A Clinico-microbiological Study of Urinary Tract Infections in Pregnant Women attending Antenatal Clinic of a Tertiary-level Hospital with Special Reference to Antimicrobial Sensitivity Pattern

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Background and study aim: A study of urinary tract infections (UTI) amongst pregnant women attending antenatal clinic in a tertiary care hospital was taken up as an initiative to investigate vulnerable population which were known to be more prone to infections.

Patients and Methods: Consenting pregnant population of all gestational age, between the ages of 20 to 40 years, attending antenatal clinic of the hospital, were selected, and recruited in this observational study. Urinalysis report, details of isolated uropathogen including antibiotic susceptibility pattern and patient details were collected and analyzed.

Results: Our study revealed a significant association between UTI and demographic status, with common affection in young, illiterate, and rural population with higher incidence in multigravida (72.31%) and multiparity (50.82%) and more commonly in third trimester (47.54%) It also revealed: high prevalence of UTI (30.35%); asymptomatic UTI (21.39%) more than symptomatic UTI (8.96%); Escherichia coli as the commonest isolated uropathogen. Most uropathogens showed high resistance to Co-trimoxazole and Penicillin; whereas demonstrated overall sensitivity to Carbapenems and Fosfomycin, raising the issue of feasible, cheap, and safe treatment strategies in this vulnerable population vis a vis applicability and usefulness of empirical antimicrobial therapy.

Conclusion: The difference in prevalence rates of UTI in pregnancy is attributed to variations in socio-economic status, education, demography, social practices, and environment. The high observed prevalence rate calls for routine screening in all three trimesters of pregnancy and most importantly in the first visit and rational antimicrobial therapy for UTI in pregnancy as part of standard obstetric care.

INTRODUCTION

The establishment and multiplication of microorganisms in the urinary tract is termed Urinary tract Infection (UTI) **[1-3].** The frequency of UTI in pregnant females is twice that of non-pregnant females of similar age group **[7-9]**.

Pregnancy increases the probability of urinary tract infections due to ureteric dilatation (hydronephrosis of pregnancy), increased bladder volume and decreased bladder tone causing non-functional ureteric valves, urinary stasis and vesicoureteral reflux which facilitates bacterial colonization and subsequent infection. UTI during pregnancy, if left untreated might result in significant maternal and fetal morbidity **[2-7]**.

The maternal complications associated with UTI in pregnancy includes pre-eclampsia, premature labour, amnionitis, anaemia etc. whereas the

foetal complications of UTIs in pregnancy included low birth weight, Intrauterine Growth Retardation (IUGR) and premature delivery **[8]**.

Most studies have reported Escherichia coli as the most common uropathogen **[2, 8, 10, 14]**. Urine culture continues to be the gold standard for diagnosis of UTI **[9]**.

The treatment of UTI in pregnancy must ensure safety of the mother, the foetus and prevent the development of anti-microbial resistance in uropathogens **[10]**. This requires judicious selection of drugs with low resistance rates in population, high efficacy, and minimal potential side effects on maternal and foetal health **[10]**.

Drugs considered safe for administration in pregnancy are fewer and include: Nitrofurantoin, Fosfomycin and co-trimoxazole and β-lactam antibiotics like penicillin, cephalosporins and carbapenems **[11, 12, 13]**.

Antimicrobial resistance among uropathogens due to misuse and overuse of antibiotics has emerged as a worldwide problem in current years **[10, 14].** The Infectious Diseases Society of America (IDSA) recommends regular monitoring of sensitivity patterns of local uropathogens **[15]**.

Antimicrobial sensitivity pattern varies considerably with time and place **[5]**. Thus, it is essential to obtain current data on species of local uropathogens and their antimicrobial sensitivity pattern for prudent therapy **[10]**. This in turn will contribute in reducing maternal and childhood morbidity and stem antimicrobial resistance. The high frequency of UTI in pregnancy coupled with rising antimicrobial resistance of uropathogens created a pressing need for carrying out this study.

