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PREVALENCE, ASSOCIATED FACTORS, BACTERIAL AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF URINARY TRACT INFECTIONS IN A SAMPLE OF IRAQI PREGNANT WOMEN IN AL-NAJAF

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ABSTRACT: *Urinary tract infections (UTIs) are rendered as the most common bacterial infections prevailing among humans, both in the community and hospital settings. In pregnancy, UTI can lead to poor maternal and perinatal outcomes. The current cross-sectional study was undertaken to estimate the prevalence of UTI in pregnant women, to determine its association with sociodemographic, obstetrical and other factors, and to identify causative agents with antibiotic sensitivity. A total of 300 pregnant women at Al-Zahraa teaching hospital / Al-Najaf from the 1st of April 2014 to 30th July 2014, with and without the symptoms of urinary tract infection (UTI), were recruited for this study. Midstream urine samples were taken and general urine examination with culture was performed. Sensitivity tests were also performed for the isolated organisms. The data pertaining to the associated risk factors were collected by using a structured questionnaire form. The results revealed that the overall prevalence of significant bacteriuria in pregnant women was 37 %, representing symptomatic and asymptomatic (23%, 14% respectively). The predominant bacterial pathogen was Escherichia coli (28.8 %), which was found to be resistant to penicillin (100 %) and cephalosporins group (40%), but sensitive to garamycin (95%) and Amikacin (90%). Factors such as type of past delivery, previous history of UTI, symptomatic patients and vaginitis were found to be significantly associated with higher rates of UTI. Significant bacteriuria was found in both symptomatic and asymptomatic pregnant women, which was significantly higher among those with lower age.*

KEYWORDS: Significant bacteriuria, UTI, Pregnant women, Asymptomatic bacteriuria, Antenatal care.

INTRODUCTION

Urinary tract infection (UTI) is a recurrent infection that can occur anywhere along the urinary tract, caused by the presence and growth of microorganism.[1] UTIs are the most common cause of hospital acquired infections accounting for approximately 40%. They occur four times more frequently in females than males.[2] Due to several anatomical and hormonal changes, pregnant women are more susceptible to develop UTIs [3], and it is found to be the most common cause of admission in obstetrical wards.[4] At around the 6th week of pregnancy, the risk of UTI increases due to the physiological changes of pregnancy where the ureters dilates. This is also known as "hydronephrosis of pregnancy".[4,5]

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The prevalence rate of UTI in developing countries is higher than the developed countries such as United States (5%–6%). In pregnant women, the hospital-based studies in multiple developing countries revealed the UTI prevalence of 12.7% in Abha-Saudi Arabian[6], 31.3% in Egypt[7], 47.5% in Nigeria[8] and 56.5% in Ghana[9]. Also, the prevalence of UTI from different studies in Iraq ranged from 29% - 47%. [10, 11, 12]

Significant bacteriuria is defined as the presence of 10^5 colony form unit per one milliliter of urine ($\geq 10^5$CFU/ml).[13] Symptomatic bacteriuria (SBU) refers to patients whose urine is yielding positive cultures ($\geq 10^5$CFU/ml) and who have symptoms related to the urinary tract, which could either be lower (acute cystitis) or upper UTI (Pyelonephritis).[14]

Asymptomatic bacteriuria (ASB) screening is included in the WHO recommended antenatal care (ANC) package.[15,16] It is defined as a pure culture of at least 10^5 organisms/ml of urine ($\geq 10^5$CFU/ml) in the absence of symptoms. A prevalence of 2 -10% has been reported for ASB in pregnancy.[17, 18] One of the study estimated that screening or treatment of bacteriuria in pregnancy is likely to reduce the incidence of prematurity and low birth weight by 20% to 55%, and also reduce neonatal mortality by 5% to 14%.[15]

Apart from the pregnancy related factors, there are other risk factors that facilitates the infection, which are; dehydration, carrying twins, kidney stones[19], genetic history of UTIs and childhood history of UTI[4], low socio-economic status and certain pre-existing medical conditions such as diabetes mellitus, sickle cell disease, immuno-deficiency states[14], neurogenic bladder retention and psychiatric illnesses.[4]
The most common cause of UTI is the infection with Escherichia coli (E. coli) [20], which causes approximately 80% of acute uncomplicated UTIs. Another cause that leads to UTI is Staphylococcus saprophyticus that is accountable for 5-15% rate of incidence.[20] Enterococcus and a variety of other primarily Gram-negative aerobes (Proteus mirabilis, Klebsiella species and Pseudomonas species) are also accountable for the other 5–10% of UTI infected people.[2] More than 95% of UTIs are caused by a single bacterial specie, less frequently are other Gram-positive cocci such as group B hemolytic streptococci, while Staphylococcus aureus (S. aureus) is less common.[21]

Complicated UTIs are defined as those which are occurring in a functionally, metabolically, or anatomically abnormal urinary tract or are caused due to the bacteria resistant to antibiotics (ATB).[2] In complicated UTIs, E. coli is recovered in approximately 34.5% of cases, Streptococcal faecalis is in 16%, and Staphylococcus epidermidis and Proteus mirabilis in 13% of cases. Complications are either primary or secondary. The primary complications are pertaining to the recurrent infection and a lack of response towards treatment. On the other hand, the secondary complication is related to maternal outcomes such as disseminated intra vascular coagulation (DIC), Bacteremia, septic shock, hypertension, preeclampsia, adult respiratory distress syndrome (ARDS) and respiratory insufficiency, endometritis, chorioamnionitis, anemia, prolonged pyrexia and poor perinatal outcomes such as Preterm labor, premature rupture of membranes, intrauterine growth restriction (IUGR) and low birth weight (LBW). [22]

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The test and procedures adopted for the diagnosis of UTI are general urine examination Qualitative (Dipstick) test and quantitative (Microscopical) test). Table -1 shows the criteria of urinalysis results of UTI.[23]

Table (1) Urinalysis results (Interpretation of Urinalysis for UTI)

Test	Usual range	Indicators of infection	Accuracy
Bacteria	Absent	Any amount	Low sensitivity [a] High specificity [b]
Leukocyte esterase	Absent	Positive=pyuria, presence of WBCs in urine	High sensitivity Low specificity
WBC	< 5	Pyuria: WBC > 10	High sensitivity Low specificity
Nitrite	Absent	Positive = presence of bacteria that reduce nitrate	Low sensitivity High specificity
RBC	< 5	Hematuria common in infection	Low sensitivity High specificity
Epithelial cells	< 5	< 5 = good urine sample	High epithelial cells indicate contamination with skin flora
PH	4.5 - 8	PH ↑ if urea-splitting organism (e.g. *Proteus mirabilis*) is present	Low specificity (there are many other causes of alkaline urine)

