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Original Research Article

Urinary Tract Infections: Prevalence, Risk Factors, and Antimicrobial Susceptibility Profile of Associated Bacterial Pathogens among Pregnant Women Visiting Teaching Hospitals, Khartoum, Sudan

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Abstract

Pregnancy causes numerous changes in the woman's body that increase the likelihood of Urinary Tract Infections (UTI's). UTI's during pregnancy is associated with risks to both the fetus and the mother, and *Escherichia coli (E.coli)* is the most common cause. The aim of this study was to determine prevalence of urinary tract infections (UTI's) during pregnancy, risk factors and antimicrobial susceptibility profiles of associated bacterial pathogens in Khartoum Hospitals. A cross-sectional hospital-based study, conducted among 230 pregnant women attending antenatal clinics. Their socio-demographic profile and risk factors obtained using a structured questionnaire. Urine samples tested microbiologically by standard procedures. Kirby-Bauer technique performed for testing commonly used antimicrobial agents by measuring the susceptibility of the isolated organisms according to CLSI guidelines. Out of 230 pregnant women included; 47 (20.4%) had a significant bacteriuria, (40.4%; 19/47) was symptomatic, and (59.6%; 28/47) was asymptomatic UTIs. Among pregnant women who had significant bacteriuria, only 1 (2.1%) had history of UTI during this pregnancy and 46 (97.9%) had no history. Gram-negative bacteria were more prevalent (68.1%). *E.coli* was the common isolate (31.9%; 15/47). More than 60% of the total isolated bacterial pathogens were resistance to ampicillin, amoxyclave and clindamycin, followed by ≥ 35% to 3rd generation cephalosporins, nitrofurantoin and norofloxacin. UTI are prevalent in pregnant women in Sudan, regardless age, parity and gestational age. The significant bacteriuria, signs and symptoms, and a previous UTI were found significantly associated with UTI's during pregnancy. Resident social class and employment status were protective, while other factors such as high level of education, parity, history of abortion were not protective. The *E. coli* was the common isolate and carbapenems, aminoglycosides, quinolones were the drug of choice. Therefore, UTI screening is essential during pregnancy.

Keywords: Asymptomatic bacteriuria, Etiology, Pregnant women, Sudan, Urinary Tract Infection

INTRODUCTION

UTI's are the most common infection in women throughout the world (Dielubanza and Schaeffer, 2011; Schnarr and Smaill, 2008). They can range from asymptomatic presence of bacteria (ASB) in urine to infections with pronounced bladder symptoms (Schnarr and Smaill, 2008). The condition affects 20% of pregnant women, and it is the most common reason for women admitted to obstetrical wards (Schnarr and Smaill, 2008; Bacak et al., 2005; Tolulope and Deborah, 2015). During pregnancy, physiological changes in the urinary tract and immune system along with hormonal changes contribute to an increased risk of ASB, resulting in serious risks for both mother and fetus. There may be independent risk factors for UTI when pregnant, such as age, parity, diabetes, Sickle cell anaemia, history of UTI, urinary tract disorders, and immune deficiency (Schnarr and Smaill,

2008; Bacak et al., 2005; Tolulope and Deborah, 2015). The treatment of pregnancy-related ASB and acute cystitis is often empirical before culture and antibiotic sensitivity testing done. *E. coli* and other coliforms account for a large majority of these naturally acquired infections (Hooton, 2000; Sefton, 2000). Depending on geography, these bacteria differ in their susceptibility to antimicrobials (Sefton, 2000). Thorough knowledge of the bacterial species involved and their antibiotic susceptibility patterns in a particular geographic location is necessary, to adequately treat these patients. There are limited data on the distribution and susceptibility patterns of urinary bacterial isolates, particularly in the study area, among pregnant women in Sudan. Accordingly, this study aimed to determine the bacterial profile, antibiotic susceptibility pattern, and risk factors associated with UTIs among pregnant women visiting Sudanese hospitals.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted during the period from February to July 2018, in Khartoum Hospitals (Academic Charity Teaching Hospital, Ibrahim Malik Teaching Hospital, Yastabshiroon Hospital, Omdurman Maternity Hospital, Soba University Hospital, and family clinic).