The antibiotic sensitivity patterns from this study might aid in devising rational empirical treatment guidelines considering the local variations in antimicrobial sensitivity. It will also provide helpful background data for implementing Antimicrobial Stewardship Programme (AMSP) and boost the efforts of Antimicrobial Resistance Surveillance and Research Network (AMRSN) and other interventions.

This study aimed at determination of profile of bacterial uropathogens in pregnant women including their respective antimicrobial sensitivity pattern along with socio-demographic and obstetric data, estimation of prevalence of UTI in this vulnerable population and comparison with reference studies.

PATIENTS/MATERIALS AND METHODS

Study type and design:

This study was an observational study with cross-sectional design.

Study area and duration:

This study was conducted on patients attending the Department of Obstetrics and Gynecology of the tertiary level hospital under the guidance of faculty members of Department of Microbiology at a tertiary-level hospital over a period as depicted in **Table 1.**

Study population:

Pregnant women in the age group between 20 – 40 years in different trimesters of pregnancy attending the Antenatal clinic of the Department of Obstetrics and Gynecology were included.

Selection criteria:

(i) Inclusion criteria:

1. Pregnant women in the age group of 20–40years.
2. Consenting pregnant women visiting the Antenatal clinic with their urine culture and sensitivity reports.

(ii) Exclusion criteria:

1. All non-pregnant females and
2. Pregnant women did not provide informed consent for participation in this study.
3. Pregnant women had a history of urological surgery, urogenital fistula, urolithiasis, and congenital anomalies of urinary tract.
4. Pregnant women were immune-compromised (as in HIV-AIDS, Malignancy, Diabetes Mellitus, etc.).
5. Pregnant women had a recent history of instrumentation (like urinary catheterization).
6. Pregnant women were suffering from recurrent urinary tract infection.
7. Pregnant women carried fetal compromise.
8. Pregnant women were on antimicrobial therapy at the time of diagnosis of UTI

Sample size:

Sample size was calculated using the Cochran's

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formula **[41]**, n= Z_α^2pq/d2 (Where, n= sample size, Z_α=standard normal variety with type-I errors as 5%, and confidence interval (CI) = 95%, p= prevalence. We took the prevalence as 51.2% which was a finding from the study by Rizvi et al **[14]**, as this study matched our study design, detail, and milieu) q = 1– p, d=relative error (taken as 10% of p in this study) Putting the values, we calculated n as $(1.96)^2$x 51.2 x 48/ $(5.12)^2$= 366 Taking 10% as non-response rate, sample size was calculated as 402**.**

Study procedure:

The participants were explained about the rationale and objectives of the study followed by collection of written free informed consent. Systematic sampling technique was used to select the pregnant woman. Data was collected from every third pregnant woman visiting the clinic with their urine culture and sensitivity report. Socio-demographic data (pregnant woman's age, type of residential area – urban or rural, educational qualification – literate or illiterate, occupation) and Obstetric data (gravida, parity, and gestational age) of the study participants were recorded using a pre-tested, pre-designed, validated structured case study record form. The antibiotic sensitivity testing (AST) was carried out using Kirby Bauer disc diffusion method as per current Clinical and Laboratory Standards Institute (CLSI) guidelines [**16]**. Data of causative bacteria and their antimicrobial sensitivity pattern were collected and recorded on the case study record form designed with Reference to guidelines of Indian Council of Medical Research (ICMR) and National Centre for Disease Control (NCDC), New Delhi, India **[11, 12]**. Antimicrobials which are considered safe in pregnancy were only considered while noting the antimicrobial sensitivity pattern of bacterial uropathogens **[5, 11, 12]**.

Study variables:

The independent variables include socio-demographic variables (age, residence type- rural or urban, educational qualification-literate or illiterate, occupation) and obstetric variables (gravida, parity, and gestational age). The outcome variables included prevalence of UTI, prevalence of asymptomatic and symptomatic UTI and the antibiotic sensitivity pattern of different isolated uropathogens.