[a] *Sensitivity = likelihood of positive test when disease is present.*
[b] *specificity = likelihood of negative test when disease is not present*
Source: Reference 20

The culture and sensitivity test is considered as the gold standard for laboratory diagnosis of UTI. It is the most accurate method to identify and quantify bacteria in the urine with high sensitivity. However, there are certain drawbacks to this method such as the relatively higher costs, the higher time duration for achieving the number of bacterial colonies necessary for a sensitive result and the need for professionals with qualified laboratories to interpret the test results.[4] The other tests that support the diagnosis of UTI are Complete blood count (Hemoglobin, RBC, WBC, and Platelet count) and Biochemical test (Blood urea and serum creatinine), both of which help to identify the severity of the infection that is reflected in the hematologic and renal function parameters. However, they are not essential for the monitoring of patients with uncomplicated UTIs. Ultrasound of kidneys and urinary tract can be considered as a complementary examination that offers rapid, inexpensive, easy accessibility and higher safety for both mother and fetus.[4]

The American College of Obstetrics and Gynecology recommends that a urine culture be obtained at the first prenatal visit. Also, a repeat urine culture should be obtained during the third trimester, because the urine of treated patients may not remain sterile for the entire pregnancy.

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Screening and treatment of asymptomatic UTI during pregnancy recommended by united state Preventative Services Task Force is to obtain a urine culture between (12 – 16) weeks of gestation.[24]

The financial constraints in several developing countries may limit the feasibility of performing general screening for UTI among the pregnant women. Routine screening in populations with low prevalence of ASB is less cost-effective due to the high laboratory charges of urine culture. The practice of diagnosing ASB by urine microscopy is inadequate, and bacterial culture from a midstream clean-catch urine sample in each trimester is considered the best diagnostic test available in all the settings.[25,26]

There is no clear consensus on the choice of antibiotic or duration of therapy, which is why the practice is more likely guided by local resistance patterns and national patterns of practice than by evidence from clinical trials. No systematic review is found pertaining to which antibiotic is best for the treatment of asymptomatic bacteriuria. Antibiotic regimens for both symptomatic and asymptomatic bacteriuria in pregnancy were suggested by many studies, although increasing antibiotic resistance may complicate empirical regimens. The selected antibiotic must have a low resistance rate and excellent efficacy in a given population with adequate maternal safety profile. Amoxicillin and Cephalexine (CEX) and Cephalosporins are considered as safe to be used during pregnancy. While ciprofloxacin and ofloxacin are the most extensively used fluoroquinolones for the treatment of UTIs, the resistance to ciprofloxacin has emerged in a variety of genera belonging to the family Enterobacteriaceae. [25, 27, 28]

METHODS

A cross-sectional study was conducted in AL-Zahraa Teaching Hospital of Kufa University in Al Najaf governorate, from the 1st of April to 30th of July, 2014. A consecutive sample of 300 pregnant women was recruited from outpatient clinic of gynecology and obstetrics at Al-Zahraa teaching hospital. Pregnant women with the history of antibiotic therapy during the last one week or those having vaginal bleeding at the time of data collection were excluded from the study.

A single proportion formula was used to calculate the sample size:

$n = Z^2 p\ (1\text{-}p)/d^2$,

Where, Z = Z score for 95 % confidence interval = 1.96, p = prevalence, d = tolerable error =5 %. The prevalence of 27 % was considered in this formula, which is the average prevalence of the rates acquired from the previous studies in Iraq (Kirkuk (29%), Baghdad (15.6%), and Mosul (37.4%)). After applying the above formula, the sample size was found to be 300. [10, 11, 29]

Data collection was performed 3 days a week, 3 hours per day throughout the four month period of the study. Each pregnant lady was interviewed and inquired about UTI with the aid of a structured questionnaire. The questionnaire was segregated into four parts, where the first component addressed the socio demographic characteristics, age, residence, level of education

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and occupation of pregnant women and her husband, family type, and the monthly family income.

The second part was related to Obstetrical, Gynecological, and medical history data such as the presence of genitourinary abnormality like single kidney and cystocele, previous genitourinary surgical operations, number of pregnancies (gravidity), number of children or parity (all deliveries above 24 week gestation), type of previous deliveries (whether normal vaginal delivery (NDV), cesarean section (CS), or both), and the history of previous abortions (spontaneous loss of pregnancy at or before 24 weeks of gestation and weight less than 500 gm). The gestational age of pregnant women was calculated from their last menstrual period (LMP) and by comprehending the information obtained from the ultrasound done in early pregnancy.[30] The women were then categorized according to their gestational age into first, second, and third trimester of pregnancy. The other data obtained from the pregnant women were: past history of UTI that was diagnosed by physician, history of anemia (hemoglobin concentration less than 11 g/dl), and the frequency of sexual intercourse per week and history of urinary catheterization.

The third section of the questionnaire acquired the data related to: patient complaints and clinical findings such as dysuria (burning sensation feeling internally or pain during urination); blood in urine or cloudy urine or foul smell; urgency (which may occur with or without voiding and frequently culminates in incontinence), with severe lower urinary tract inflammation, where the desire to urinate may be constant with only a few milliliters of urine eliminated with each voiding[31]; frequency (need to urinate many times during day or night in normal or less than normal volume i.e. >7 times urination per day and >3 during the night is considered as abnormal)[32]; presence of supra pubic pain, (suprapubic discomfort in the first trimester may be related to a retroverted uterus, however, in late gestation, it can be due to compression of the bladder by the fetal head). The diagnosis of urinary tract infection by symptoms is more difficult in late pregnancy as the symptoms of urgency, frequency, and suprapubic pressure are also considered as normal in the later stage. Thus, the pregnant women were inquired about developing attacks of fever, rigors, nausea with vomiting and loin pain or controvertible pain and tenderness. At the same time, inquiries were posed about the amount and color of vaginal discharge and whether or not it was associated with itching and dysuria externally feeling. More than or equal to 2 symptoms confirmed the infection as vaginitis. Therefore, any of the above mentioned symptoms with dysuria, either in cystitis or pyelonephritis, would be considered as symptomatic cases, i.e. ≥ 2 symptoms are considered if the number of urination at day and night are abnormally increased.[30]

The fourth part of the questionnaire consisted of the investigation results, which were done using scientific methods at Medical Microbiology and Parasitology laboratory department in Al-Zahraa teaching Hospital. Each pregnant woman had a brief explanation concerning the method of collecting urine sample, and the importance of quick delivery of sample to the laboratory (within 30 minutes to one hour from collection) by the researcher.[14] Therefore, to collect a clean sample, the pregnant lady was told to clean the periurethral area and perineum with two or three cleansing pads by front-to-back wiping to reduce the potential contamination. While holding the labial folds apart, the women should void the first few milliliters of urine to flush bacteria from the urethra. Without stopping the stream, the patient used a wide mouthed two sterile containers

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to collect the midstream portion of the urine (5 ml) in each cup. The container is equipped with a tight-fitting lid to avoid any leakage of contents. From the time of collection, the urine was processed within 30 minutes to one hour and not more than a maximum of 2 hours[14] for minimizing the chances of increasing the actual colony count of any present pathogen.