Data collection

A face-to-face interview with pre-tested questionnaire, was conducted after signing informed consent. The questionnaire asked about several socio-demographic characteristics associated with UTI, such as age, employment status, and education level. In addition, signs and symptoms, gestational age, multiparity, medical history, and obstetric history, are considered as risk factors for UTI.

Collection of urine samples

Patients provided with clear instructions on how to avoid contamination of urine samples. Two hundred and thirty midstream urine samples collected from pregnant women and immediately transported to the laboratory in sterile universal containers.

Isolation and identification of bacteria from urine samples

As part of the standard microbiological procedures, the samples examined microscopically for pus cells and casts. Samples cultured immediately on Cystinelactose electrolytes deficient (CLED) media (Oxoid, Ltd., Basingstoke, Hampshire, England) by the 0.01 ml standard loop and incubated in the aerobic atmosphere at 37^{o}C for 24 h. The total number of colonies counted to determine the presence of significant bacteriuria, and results of culture plates interpreted as significant, or insignificant. Significant bacteriuria defined as a growth of 10^5 colony-forming units/ml. From samples showing significant bacteriuria, colonies were selected and characterized on basis of morphology, and gram stain, while biochemical features were used to identify the isolated organisms (Old et al., 1996).

Antimicrobial susceptibility testing

The Kirby-Bauer technique was carried out for antimicrobial susceptibility testing, of all identified isolates, and interpretations to all antibiotics used for UTI in pregnant women irrespective of the hospital antibiotic policy. From a pure culture, loopful bacterial colonies taken and transferred to a tube containing 5 ml of normal saline and mixed gently until it forms a homogenous suspension. The turbidity of the suspension was then adjusted to the density of 0.5 McFarland to standardize the inoculum (Forbes et al., 2007). A sterile cotton swab was then deep into suspension and the excess removed by gentle rotation of the swab against the surface of the tube. The swab was then used to distribute the bacteria evenly over the entire surface of Muller Hinton agar. The inoculated plates were left at room temperature to dry for 3-5 min. With the aid of sterile forceps, the antibiotic disc was put on the surface of Muller-Hinton agar (Oxoid). The plates were then incubated at 37°C for 24 h. Diameters of the zone of inhibition around the discs were measured using a digital caliper, and the isolates were classified as sensitive and resistant according to the standardized table supplied by CLSI 2014 (Forbes et al., 2007; Miller et al., 2014).

Data analysis

Data entered, and organized into Microsoft Office Excel 2007 datasheet, then subjected to statistical analysis using the software statistical package for social science program (SPSS) version 16. Chi-square analysis ($\chi 2$) used in findings on the comparison of positively UTI cases according to individual characteristics. Evaluations carried out at a 95% confidence level and $P < 0.05$ considered statistically significant.

Ethical consideration

The study approved by the ethical committee of the University of Medical Sciences and Technology.

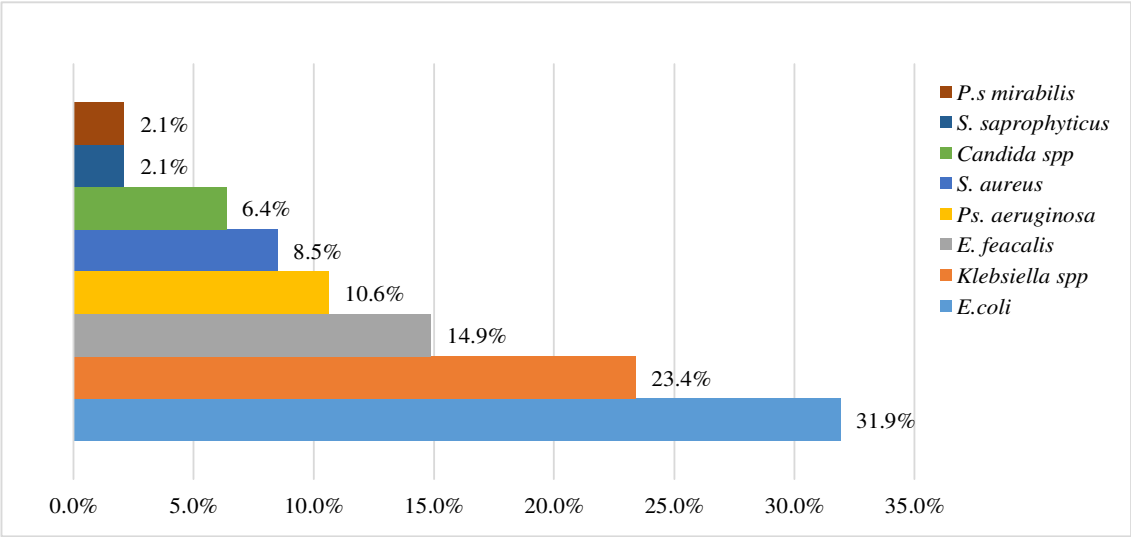

Figure 1. Distribution of isolates (*n*=47)