Statistical analysis

Data collected was verified to ensure accuracy and completeness and was entered into Microsoft Office Excel2007 ™ (Microsoft Corporation, Redmond, WA, USA) followed by analysis using Statistical Package for the Social Sciences (SPSS) software ™ (version 25.0, IBM). Association between prevalence of UTI and socio-demographic and obstetric variables was determined using Chi-square test. p value < 0.05 was taken to be statistically significant. Simple descriptive and inferential statistics were used to determine:

1. The prevalence of urinary tract infection including symptomatic and asymptomatic bacteriuria in pregnancy and its association with socio -demographic and obstetric data.
2. The profile of bacterial uropathogens isolated and their antibiotic sensitivity patterns.

RESULTS

During our study, we recruited a total of four hundred and two pregnant women who had attended the Antenatal clinic of the Department of Obstetrics and Gynaecology of the tertiary-level hospital after screening and scrutiny of their urine culture and sensitivity reports. The prevalence of UTI in pregnant women in our study was calculated as 30.35% (Table 2). Among the pregnant women screened; asymptomatic bacteriuria was prevalent in 21.39% while symptomatic bacteriuria was observed in 8.96% of our study population (Figure 2).

The highest proportion of pregnant women with UTI belonged to the age group of 20-25 years (42.62%), who were homemakers (55.74%) and illiterate (69.67%), and resided in rural areas (67.21%). The association between prevalence of UTI and socio-demographic variables like age, educational status and residence were found to be statistically significant (p < 0.05). No significant association was found between prevalence of UTI and type of occupation in our study. The highest proportion of women with UTI in our study was in third trimester of pregnancy (47.54%), with multigravida (72.31%)

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and multiparity (50.82%). The association between prevalence of UTI and obstetric variables like gestational period(trimester), gravid and parity were found to be statistically significant (Table3).

The most common bacterial uropathogen isolated was Escherichia coli which accounted for 68.03% of the total cases of UTI followed by Klebsiella pneumoniae (18.85%), Pseudomonas aeruginosa (4.1%), Proteus vulgaris (3.28%), Staphylococcus saprophyticus (2.46%), Staphylococcus aureus (1.64%) and Enterococcus faecalis (1.64%) (Figure 3).

The bacterial uropathogens showed high overall resistance to ampicillin (86.88%), amoxicillin-clavulanic acid (88.52%) and co-trimoxazole (68.03%), and high sensitivity for imipenem (90.98%), meropenem (81.96%), fosfomycin (81.97%) and cefepime (67.21%) (Figure 4).

Escherichia coli demonstrated a high resistance to amoxicillin-clavulanic acid (91.57%), ampicillin (86.75%) followed by co-trimoxazole (66.27%) and relatively higher sensitivity to Fosfomycin (93.98%), imipenem (92.77%) and meropenem (80.72%). Klebsiella pneumoniae showed high resistance to amoxicillin-clavulanic acid (82.61%), ampicillin (91.3%), cefixime (91.3%), nitrofurantoin (82.61%) and high sensitivity to imipenem, meropenem and cefepime. Multidrug resistance was also observed in Proteus vulgaris and Pseudomonas aeruginosa (Table 4). Staphylococcus saprophyticus showed complete resistance to ampicillin, amoxicillin-clavulanic acid and cefixime and high sensitivity to imipenem and piperacillin-tazobactam. Staphylococcus aureus showed 100% resistance to amoxicillin-clavulanic acid, ampicillin, cefixime, cefoperazone-sulbactam and cotrimoxazole. Enterococcus faecalis showed a very high sensitivity to amoxicillin-clavulanic acid, ampicillin, imipenem, nitrofurantoin and piperacillin-tazobactam (Table 5).