The first sample was rapidly screened by non-microscopic (urinary dip stick) by using reagent strips. Dipstick tests are most useful in screening symptomatic patients as they are inexpensive and simple to perform. However, in patients who urinate frequently, dilution of the two enzymes may result in reduced detection that may result into false negative results. The nitrate test and a test for leukocyte esterase (along with the other chemical parameters) were present on a single reagent strip that could be read in less than 2 minutes. The reagent strip was dipped into the urine and read by comparing the reactions to a color chart or in an automated reagent strip reader. Catalase, another commercially available tests such as Uriscreen was deployed, where the release of catalase from bacteria, leukocytes, and erythrocytes in urine was extracted. This test was primarily intended for the screening of symptomatic patients.

Microscopical examination was performed by first putting 5-10ml urine in a tube, and centrifuging it. The samples were then examined at low power (×10) and at high power (×40) on the bright-field microscope for determining the bacteria rapidly, while emphasizing on the white blood cell (pus cell) and red blood cell count.[33] The gram stains were done, which are useful as initial tests for detecting and identifying general types of bacteria or fungi and also enables the doctor in determining the best type of treatment for an infection.[34]

The second urine sample was sent for culture and sensitivity at the same time, but in a specific lab room. Samples that have positive growth by culture had undergone the antibiotic sensitivity test using Mueller-Hiuton agar (yellow colour) by Kirby-Bauer method. All these biochemical tests were done after the gram stain.

The interpretation of quantitative urine culture results are shown in figure-1 as conversion from number of colonies to number of bacteria per ml. The general recommendations for reporting are as follows:

1. Category 1: Less than 10^4CFU per ml. In such as case, the UTI was rendered as absent in the report.
2. Category 2: 10^4-10^5 CFU per ml. If the patient is asymptomatic, a second urine specimen was requested and the count repeated. If the patient had symptoms of UTI, both the identification and susceptibility tests were executed when one or two different colony types of bacteria were present. Bacterial counts in this range strongly suggest UTI in symptomatic patients, or in the presence of leukocyturia. If the count, the quality of the urine specimen, or the significance of the patient's symptoms were in doubt, a second urine specimen was obtained for retesting.
3. Category 3: More than 10^5 CFU per ml. The count to the physician was reported and further proceeding with identification and susceptibility tests, if one or two different colony types of bacteria were present, was carried out. These bacterial counts are strongly suggestive of UTI in all the patients, including asymptomatic females. If more than two species of bacteria were present in urine samples as estimated under categories 2and 3. This report was written as: "Probably contaminated; please submit a fresh, clean-catch specimen".[35]

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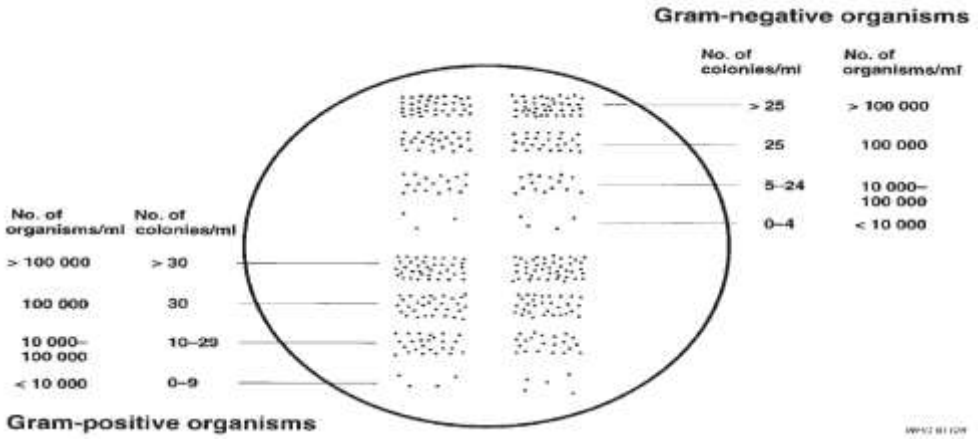

Figure-1: quantitative urine culture results (WHO)

Haemoglobin (Hb) measurement was done reading Hb meter gm/dl or Hb spectrophotometer directly after withdrawing 2 ml of venous blood sample from each of the pregnant women.

Ethical considerations: The study procedure was discussed and approved by the scientific committee of Family and Community Medicine department in Al-Nahrain college of Medicine. Approvals of Scientific Committee of Research at Najaf Health Directorate, and Iraqi Board for medical specialization were obtained before conducting the study. Prior to data collection, the pregnant women were informed about the nature and aim of the research that addressed their potential contribution in the study. A verbal informed consent was obtained from each of the participant.

Initially, a pilot study was carried out, which included 15 pregnant women attending the same hospital. The aim of the pilot study was to assess the feasibility of questionnaire and the time required for each interview; to find out whether or not there are any difficulties during the laboratory investigations; and to make possible changes or corrections to the questionnaire if needed. These 15 women were not included in the study.

Statistical package for social sciences (SPSS) version 20, US, IBM, 2013 was used for data analysis of this research. Descriptive statistics were presented as frequencies, proportions (%), means and standard deviation (SD) were evaluated. Chi square test was used to find the association between two categorical variables along with student t-test to estimate the difference between the two means of numerical variables. Shapiro-Wilk's test was also used for testing the normality of data. For these tests, the level of significance of < 0.05 was considered as significant.

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RESULTS

The prevalence of UTI (significant bacteriuria) was found to be 37% of the total 300 pregnant women included in this study (figure 2). The demographic results of the study suggested that half of the pregnant women were aged between 15-24 years, the majority of them (81.7%) belonged to urban areas, and 37.3% of the women were illiterate, where 28.3% of their husbands were also uneducated. On the other hand, the rates of women and husbands with college and higher education were 9.3% and 10.7% respectively.

