionally aggravates as a result of pressure from the enlarging uterus.

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Table 4. Antimicrobial susceptibility patterns of Gram-positive bacterial isolates retrieved from pregnant women with asymptomatic bacteriuria

Bacterial isolates (no.)		Antimicrobial agents tested											
		CLN	Ery	Pen	Chl	Tet	CPR	STX	Nit	Nor	Cefr	Amp	Vac
S. aureus (18)	S	14 (77.8)	5 (27.8)	1 (5.6)	14 (77.8)	5 (27.8)	14 (77.8)	2 (11.1)	17 (94.4)	13 (72.2)			
	NS	4 (22.3)	13 (72.2)	17 (94.4)	4 (22.3)	13 (72.2)	4 (22.2)	16 (88.9)	1 (5.6)	5 (27.8)			
CONS (17)	S	8 (47.1)	9 (52.9)	2 (11.8)	9 (52.9)	8 (47.1)	12 (70.6)	5 (29.4)	16 (94.1)	13 (76.5)			
	NS	9 (52.9)	8 (47.1)	15 (88.3)	8 (47.1)	9 (52.9)	5 (29.4)	12 (70.6)	1 (5.9)	4 (23.6)			
S. agalactae (2)	S	1 (50.0)	2 (100.0)	2 (100.0)	1 (50.0)	1 (50.0)					2 (100.0)	2 (100.0)	2 (100.0)
	NS	1 (50.0)	0 (0)	0 (0)	1 (50.0)	1 (50.0)					0 (0)	0 (0)	0 (0)
Total (n=37)	S	23 (62.2)	16 (43.2)	5 (13.5)	24 (64.9)	14 (37.8)	26 (74.3)	7 (20.0)	33 (94.3)	26 (74.3)	2 (100.0)	2 (100.0)	2 (100.0)
	NS	14 (37.8)	21 (56.7)	32 (86.5)	13 (35.1)	23 (62.2)	9 (25.7)	28 (80.0)	2 (5.7)	9 (25.7)	0 (0)	0 (0)	0 (0)

CLN: clindamycin; Ery: erythromycin; Pen: penicillin; Chl: chloramphenicol; CPR: ciprofloxacin; Tet: tetracycline; STX: trimethoprim-sulfamethoxazole; Nit: nitrofurantoin; Nor: norfloxacin; Cef: ceftriaxone; Am: ampicillin; Vac: vancomycin; S. sensitive; NS: non-susceptible

Table 5. Multidrug resistance patterns of bacterial isolates in asymptomatic pregnant women

		Antimicrobial resistance patterns					
Bacterial isolates	Total (%)	R0	R1	R2	R3	R4	>R5
Gram-negative	21 (36.3)	2 (9.5)	1 (4.8)	3 (14.3)	2 (9.5)	5 (23.8)	8 (30.1)
E. coli	18 (85.7)	2 (11.1)	1 (5.6)	3 (16.7)	2 (11.1)	4 (22.2)	6 (33.3)
K. pneumoniae	2 (9.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)
E. aerogenes	1 (4.8)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)
Gram-positive	37 (63.7)	1 (2.7)	3 (8.1)	6 (16.2)	5 (13.5)	7 (18.9)	15 (40.5)
S. aureus	18 (48.6)	0 (0)	0 (0)	2 (11)	3 (16.7)	7 (38.9)	6 (33.3)
CoNS	17 (45.9)	0 (0)	2 (11.8)	4 (23.5)	2 (11.8)	0 (0)	9 (52.9)
S. agalactiae	2 (5.4)	1 (50)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)
Total	58 (100)	3 (5.2)	4 (6.9)	9 (15.5)	7 (12.1)	12 (20.7)	23 (39.7)

R0: no resistance; R1: resistence to one; R2: resistance to two; R3: resistance to three; R4: resistance to four; R5: resistance to five antibiotics

All of these factors bring urinary stasis, dysfunctional ureteric valves and vesico-ureteral reflux, which assists bacterial colonization and rising infection.[5] This environment is suitable to *E. coli*. The current study also reported high prevalence rate of *S.aureus* (31.04%). This finding was in agreement with the previous report in Abakaliki, Nigeria (34%).[8] A rising trend in the prevalence of *S. aureus* was found among pregnant mothers.[26] Moreover, 3.4% of GBS isolates were identified. This finding is similar to others findings reported for pregnant women in Northwest Ethiopia 3.6%.[27] In general, the varia-