Table 1: Gantt Chart showing duration of different phases of the study

	Study duration in weeks (Total study duration = 8 weeks)							
	1st week	**2nd week**	**3rd week**	**4th week**	**5th week**	**6th week**	**7th week**	**8th week**
Data Collection								
Data Compilation and Cleaning								
Data analysis								
Report Preparation								

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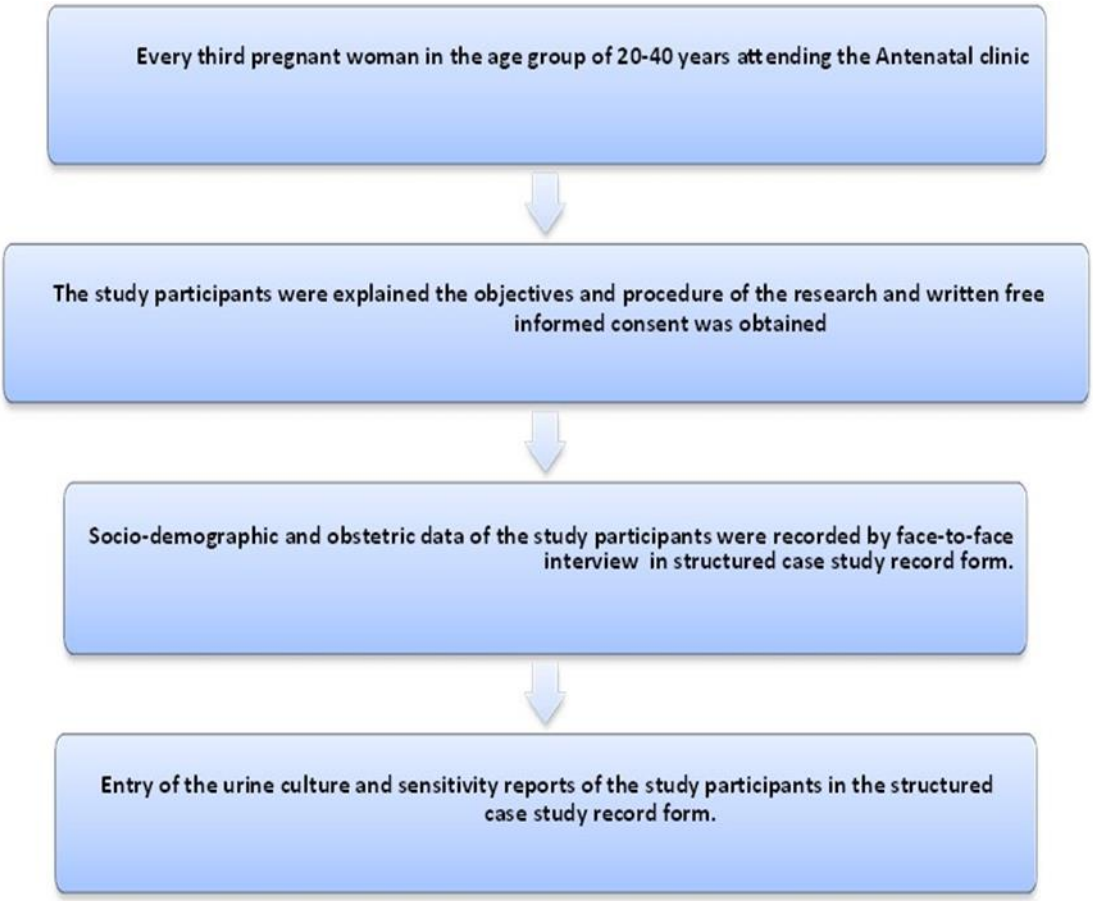

Figure 1. Flow Chart depicting the procedure followed for data collection during the course of our study.