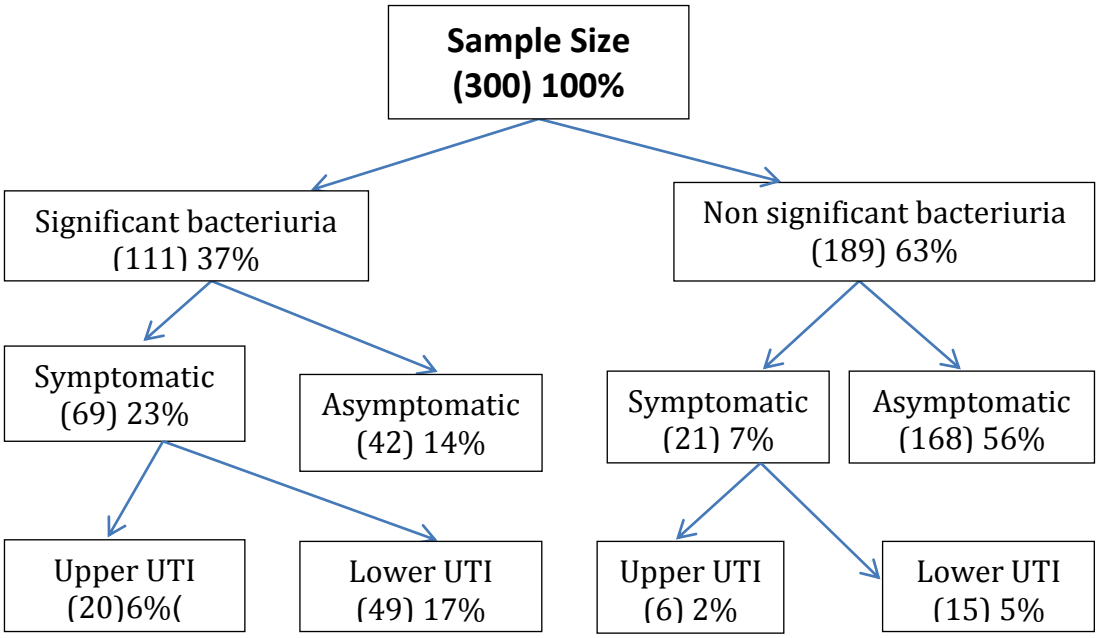

Figure-2: Number and Percentage of sample size categories

A high proportion of women (88.7%) were housewives (unemployed), while 71% of their husbands were self-employed. 182 women (60.7%) had monthly income less than $400 and 24 (8%) women earned more than $1000 monthly income. Also, about two thirds of the women (202) had extended type of family (Table 2).

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Table(2): Socio-demographic characteristics of the pregnant women by bacteriuria

Variable		***Significant bacteriuria (N=111) N(%)***	***Non- significant Bacteriuria (N=189) N(%)***	***Total N(%)***	***P value****
Age group	*15-24*	*65(42.5)*	*88(57.5)*	*153(51)*	*0.127*
	25-34	*34(32.1)*	*72(67.9)*	*106(35.3)*	
	35-44	*12(29.3)*	*29(70.7)*	*41(13.7)*	
Mean= 25.15 Y Range= 28					
Residence	*Urban*	*85(34.7)*	*160(65.3)*	*245(81.7)*	*0.081*
	Rural	*26(47.3)*	*29(52.7)*	*55(18.3)*	
Educational Level of Husband	*Illiterate*	*33(38.8)*	*52(61.2)*	*85(28.3)*	*0.961*
	Read and write	*8(33.3)*	*16(67.7)*	*24(8)*	
	Primary school	*24(39.3)*	*37(60.7)*	*61(20.3)*	
	Intermediate school	*28(37.8)*	*46(62.2)*	*74(24.7)*	
	Secondary school	*8(33.3)*	*16(66.7)*	*24(8)*	
	High education	*10(31.2)*	*22(68.8)*	*32(10.7)*	
Educational Level of women	*Illiterate*	*42(37.5)*	*70(62.5)*	*112(37.3)*	*0.742*
	Read and write	*7(35)*	*13(65)*	*20(6.7)*	
	Primary school	*32(42.7)*	*44(57.3)*	*76(25.3)*	
	Intermediate school	*18(37.5)*	*30(62.5)*	*48(16)*	
	Secondary school	*4(25)*	*12(75)*	*16(5.3)*	
	High education	*8(28.6)*	*20(71.4)*	*28(9.3)*	
Occupation of women	*Housewife*	*104(39.1)*	*162(60.9)*	*266(88.7)*	*0.108*
	Employed	*5(20)*	*20(80)*	*25(8.3)*	
	Student	*2(22.2)*	*7(77.8)*	*9(3)*	
Occupation of Husband	*Governmental Employment*	*24(33.3)*	*48(66.7)*	*72(24)*	*0.813*
	Non-Governmental Employment	*4(44.4)*	*5(55.6)*	*9(3)*	
	Unemployed	*0(0)*	*1(100)*	*1(0.3)*	
	Self-employed	*82(38.5)*	*131(61.5)*	*213(71)*	
	Students(others)	*1(20)*	*4(80)*	*5(1.6)*	
Family monthly Income	*(<500,000ID)*	*70(38.5)*	*112(61.5)*	*182(60.7)*	*0.108*
	(500,001-900,000ID)	*30(42.9)*	*40(57.1)*	*70(23.3)*	
	(900,001-1,250,000ID)	*4(16.7)*	*20(83.3)*	*24(8)*	
	(>1,250,000ID)	*7(29.2)*	*17(70.8)*	*24(8)*	
Type of family	*Nuclear*	*34(34.7)*	*64(65.3)*	*98(32.7)*	*0.564*
	Extended	*77(38.1)*	*125(61.9)*	*202(67.3)*	

**Chi square test*

Results concerning with the obstetrical and genitourinary characteristics of the pregnant women revealed that 11 (3.7%) women had genitourinary abnormalities such as the existence of only a

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single kidney, and cystocele and previous genitourinary surgical operation, (Table 2). Six of them (54.5%) had significant bacteriuria, of which 66.6% were infected with klebsiella spp.

Regarding the gravidity of women in this study, the rate of primigravida was 26.3%, multigravida (2-4 pregnancies) was 44.3% and grand multigravid (≥5 pregnancies) was 29.3%. Parity, on the other hand, was as follows: nullipara was 31%, 18% of para one, 42% multipara, and 9% grand multipara. The prevalence of previous cesarean section was 34.6%, but more than half of the women (121) had vaginal delivery (57.3%), while 8.1% were with both types (cesarean and vaginal). More than half of the pregnant women (51.4%) were in the third trimester, 36.3% at second trimester, and lowest rate (12.3%) at first trimester of their pregnancy. The history of UTI was positive in 70% of the pregnant women and majority of the sample (94%) had three and above sexual intercourse per week, and only 12% had positive history of urinary bladder catheterization (Table 3).

No significant association was found between significant bacteriuria and sociodemographic characteristics of the pregnant women (Table 1). However, the rate of significant bacteriuria was significantly higher among the women with previous NVD (41.3%) than with C/S (21.9%) and higher rate was also estimated among those with positive history of UTI (41.6%), which was also significant (Table 3).