Permission from the Medical Director of different hospitals applied and verbal consent was obtained from all subjects enrolled in the study. For each confirmed infection case, the responsible clinician of the participant was informed and treatment started as per the culture result and drug susceptibility pattern.

RESULTS

Prevalence of urinary tract infection

In total, 47 (20.4%) out of the 230 samples of pregnant women had significant bacteriuria. The majority of the pregnant women were asymptomatic 164 (71.3%), while only 66 (28.7%) of the pregnant women were symptomatic. In samples showing growth on culture, ASB (12.2%) was identified, whereas symptomatic UTI was only found in (8.3%) of pregnant women (*P*=0.037). Of the culture-positive urine samples, Gram-negative bacteria were the most common of uropathogens responsible for UTI with a (68.1%; 32/47) in comparison to (25.5%; 12/47) for gram-positive bacteria, and (6.4%; 3/47) for gram-positive budding yeast. Seven bacterial species of UTI were isolated in which the majority were *E. coli* accounting for 15 (31.9%) of the total isolated bacterial pathogens, followed by *Klebsiella spp* 11 (23.4%). Other isolates were *Enterococcus feacalis* 7 (14.9%), *Pseudomonas aeruginosa* 5 (10.6%), *Staphylococcus aureus* 4 (8.5%), *Candida spp.* 3 (6.4%), *Staphylococcus saprophyticus* and *Proteus mirabilis* 1 (2.1%) each. (Figure 1)

Socio-demographic characteristics

The Socio-demographic characteristics of 230 pregnant women found in (Tables 1). Pregnant women enrolled in this study with the age range of 15–42 years with the mean (standard deviation) of 25 (+4.7) years. Among the study subjects, 122 (53.0 %) had an educational level of secondary school or less, and 148 (64.3%) were of medium social class. Regarding employment status 29 (12.6%) of women were employed, and 201 (87.4) were housewife.

Factors associated with UTI

Of all considered variables associated with risk factors, only signs and symptoms, and history of UTI during this pregnancy were significantly associated with UTI's, nineteen (27.7 %) had symptoms, and 28 (71.3 %) were asymptomatic (P=0.037), while 20 (8.7 %) and 68 (29.6 %) of study subjects had UTI during this pregnancy, respectively. (P=0.05). The study found that the frequency of patients with UTI were in the first trimester of pregnancy (59%), followed by the third trimester (38%), only (3%) had bacteriuria in the second trimester of pregnancy. Based on their parity, 61 (37.4 %), 169 (21.6 %), were primigravidae, and multigravidae, respectively. There was no significant association between, between UTI and parity, gravidity, and trimester (Table 2).

Antimicrobial resistance pattern of isolates

The overall antimicrobial resistance pattern of the isolated pathogens is shown in Table 3. Among the tested antibiotics the highest resistant range (70.5%-43.5%) to ampicillin, amoxyclave followed by clindamycin, 3rd generation cephalosporins, nitrofurantoin and norofloxacin. Of these isolates were relatively low

Table 1. Socio-demographic characteristics of pregnant women (*n*=230)

UTI infection ?	Yes n(%)	No n(%)	Total n(%)	*P*-value
Age Group				0.539
15-25 Yrs	15(6.52)	74(32.2)	89(38.7)	
26-35Yrs	26(11.3)	86(37.4)	112(48.7)	
36-42Yrs	6(2.6)	23(10)	29(12.6)	
Educational status				0.579
Illiterate	8(3.5)	42(18.3)	50(21.7)	
Secondary school or less	25(10.9)	97(42.2)	122(53.0)	
University school or more	14(6.1)	44(19.1)	58(25.2)	
Employment status				
Employed	10(4.4)	19(8.3)	29(12.6)	0.044*
Housewife	37(16.1)	164(71.3)	201(87.4)	
Resident social class				
Low social class	5(2.2)	57(24.8)	62(27.0)	0.009*
Medium social class	39(17.0)	109(47.4)	148(64.4)	
High social class	3(1.3)	17(7.4)	20(8.7)	
Total	47(20.4)	183(79.6)	230(100)	