Table 6. Bivariate and multivariate analysis of risk factors associated with asymptomatic bacteriuria among pregnant women

	Asymptomatic bacteriuria						
Variables	**Positive No (%)**	**Negative No (%)**	**Total No (%)**	**COR (95%CI)**	**p**	**AOR (95%CI)**	**p**
History of catheterization							
Yes	11 (28.2)	28 (71.8)	39 (10.9)	2.392 (1.113-5.142)	0.026	2.279 (1.025-5.1)	0.043
No	45 (14.1)	274 (85.9)	319 (89.1)		1.00		
Hgb level							
Anemia (<11 g/dL)	16 (42.1)	22 (57.9)	38 (10.6)	5.091 (2.468-10.503)	0.00	4.977 (2.4-10.3)	0.000
Normal (>11 g/dL)	40 (12.5)	280 (87.5)	320 (89.4)		1.00		
Parity							
Nulliparous	18 (12.0)	132 (88.0)	150 (41.9)				*
Primiparous	25 (20.5)	97 (79.5)	122 (34.1)	1.890 (0.977-3.657)	0.059		
Multiparous	13 (15.1)	73 (84.9)	86 (24.0)	1.306 (0.606-2.816)	0.496		
Gestational period							
1st trimester	5 (1.4)	32 (8.9)	37 (10.3)				*
2nd trimester	21 (5.9)	93 (26.0)	114 (31.8)	1.445 (0.503-4.150)	0.494		
3rd trimester	30 (8.4)	177 (49.4)	207 (57.8)	1.085 (0.392-3.005)	0.76		
Educational status							
Illiterate	10 (20.8)	38 (79.2)	48 (13.4)	1.974 (0.786-4.957)	0.148		*
Literate	4 (25.0)	12 (75.0)	16 (4.5)	2.5 (0.694-9.009)	0.161		
Primary school	15 (16.9)	74 (83.1)	89 (24.9)	1.52 (0.67-3.448)	0.316		
Secondary school	15 (14.6)	88 (85.4)	103 (28.8)	1.278 (0.566-2.885)	0.554		
Higher education	12 (11.8)	90 (88.2)	102 (28.5)		1.00		
History of UTI							
Yes	19 (21.3)	70 (78.7)	89 (24.9)	1.702 (0.921-3.146)	0.09		*
No	37 (13.8)	232 (86.2)	269 (75.1)		1.00		
Average monthly income level (in Ethiopian Birr)							
<500	6 (23.1)	20 (76.9)	26 (7.3)	1.4 (0.52-3.8)	0.50		*
501-1000	12 (14.6)	70 (85.4)	82 (22.9)	0.8 (0.388-1.66)	0.55		
1001-1500	4 (9.1)	40 (90.9)	44 (12.3)	0.468 (0.156-1.4)	0.18		
1501-2000	3 (10.0)	27 (90.0)	30 (8.40)	0.52 (0.148-1.82)	0.31		
>2000	31 (17.6)	147 (82.4)	178 (49.7)		1.00		

*After multivariate analysis no statistical significant association was found (p-value >0.05). COR: crude odds ratio; CI: confidence interval; AOR: adjusted odds ratio; Hgb: hemoglobin; UTI: urinary tract infection

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tion of prevalence of ASB from one country to a different and among regions of similar country in studies could be attributed to differences in geographical location, socio-economic state at the time of the study, sample size of the study and variations in screening tests. Pregnancy itself is one of the factors, which increase the risk of UTI partly, due to the combination of alterations in hormonal, anatomical, mechanical, physical and maternal immunity during the period of pregnancy. This contributes to major alterations in the urinary tract, which have a reflective impact on the attainment of bacteriuria.[4]