Table(3): Obstetrical and genitourinary history of the pregnant women by bacteriuria

Variable		***Significant bacteriuria* (N=111) *N(%)***	***Non-significantbacteriuria (N=189) N(%)***	***Total N(%)***	***P value***
Presence of genitourinary abnormality	*Yes*	*6(54.5)*	*5(45.5)*	*11(3.7)*	*0.34*
	No	*105(36.5)*	*184(63.5)*	*289(96.3)*	
Range of Gravidity	*Primigravid*	*34(43)*	*45(57)*	*79(26.3)*	*0.325*
	multigavid	*49(36.8)*	*84(63.2)*	*133(44.3)*	
	Grand multigravid	*28(31.8)*	*60(68.2)*	*88(29.3)*	
Range of Parity	*Nullipara*	*42(45.2)*	*51(54.8)*	*93(31)*	*0.230*
	Primipara	*20(37)*	*34(63)*	*54(18)*	
	Multipara	*40(31.7)*	*86(68.3)*	*126(42)*	
	Grand multipara	*9(33.3)*	*18(66.7)*	*27(9)*	
Type of past delivery	*NVD*	*50(41.3)*	*71(58.7)*	*121(57.3)*	*0.014*
	C/S	*16(21.9)*	*57(78.1)*	*73(34.6)*	

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	NVD+C/S	*4(23.5)*	*13(76.5)*	*17(8.1)*	
Gestational age of the current pregnancy in weeks	*1-12*	*13(35.1)*	*24(64.9)*	*37(12.3)*	*0.770*
	13-27	*38(34.9)*	*71(65.1)*	*109(36.3)*	
	28-birth	*60(39)*	*94(61)*	*154(51.4)*	
History of anemia in current pregnancy	*Yes*	*32(33.7)*	*63(66.3)*	*95(31.7)*	*0.523*
	No	*79(38.5)*	*126(61.5)*	*205(68.3)*	
History of UTI	*Yes*	*87(41.6)*	*123(58.4)*	*210(70)*	*0.036*
	No	*24(26.7)*	*66(73.3)*	*90(30)*	
Frequency of sex in week	*≤3*	*106(37.6)*	*176(62.4)*	*282(94)*	*0.403*
	>3	*5(27.8)*	*13(72.2)*	*18(6)*	
History of use catheterization	*Yes*	*12(33.3)*	*24(66.7)*	*36(12)*	*0.627*
	No	*99(37.5)*	*165(62.5)*	*264(88)*	

Women with significant bacteriuria had a significantly lower mean age than those with non-significant bacteriuria, while no significant difference was estimated between the two groups when considering the means of gestational age, gravidity, parity, and hemoglobin level (Table 4)

Table(4):Mean age, gestational age, gravidity, party, and Hb level of pregnant women by bacteriuria

characteristics	***Significant bacteriuria (n=111)***	***Non-significant bacteriuria (n=189)***	***P value****
Age/years M±SD	*24.05±6.57*	*25.79±6.48*	*0.026*
Gestational age/weeks	*27.04±10.02*	*25.78±10.51*	*0.31*
Gravidity	*3.28±2.29*	*3.48±2.26*	*0.47*
Parity	*1.74±1.96*	*2.05±1.96*	*0.182*
Hb (mg/100ml)	*11.5±1.42*	*11.16±1.73*	*0.081*

*Student t-test

Significantly higher rates of significant bacteriuria were estimated among pregnant women with almost all genitourinary symptoms as illustrated in Table 5. In general, 69 (76.7%) women had significant bacteriuria of the total 90 (30%) symptomatic pregnant women, while only 42 (20%) participants of 210 (70%) asymptomatic women were found to have significant bacteriuria. Similarly, a highly significant association was estimated between significant bacteriuria and laboratory urinalysis results with higher rates among pregnant women with positive urinalysis Results (Table 6).

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Table(5):Distribution of pregnant women by bacteriuria and genitourinary symptoms

Genitourinary Symptoms	*Significant bacteriuria (n=111) N(%)*	*Non-significant bacteriuria. (n=189) N(%)*	*P value*
Symptomatic UTI (n=90)	*69(76.7)*	*21(23.3)*	*<0.0001*
Frequency of urine (n=69)	*63(91.3)*	*6(8.7)*	*<0.0001*
Nocturia (n=64)	*58(90.6)*	*6(9.4)*	*<0.0001*
Presence supra pubic pain (n=73)	*63(86.3)*	*10(13.7)*	*<0.0001*
Fever (n=47)	*37(78.7)*	*10(21.3)*	*<0.0001*
Rigor (n=1)	*1(100)*	*0(0)*	*0.37*
Nausea (n=24)	*21(87.5)*	*3(12.5)*	*<0.0001*
Vomiting (n=7)	*7(100)*	*0(0)*	*0.00084*
Loin pain (n=47)	*42(89.4)*	*5(10.6)*	*<0.0001*
Costovertebral tenderness (n=18)	*13(72.2)*	*5(27.8)*	*0.001*
Dysuria (n=81)	*71(87.7)*	*10(12.3)*	*<0.0001*
Urgency (n=73)	*62(84.9)*	*11(15.1)*	*<0.0001*
Presence of blood in urine (n=20)	*16(80)*	*4(20)*	*0.00004*
Cloudy or foul smell urine (n=60)	*49(81.7)*	*11(18.3)*	*<0.0001*
Incomplete voiding of urine (n=70)	*63(90)*	*7(10)*	*<0.0001*
Vaginal discharge-Heavy amount (n=15)	*6(40)*	*9(60)*	*0.805*
Vaginal discharge-Color change (n=69)	*30(43)*	*39(57)*	*0.204*
Vaginal discharge-Itching (n=90)	*41(46)*	*49(54)*	*0.045*
Vaginal discharge-External Dysuria (n=24)	*8(33)*	*16(67)*	*0.698*
Vaginitis >= 2 Symptoms (n=65)	*32(49)*	*33(51)*	*0.021*

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Table(6):Lab. Results of urinalysis of the pregnant women by bacteriuria

Lab. Results of urinalysis	***Significant bacteriuria (n=111) N(%)***	***Non-significant bacteriuria(n=189) N(%)***	***P value***
Turbidity (n=53)	*43(81.1)*	*10(18.9)*	*<0.0001*
WBC (n=123)	*105(75.5)*	*18(24.5)*	*<0.0001*
RBC (n=49)	*39(79.6)*	*10(20.4)*	*<0.0001*
RBC cast (n=4)	*4(100)*	*0(0)*	*0.018*
Bacteria (127)	*103(81.1)*	*24(18.9)*	*<0.0001*
Crystal (n=175)	*81(46.3)*	*94(53.7)*	*0.00008*
Albumin (n=30)	*18(60)*	*12(40)*	*0.006*
RBC(dipstick) (n=53)	*39(73.6)*	*14(26.4)*	*<0.0001*
Leukocyte esterase(dipstick) (n=120)	*100(83.3)*	*20(16.7)*	*<0.0001*
Nitrite(dipstick) (n=19)	*15(78.9)*	*4(21.1)*	*0.00009*