Table 2. Factors associated with UTI's among pregnant women (*n*=230)

UTI infection	Yes n(%)	No n(%)	Total n(%)	*P*-value
Sign and symptoms?				
Yes	19(8.3)	47(20.4)	66(28.7)	0.037*
No	28(12.2)	136(59.1)	164(71.3)	
Parity				
Primigravida	15(6.5)	46(20)	61(26.5)	0.223
Multigravida	32(13.9)	137(59.6)	169(73.5)	
History of abortion				
Yes	9(3.9)	36(15.7)	45(19.6)	0.56
No	38(16.5)	147(63.9)	185(80.4)	
Gestational age				
First trimester	5(2.2)	33(14.4)	38(16.5)	0.348
Second trimester	23(10)	72(31.3)	95(41.3)	
Third trimester	19(8.3)	78(33.9)	97(42.2)	
History of UTI's				
Yes	16(7.0)	52(22.6)	68(29.6)	0.28
No	31(13.5)	131(57)	162(70.4)	
How many times				
Once	13(5.7)	31(13.5)	44(19.0)	0.26
Two Times	3(1.3)	19(8.3)	22(9.6)	
Three Times	0(0.0)	2(8.7)	2(8.8)	
History during this pregnancy				
Yes	1(0.4)	19(8.3)	20(8.7)	0.050*
No	46(20.0)	164(71.3)	210(91.3)	
History of antibiotics				
Yes	15(6.5)	53(23.0)	68(29.6)	0.409
No	32(13.9)	130(56.5)	162(70.4)	
History of any other disease				
D.M	2(0.8)	7(3.0)	9(3.9)	0.776
Hypertension	0(0.0)	4(1.7)	4(1.7)	
Other	1(0.4)	3(1.3)	4(1.7)	
No	44(19.1)	169(73.5)	213(92.6)	
Haemoglobin level				
Yes	3(1.3)	25(10.9)	28(12.2)	0.131
No	44(19.1)	158(68.7)	202(87.8)	
Total	47(20.4)	183(79.6)	230(100)	

Table 3. Antimicrobial resistant pattern of the isolates (*n*=44)

Isolates	Gram negative n(%)				Gram positive n(%)			UTI isolates n(%)
A. agents	*E.coli* (n:15)	*Klebs.sp* (n:11)	*P.mirabilis* (n:1)	*P.aureg* (n:5)	*S.aureus* (n:4)	*E.faecalis* (n:7)	*S.saprophyticus* (n:1)	*Total* (n:44)
AMP	15(100)	11(100)	1(100)	NT	2(50)	1(14.3)	1(100)	31 (70.5)
AMC	13(86.7)	9(81.8)	1(100)	5(100)	0(0)	2(28.6)	0(0)	30 (68.2)
AK	0(0)	0(0)	0(0)	1(20)	0(0)	0(0)	1(100)	2(4.5)
CD	11(73.3)	8(72.7)	1(100)	5(100)	1(25)	1(14.3)	1(100)	28(63.6)
CFX	5(33.3)	8(72.7)	1(100)	5(100)	1(25)	1(14.3)	1(100)	22(50.0)
CXM	5(33.3)	6(54.5)	1(100)	3(60)	3(75)	0(0)	1(100)	19(43.2)
CAZ	5(33.3)	5(45.5)	0(0)	1(20)	3(75)	0(0)	1(100)	15(34.1)
CRO	4(26.7)	4(36.4)	0(0)	4(80)	3(75)	0(0)	1(100)	16(36.4)
CTX	11(73.3)	3(27.3)	0(0)	4(80)	100	0(0)	1(100)	23(52.3)
CIP	6(40)	2(18.2)	1(100)	1(20)	1(25)	0(0)	0(0)	11(25.0)
COT	2(13.3)	2(18.2)	1(100)	NT	3(75)	1(14.3)	0(0)	9(20.5)
E	NT	NT	NT	NT	0(0)	2(28.6)	1(100)	3(6.8)
F	1(6.7)	4(36.4)	1(100)	2(40)	3(75)	7(100)	1(100)	19(43.2)
GEN	4(26.7)	5(45.5)	0(0)	1(20)	0(0)	0(0)	0(0)	10(22.7)
IMP	0(0)	1(9.1)	0(0)	0(0)	0(0)	0(0)	0(0)	1(2.3)
MEM	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
NA	3(20)	2(18.2)	1(100)	NT	3(75)	2(28.6)	1(100)	12(27.3)
NOR	2(13.3)	3(27.3)	0(0)	2(40)	100	7(100)	1(100)	19(43.2)
OFL	1(6.7)	2(18.2)	0(0)	3(60)	0(0)	0(0)	0(0)	6(13.6)
PEN	NT	NT	NT	NT	3(75)	1(14.3)	1(100)	5(11.4)
TE	0(0)	1(9.1)	0(0)	NT	0(0)	5(71.4)	0(0)	6(13.6)
V	NT	NT	NT	NT	0(0)	0(0)	0(0)	0(0)