In this study, antimicrobial susceptibility pattern of Gram-negative bacteria demonstrated that the majority of isolates showed susceptibility to nitrofurantoin (95.2%), norfloxacin (85.7%), ciprofloxacin and ceftriaxone (for each, 80.95%), amikacin (76.2%), ceftazidime (71.4%), gentamycin (66.7%), trimethoprim-sulfamethoxazole and tetracycline (for each, 57.1%), cefotaxime (52.4%) and amoxicillin-clavulanic acid (38%). In contrary, a study in Adama, Ethiopia[7] pointed out that Gram-negative bacteria were susceptible to ciprofloxacin and norfloxacin (100%), cefotaxime (92.2%), tetracycline and gentamicin (64.7%), nitrofurantoin (60.8%), trimethoprim-sulfamethoxazole (51.9%) and amoxicillin clavulanic acid (48%). The easy accessibility and indiscriminately, and frequently used drugs such as amoxicillin-clavulanic acid may result in an increase in resistance. Among Gram-positive bacteria tested with commonly used antibiotics, resistance patterns of the isolates revealed a high level of non-susceptibility to penicillin (n=17; 94.44%), trimethoprim-sulfamethoxazole (n=16; 88.89%), erythromycin and tetracycline (for each, n=13; 72.22%). The majority of bacterial isolates were sensitive to nitrofurantoin (94.3%), ciprofloxacin and norfloxacin (for each, 74.3%), and chloramphenicol (64.7%). This is not in line with the report published in Adama, Ethiopia[7] which showed 100% susceptibility to ciprofloxacin and norfloxacin, 80% to chloramphenicol and 0% to nitrofurantoin and tetracycline. In the present study, the efficacy of ciprofloxacin and norfloxacin to both gram negative and gram- positive bacteria and chloramphenicol to Gram-positive bacteria is lower than that of a comparable study. This might be due to the use of ciprofloxacin, norfloxacin, chloramphenicol, tetracycline, erythromycin, trimethoprim-sulfamethoxazole, amoxicillin-clavulanic acid and penicillin for empirical therapy. In this study, the resistance rate of Gram-positive bacterial isolates to nitrofurantoin was 5.7%. which is lower relative to that indicated in a report from Adama, Ethiopia[7] in which Gram-positive bacteria showed 100% resistance to nitrofurantoin which could be explained by less frequent utilization of nitrofurantoin in study area.

In our study, multidrug resistance was seen in 72.4% of the the cases with isolated bacteriuria. Similar result was reported in Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia (74%).[23] Therefore; in this study, multidrug resistance was found to be incredibly high to the frequently used antimicrobials. Antimicrobial resistance is more likely to develop in patients that do not comply with the full duration of antimicrobial treatment[3] and in the community, lack of proper infection control strategies, which can cause a shift to increase in the prevalence of resistant organism(s). In addition to these, the reasons for this alarming number of multidrug resistant cases might be due to the prescription of antimicrobials without laboratory guidance and unsuitable and wrong administration of antimicrobial agents in empirical treatment. Besides, over-the-counter sales of antimicrobials without prescription are probable factors for increased bacterial resistance to antimicrobial agents.

The present study showed that previous catheterization and anemia are associated risk factors with respect to asymptomatic UTI among pregnant women. Previous history of catheterization was one of the factors that were significantly associated with increased rates of ASB. Pregnant women who had history of previous catheterization were 2.28 times more likely to develop ASB compared with those without any history of catheterization. This finding was in concordance with the previous report concerning a study in Gondar, Ethiopia which was conducted with pregnant women.[28] Pregnant women who had hemoglobin levels <11 mg/dL was 4.98 times more likely to develop ASB compared to those with hemoglobin levels >11 mg/dL. Similar findings were also reported in Northwest Ethiopia and in Iran.[22,29]

Study limitations

In this study, the sample size was inadequate for the determination of the prevalence of ASB and assessment of risk factors in pregnant women. Therefore, larger group of pregnant women need to be studied in the study area for confirmation of the results. In addition, though fosfomycin is approved mainly for the treatment of uncomplicated UTIs during pregnancy, it was not assessed for antimicrobial susceptibility testing in this study.

In conclusion, the overall prevalence rate of ASB among pregnant women in our study was higher. The majority of bacterial isolates detected in the urine specimens of pregnant women in Dessie Referral Hospital were *Staphylococcus aureus, Escherichia coli* and Coagulase-negative Staphylococcus. The majority of isolates were sensitive to nitrofurantoin. Most of the isolates were resistant to the commonly used antimicrobials as ampicillin, tetracycline, and trimethoprim-sulfamethoxazole. Our findings have showed that bacteriuria was resistance to frequently used antimicrobial agents and aynı anda increase in multidrug resistance rates. It is essential to consider that treatment must be safe for the mother and the fetus. In addition, prevalence of ASB was positively correlated with prior history of catheterization and anemia.

Ethics Committee Approval: Ethical clearance was obtained from the University of Gondar, School of Biomedical and Laboratory Sciences, Ethical Review Committee.

Informed Consent: Written informed consent was obtained from each study participants, after explaining the purpose and objective of the study. All the information obtained from each study participants was kept confidential. Laboratory results of the study participants were delivered to their attending physicians for appropriate treatment.

Peer-review: Externally peer-reviewed.

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