Among a total of 111 pregnant women with significant bacteriuria, the predominant growth of single bacteria was that of Escherichia coli (n=32, 28.8%), which had high sensitivity towards amikacin and garamycin but 100% resistance to ampicillin, cloxacillin and amoxicillin. The next common bacteria was staphylococcus aureus (n=31, 27.9%), which was highly sensitive to furadantine but resilient towards amoxicillin. Lastly, klebsiella spp. (n=17, 15.3%) was found to prevail with a sensitivity to amikacine and garamycine and resistance towards ampicillin, cloxacillin, and amoxicillin, as shown in Table 7. The other less common pathogens, which are, proteus mirabilis (4.5%), streptococcus pyogeneous (3.6%), and pseudomonas aerogenosa (2.7%), were also detected.

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Table(7): Antibiotic Sensitivity & Resistance Pattern of Isolated Organism in UTI

Staph. Aurous+ E. coli		*Klibesila + E. coli*		*Staphylococcus ,candidia*		*Stereptococcuspyogeneous*		*Pseudomonas aeruginosa*		*Proetus mirabilis*		*Staphylococcus aureus*		*Escherichia coli*		*Klebsiella spp.*	
N=6(5.4%)		*N=5 (4.5%)*		*N=8(7.2%)*		*N=4(3.6%)*		*N=3(2.7%)*		*N=5(4.5%)*		*N=31(27.9%)*		*N=32(28.8%)*		*N=17 (15.3%)*	
R	*S*	*R*	*S*	*R*	*S*	*R*	*S*	*R*	*S*	*R*	*S*	*R*	*S*	*R*	*S*	*R*	*S*
100%	*0%*	*100%*	*0%*	*100%*	*0%*	*100%*	*0%*	*100%*	*0%*	*100%*	*0%*	*87.1%*	*12.9%*	*100%*	*0%*	*100%*	*0%*
83.3%	*16.7%*	*100%*	*0%*	*50%*	*50%*	*25%*	*75%*	*100%*	*0%*	*100%*	*0%*	*87.1%*	*12.9%*	*100%*	*0%*	*100%*	*0%*
16.7%	*83.3%*	*100%*	*0%*	*12.5%*	*87.5%*	*0%*	*100%*	*66.7%*	*33.3%*	*40%*	*60%*	*19.4%*	*80.6%*	*46.9%*	*53.1%*	*52.9%*	*47.1%*
100%	*0%*	*100%*	*0%*	*100%*	*0%*	*100%*	*0*	*100%*	*0%*	*100%*	*0%*	*96.8%*	*3.2%*	*100%*	*0%*	*100%*	*0%*
33.3%	*66.7%*	*0%*	*100%*	*0%*	*100%*	*25%*	*75%*	*0%*	*100%*	*20%*	*80%*	*19.4%*	*80.6%*	*6.20%*	*93.8%*	*5.9%*	*94.1%*
50%	*50%*	*80%*	*20%*	*80%*	*20%*	*75%*	*25%*	*100%*	*0%*	*100%*	*0%*	*93.5%*	*6.50%*	*96.9%*	*3.1%*	*88.2%*	*11.8%*
66.7%	*33.3%*	*20%*	*80%*	*20%*	*80%*	*75%*	*25%*	*100%*	*0%*	*60%*	*40%*	*6.5%*	*93.5%*	*43.8%*	*56.2%*	*47.1%*	*52.9%*
33.3%	*66.7%*	*0%*	*100%*	*0%*	*100%*	*75%*	*25%*	*33.3%*	*66.7%*	*0%*	*100%*	*29%*	*71%*	*0%*	*100%*	*5.9%*	*94.1%*
83.3%	*16.7%*	*80%*	*20%*	*100%*	*0%*	*80%*	*20%*	*100%*	*0%*	*80%*	*20%*	*77.4%*	*22.6%*	*87.5%*	*12.5%*	*94.1%*	*5.9%*
83.3%	*16.7%*	*60%*	*40%*	*60%*	*40%*	*50%*	*50%*	*0%*	*100%*	*80%*	*20%*	*77.4%*	*22.6%*	*71.9%*	*28.1%*	*64.7%*	*35.3%*
100%	*0%*	*60%*	*40%*	*60%*	*40%*	*75%*	*25%*	*33.3%*	*66.7%*	*60%*	*40%*	*87.1%*	*12.9%*	*78.1%*	*21.9%*	*70.6%*	*29.4%*
83.3%	*16.7%*	*40%*	*60%*	*40%*	*60%*	*75%*	*25%*	*66.7%*	*33.3%*	*40%*	*60%*	*77.4%*	*22.6%*	*68.8%*	*31.2%*	*52.9%*	*47.1%*

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		Ampicillin	*Cloxacillin*	*Pipracillin*	*Amoxicilline*	*Amikacine*	*Erythro.*	*Nitrofura.*	*Gramicyine*	*Cephalexine*	*Ceftriaxone*	*Cefotaxime*	*Cefixime*	

Multi drug resistance (MDR = resistance to 2 drugs and above) to different antibiotics was observed in 100 % of the isolated bacterial uropathogens. The antibiotic sensitivity test results showed that the highest resistance was for amoxicillin, ampicillin, cloxacillin, erythromycin and cephalexine. Apart from this, the antibiotics having the highest sensitivity were amikacine, garamycin, and pipracillin (Figure 3).