Abbreviations: A. agents: antimicrobial agents**, *Klebs. spp*:** *Klebsiella species***, *P.aureg*:** *Pseudomonas aeruginosa***, AMP**: ampicillin, **AMC**: amoxyclave, **AK**: amikacin, **CD**: clindamycin, **CFX**: cifixime, **CXM**: cefuroxime, **CAZ**: ceftazidime, **CRO**: ceftriaxone, **CTX:** cefotaxime**, CIP**: ciprofloxacin, **COT**: co-trimoxazole, **E**: erythromycin, **F**: nitrofurantoin, **GEN**: gentamicin, **IMP**: imipenem, **MEM**: meropenem, **NA**: nalidixic acid, **NOR**: norofloxacin, **OFL**: ofloxacin, **PEN**: penicillin, **TE**: tetracycline, **V**: vancomycin.

resistant to ceftriaxone (36.4%), ceftazidime (34.1%), nalidixic acid (27.3%), ciprofloxacin (25.0%), and gentamicin (22.7%). However, all gram positive isolates were very sensitive to vancomycin, and both gram positive and negative isolates were highly and fully sensitive to meropenem (100%), followed by (97.7%) to imipenem, (95.5%) to erythromycin and amikacin for each, (88.6%) to penicillin, (86.4%) to ofloxacin and tetracycline for each and (79.5%) to co-trimoxazole. In case of *E. coli*, which was the foremost isolate, most resistant antibiotics were ampicillin (100.0%), followed by amoxyclave (86.7%), clindamycin and cefotaxime (77.7%) for each. *Klebsiella* species which was the second most isolated organism, showed high resistant to ampicillin (100.0%), followed by amoxyclave (81.8%), cifixime and amikacin (72.7%) for each, (54.5%) to cefuroxime and only one strain showed resistant toward impenem (9.1%).

DISCUSSION

In this study, the prevalence of urinary tract infections among pregnant women was 20.4%. This prevalence of UTI is similar to that reported in Nepal (Raza S, Pandey S, Bhatt C (2011) (19.7%) and in Tanzania (Masinde et al., 2009) (18%). However, It is higher than the study done in Khartoum State (Hamdan et al., 2011), where the prevalence of UTI was (14.0%), in north Nigeria (Ali and Abdallah, 2019) (15.8%), and lower than study carried in Egypt (Younis et al., 2019) andin Saudi Arabia (El-Kashif, 2019), were the prevalence of UTI in pregnant women was (49.3%), and (53,5%), respectively. The reason for this variation may attribute them to differences in the environment, social habits of the community, hygiene standards and educational levels.

Asymptomatic pregnant women showed a prevalence rate of (72.3%), which is higher than in symptomatic pregnant women with a prevalence rate of (27.7%). This relatively agrees with a previous study done in Sudan (Hamdan et al., 2011), that showed a high prevalence rate of UTI's in asymptomatic pregnant women, and similar to a study conducted in North West Ethiopia (Demilie et al., 2012).