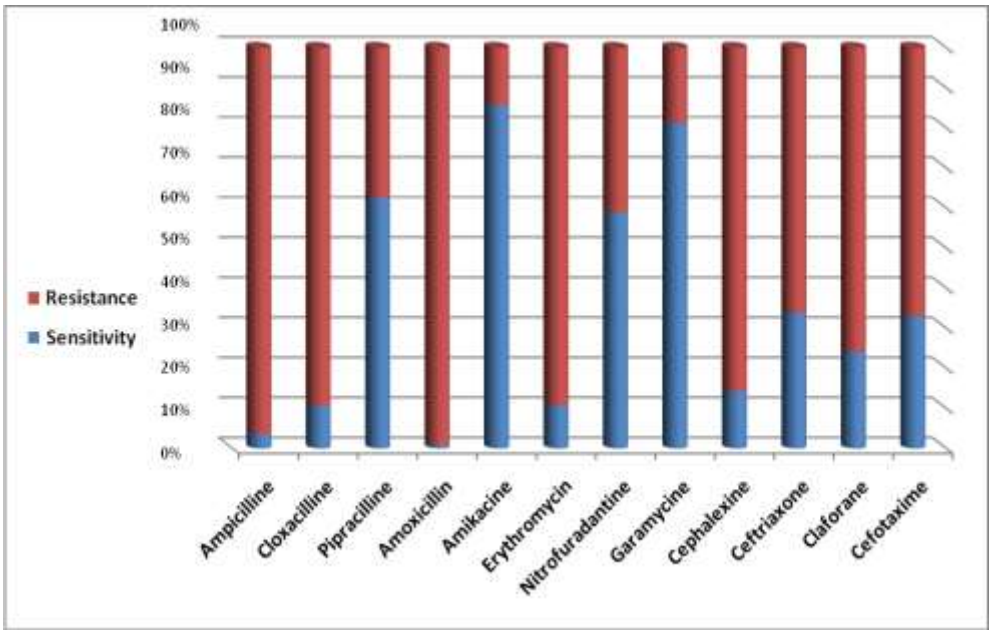

Figure-3:Antibiotic sensitivity test

DISCUSSION

Urinary tract infections (UTI) are highly frequent within a hospital setting and also among general population. Nearly 1/3rd of all the women experience UTI at some point in their life.[36] In general, the pregnant women are considered immunocompromised UTI hosts because of physiologic changes associated with pregnancy.[37] It is considered as a serious problem for women, which must be treated or it may lead to pyelonephritis, preterm labor or Group B Streptococcal infection in the newborn.[38]

The prevalence of UTI in this study was 37%, which is lower than that of other studies conducted in other governorates in Iraq; Mosul (47%), Tikrit (38%) and Kirkuk (29%).[10, 11, 12] This contrast may be due to the different study settings and designs and differences in socio-economic characteristics. This rate is observed to be higher than Abha in Saudi Arabia (12.7%)[6],

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al- komis in Libya (30%)[39], Khartoum (26.8%)[2] and Eastern Ethiopia (14%).[40] The highest rates recorded in different studies in Nigeria were 55% and 61.5%.[41, 42] Also, the prevalence rates of UTI in developing countries are higher than that of the developed countries such as United States, where it ranges from 5%–6% in women of 18–40 years of age. Most of these UTIs are uncomplicated and managed on an outpatient basis with simple antibiotic regimens. In low and middle income countries, UTI may be expected to cause higher morbidity and incur greater risk of adverse outcomes due to the lack of medical care accessibility and the inability of women to get appropriate treatments at the right time. In agreement with another study, UTI was higher among pregnant women with symptoms than those without symptoms.[40]

The rate of asymptomatic bacteriuria among 300 pregnant women in the present study was 14%, which is higher than that reported by other studies where asymptomatic bacteriuria ranged from 2.5% to 11%.[43] Screening all pregnant women for UTI should be considered as a compulsory test at antenatal care visits[44] since the untreated cases of bacteriuria is a risk factor for acute cystitis (40%) and pyelonephritis (25-30%) in pregnancy. These cases account for 70% of all the cases of symptomatic UTI among the unscreened pregnant women.[37] Treating ASB in pregnancy, thus reduces the rates of persistent bacteriuria and the women's risk of developing pyelonephritis.[45]

The results of this study revealed a higher rate of UTI among women delivered by vaginal delivery only by C/S. This observation was different from another study that found an association between cesarean delivery and UTI, however, the study was confounded by other factors such as bladder catheterization or prolonged rupture of membranes.[46]

The pregnant women with previous history of UTI had higher rate of current UTI than those with negative history. This result agrees with the existing studies conducted in eastern Ethiopia (2016)[6], Pakistan (2010) [38], Abha (2013) [39], and Libya (2013).[40] The alignment within the results might be due to the presence of resistant strains of pathogens among those who had previous history of UTI.[46] Additionally, the present study found that almost all the pregnant women with positive genitourinary and related symptoms have reported significantly higher rates of UTI, except that for rigor and vaginal discharge. This finding was in agreement with the related studies conducted in Al-Khartoum (2011)[2], Northwest Ethiopia (2012)[6] and Abha (Saudi Arabia, 2013).[47] Significant bacteriuria was also estimated with higher rates among pregnant women with positive laboratory results of urinalysis, which is similar to the finding of a study conducted in A Nepal (2012).[48] When compared with the culture, Urinalysis has a sensitivity of only 25-67% and a specificity of 97-100% in the diagnosis of asymptomatic bacteriuria.[37] A significantly higher rate of significant bacteriuria was reported in the current study among the pregnant women with positive urinalysis results.

Although, the majority of the studies revealed no significant association of almost all socio demographic characteristics of pregnant women with significant bacteriuria, only a few studies did. A study in Nigeria revealed that the maternal age and educational status did not affect the prevalence of urinary tract infection.[42] However, the current study found that the women with significant bacteriuria had a significantly lower mean age than the others. A finding similar to this revelation was reported in Mosul (2007)[11], and Northwest Ethiopia (2013)[16], but in disagreement with a study in Abha-Saudi Arabia (2013)[6]. Comparable results were reported in a

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study in southern Nigeria, which found that the younger women (14-23 years) were more infected, while the study in southeast Nigeria found that the pregnant women aged 15-20 years were the least infected, therefore, both the results were not statistically significant.[41, 49] The educational level of women, and family monthly income in the present study, have no significant association with significant bacteriuria, which is similar to Ethiopian studies in 2012 and 2013[16, 47] and Abha-Saudi Arabia (2013)[6], but differs with Libyan study (2013).[39] The other factors having no significant association with bacteriuria are women's family type and husband educational level.