According to the results, there is a statistically significant correlation between the residence social class, employment status, and UTI during the current pregnancy, which were found to be protective (P=0.009, P= 0.044). Similarly, to the study done in Haydabad (Haider et al., 2010), found that low socioeconomic group, illiteracy, history of sexual activity, UTI history, and multiparity were risk factors for UTI. Other factors such as

high level of education, parity, history of abortion, and women who had 4 or 5 pregnancies were not protective, as they were not a statistically significant predictor of bacteriuria in pregnancy (Table 1).

The assessment of associated risk factors to bacteriuria showed that signs and symptoms (*P*=0.037), and a history of UTI during this pregnancy (*P*=0.050), were significantly associated with bacteriuria. It is following the study done in India (Haider et al., 2010), which found that UTIs are significantly associated with any symptoms of UTI, while previous history of UTI or abortion, gestational age, history of antibiotics were not significant. (Table 2)

About age groups, the highest prevalence found in the age group 26-35 years (46.8%) and the lowest in the age 36-42 years (10.6%). There was no statistically significant association between the age of the pregnant women and UTI. These findings agree with the previous study in Sudan (Hamdan et al., 2011), as well as in India (Dash et al., 2013); and higher than another study done in India (Sujatha and Nawani, 2014), where the highest incidence reported in the age group of 21-30 years, and in Ghana (Turpin et al., 2007), the highest incidence was reported in the age group of 35–39 year.

The association between multiparity and UTI is due to profound physiologic changes affecting the entire urinary tract during pregnancy, and has a significant impact on the natural history of UTI during gestation (Matuszkiewicz-Rowińska et al., 2015). According to this study, parity was not significantly associated with UTI in pregnancy. Although multigravida had a high prevalence rate of 32 (68.1%) when compared to pregnant women who were primigravidae 15 (31.9%), but it is not significant. This finding is in line with different studies throughout the world such as Sudan (Hamdan et al., 2011), Tanzania (Masinde et al., 2009), Ghana (Turpin et al., 2007), and in India (Sujatha and Nawani, 2014).

Pregnant women in the second trimester had the highest prevalence rate of UTI 23 (48.9%), followed by pregnant women in the third trimester 19 (40.4%), and at the end pregnant women in the first trimester 5 (10.6%). This is in agreement with a study conducted in Nairobi (Onyango et al., 2018), concluded that the highest prevalence rate was observed in pregnant women during their second trimester (60.6%), and followed by the third trimester, followed by the first trimester.

There was no significant difference in the prevalence of UTI concerning trimester. This is similar to earlier studies on UTI in Sudan (Hamdan et al., 2011), in Pakistan (Sheikh, 2000), in Tanzania (Masinde et al., 2009), in Iran (Azami et al., 2019), and in India (Dash et al., 2013). Likewise, level of education also found to be not significantly associated with UTI. Other studies also andclindamycin (73.3%, 90.9%, and 100%), respectively. This is similar to the previous study done in Khartoum, Sudan (Hamdan et al., 2011), which showed that E. coli isolates, were resistance to ampicillin (100%), amoxyclave (86.7%). *Proteus mirabilis* also shows high resistant with nalidixic acid, nitrofurantoin, co-trimoxazole, and ciprofloxacin. *Pseudomonas aeruginosa* shows a high percentage of resistance to amoxyclav and cefixime. *E. coli* was (100%) sensitive to imipenem, meropenem, amikacin and tetracycline. In Sudan, patients can purchase and use the most commonly prescribed antimicrobials without prescription because most local pharmacies sell them, which could also contribute to drug resistance. On the other hand, in this study Gram-positive bacterial isolates found to be resistant to norofloxacin (100%), nitrofurantoin (92%) and relatively to 3rd generation cephalosporin's, aminoglycosides and co-trimoxazole which are in agreement with the finding in Saudi Arabia (El-Kashif, 2019)

CONCLUSION

The overall prevalence of urinary tract infection among pregnant women in this study is 20.4%. It was higher among pregnant women without symptoms, regardless of women's age, parity and gestational age. Therefore, UTI screening is essential. The most frequent identified isolates were *E. coli* (31.9%), followed by *Klebsiella spp* (23.4%), all Gram-negative isolates were resistant to Ampicillin at (100%). Signs and symptoms, and a history of UTI during this pregnancy, were found significantly associated with UTI's. Resident social class and employment status were protective, while other factors such as high level of education, parity, history of abortion were not protective. There is a need for periodic surveillance of the type of bacterial pathogens and their updated antimicrobial resistance profile in the study setting.

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