No significant association was estimated in this study between gravidity and parity with significant bacteriuria. This was in agreement with a study in Ethiopia (2012)[47], similarly the history of abortion had no association with significant bacteriuria as in a study conducted in Abha-Saudi Arabia (2013)[6]. The gestational age of pregnant women in the present study had no significant association with significant bacteriuria, which is similar to the findings of the two Ethiopian studies in 2012 and 2013[16, 47], while different results were reported in the other studies conducted in Mosul, Baghdad (2004), and Libya (2013).[11, 29, 50]

The disagreement between the results of this study and other studies regarding the association of significant bacteriuria with multiple variables of pregnant women may be attributed to the differences in social, economic, cultural characteristics and traditional habits of populations and living standards, availability and accessibility of health services, in addition to different research plan.[16]

The history of catheterization had no association with significant bacteriuria during pregnancy in the present study, which agrees with Ethiopian study (2012)[47], but disagrees with Ethiopian study conducted in 2013.[16] Multiple studies in Ethiopia (2013), Iran (2009) and Libya (2013) revealed significant association of UTI with sexual activity, which differs from the finding of the current study. The history of genitourinary abnormality and anemia (Hemoglobin concentration less than 11gm/dl) of pregnant women in the current study had no association with significant bacteriuria as found in the Ethiopian study (2013).[16]

E. coli, prevailing in 28.8% of women infected with UTI, is the most implicated microorganism causing UTI in pregnant women in the present study. This rate is near to that obtained in other parts of the country as in Tikrit study (31.1%)[12], while in south western Nigeria in 2010 and eastern Ethiopia (2016), E.coli was isolated from 42.1% and 34.6% of the cases of UTI respectively.[14, 40] The higher rates were also estimated at Khartoum and Ethiopia studies (42.4% and 47.5% respectively)[2, 47], while E coli was the most common uropathogen (40%) among the infected subjects in other studies.[41, 42, 49] This may be due to the ability of uropathogenic E coli to express a multitude of virulence factors to break the inertia of the mucosal barrier, and can persist within the urinary tract serving as a reservoir for recurrent infections and serious complications. It was also postulated that the receptors CD55, also called DAF, is upregulated by progesterone a hormone that increases with gestational age. E coli, which recognizes CD55, may gain an advantage in the colonization and/or invasion of tissues, a process that is directly proportional to CD55 receptor density.[51] Up to the knowledge of the researchers, no previous

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studies in this Iraqi governorate had determined the microbial and antibiotic susceptibility of UTI in pregnant women.

This study showed that E.coli has multidrug resistance (MDR = resistance to ≥ 2 drugs) of 100%, mainly to ampicillin, amoxicillin and cloxacillin, but high sensitivity to garamycine, amikacine and furadantin. These findings are in agreement with another two studies conducted in Iraq (in Kirkuk and Tikrit) and Ethiopian study.[10, 12, 47] Although, Staphylococcus aureus (S. aureus) was known for years as a rare urinary isolate, it has been reported to be the most frequent pathogen among pregnant women in Nigeria[2], and the second isolated microorganism in the current study with a rate of 27.9% of total UTI cases. This rate is more than that reported by a study in Tikrit (11.1%)[12], but slightly higher than Ethiopian study (22.5%).[47] S. aureus, in the present study, had high sensitivity to furadantin (93%), pipracilline (80%) and amikacine (80%), but was resistant towards penicillin and cephalosporin groups. These revelations were in consistency with Tikrit study, except for resistance to cephalosporin.[12]

In the present study, Klebsiella constituted 15.3% of all significant UTI, which was slightly higher than that observed in Tikrit (13.3%).[12] Different studies found that Klebsiella. spp is highly sensitive to amikacine and garamycine but highly resistant to penicillin groups, with moderate resistance to cephalexin, which is similar to results of the current study.[12, 47] The other microorganisms such as proteous mirabilis (4.5%) and mixed microorganism (klebsiela.spp with E.coli 4.5%) were far less than that seen in Tikrit study (22.2%). The above microorganisms showed resistance to penicillin, but they were sensitive to aminoglycoside and cephalosporineas as in Kirkuk study in Iraq.[10] The highest rate of the mixed microorganism growth that had been seen in the present study was of Staphylococcus aurous with candida (7.2%). This mixed growth was sensitive to gramycine and pipracillin (100% and 87.5% respectively), but 100% resilient towards penicillin and cephalexin groups. Streptococcus pyogenous rate was 3.6%, which was less than that seen in Nepal 8.3%.[48] Pseudomonus aeroginosa had the lowest rate among isolates in the current study (2.7%), which was less than that reported in Tikrit study (15.5%)[12], but near to Kirkuk study (3.4%) [10], it was highly sensitive to amikacine, with less sensitivity to garamycine and full resistance to penicillin groups. In general, the bacterial pattern of the organisms that were implicated in the current study was similar to that of other existing studies.[41, 49, 52]

The high prevalence rate of UTI reported in the present study must be greatly concerned not only for the adverse health effects on life of pregnant women and their fetuses, but also because they may impose economic and social burden due to stigma associated with these infections. In addition, the important infecting microorganisms were found to be commensals of perianal and vaginal regions, which recommends the pregnant women to increase their personal and environmental hygiene and emphasize on need to expand health services for prevention and treatment to pregnant women.[41, 49]

Multi-drug resistance was seen in 100 % of the isolated bacterial uropathogens to the commonly used antibiotics. A lower rate was estimated in Gondar Teaching Hospital in Ethiopia (95 %).[47] Antibiotic resistance has been recognized as the consequence of antibiotic use and abuse, therefore, the reasons for this alarming phenomenon might be due to the inappropriate and

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incorrect administration of antimicrobial agents in empiric therapies and the lack of appropriate infection control strategies, which can cause a shift to increase prevalence of resistant organisms in the community.[47]

LIMITATIONS OF THE STUDY:

Some of the obstacles of the present study that might have affected the results are:

1. Limited number of pure cases (cases with inclusion criteria that coincide with requirements of the study).
2. Difficulty of control on women behaviour, and the low knowledge among participants about the benefit of these investigations.

CONCLUSIONS

In the present study, the prevalence of urinary tract infection among the pregnant women was found to be 37%, which was associated with younger age, history of vaginal delivery, past history of UTI, and positive clinical and laboratory findings. Significant bacteriuria was observed in symptomatic and asymptomatic pregnant women. Escherichia coli was the most predominant microorganism, followed by coagulase positive staphylococci. Both of these were sensitive to garamycin, amikacin and resistant to penicillin and cephalosporine. A large number of the isolates were resistant to ampicillin, amoxacillin, erythromycin, cloxacillin and cephalaxin. The results of the present study may be useful for the health ministry in policy formulation, since no data is available from this part of the country, especially those related to most common microorganisms in UTI and drug sensitivities, which can be used in the development of hospital-specific treatment standards, as therapy must be initiated on an empirical basis, before culture results are available.

The study highly recommends the regular screening of all the pregnant women for UTI with urine culture. Such screening will assist in the early detection of causative agent and determine their drug susceptibility to ensure adequate treatment with appropriate antimicrobial drugs, and also to prevent any complications for mother and fetus. In addition, all the pregnant women should be educated by antenatal care providers about causes and drug use of pregnant women with UTI. For empirical treatment of pregnant women with UTI, Garamycin, Amikacin and Pipracillin can be used when there is no facilities for culture and sensitivity tests in their areas. However, they should be used with great care to reduce the further emergence of drug resistance. The knowledge of the local prevalence of bacterial organisms, antibiotic sensitivities and Institution-specific drug resistances should also be considered before selection of empirical antibiotic.[37, 40]

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