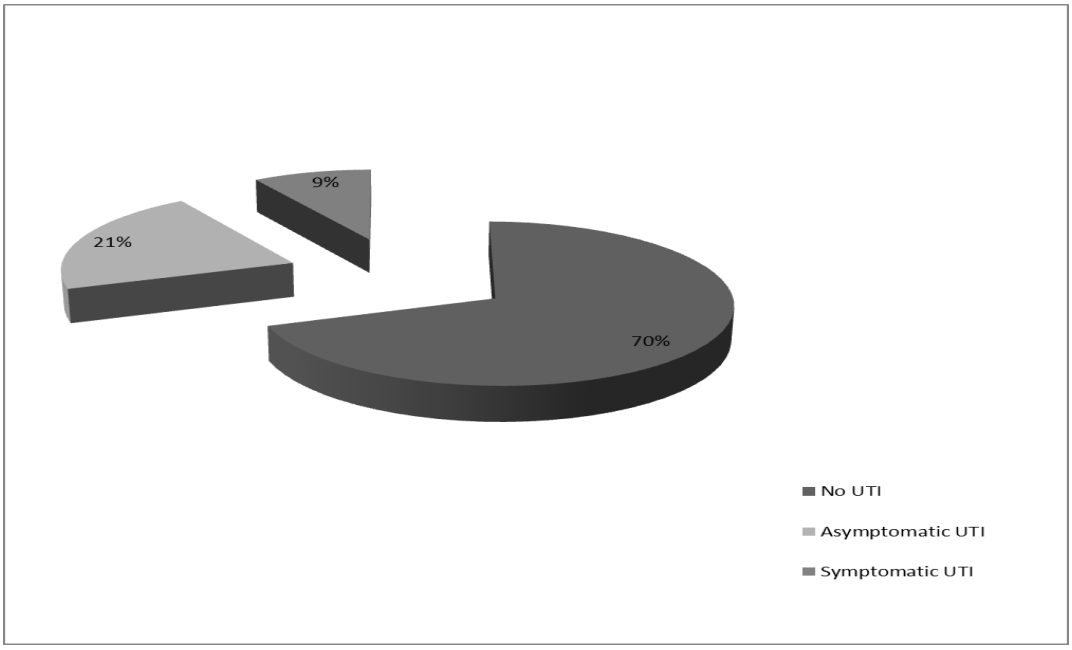

Figure2: 3D fractured Pie chart showing prevalence of asymptomatic and symptomatic UTI in pregnant population.

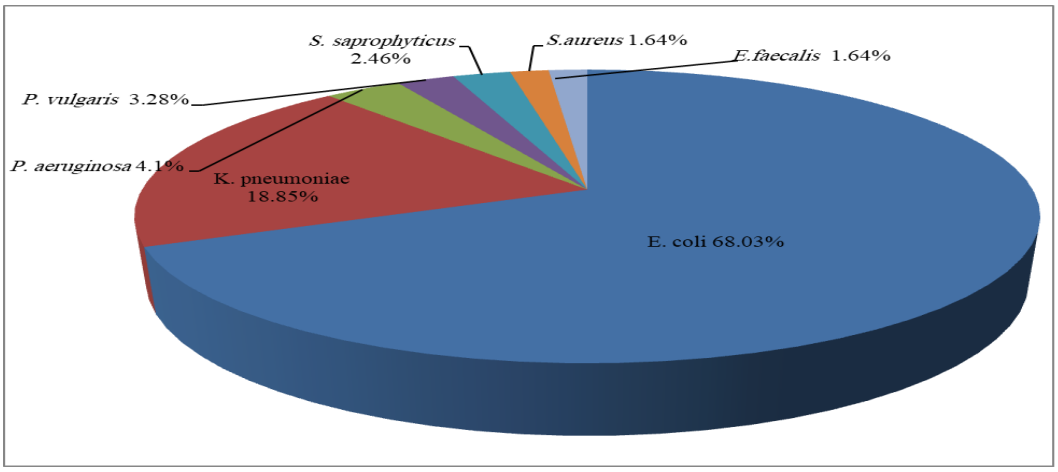

Figure3: 3D Pie chart showing isolated and identified bacterial uropathogens responsible for UTI in pregnancy.

Table 2: Prevalence of UTI among pregnant women**.**

Total number of pregnant women included in study	Number of pregnant women diagnosed with UTI	Percentage of prevalence of UTI in pregnant women (%)
402	122	30.35

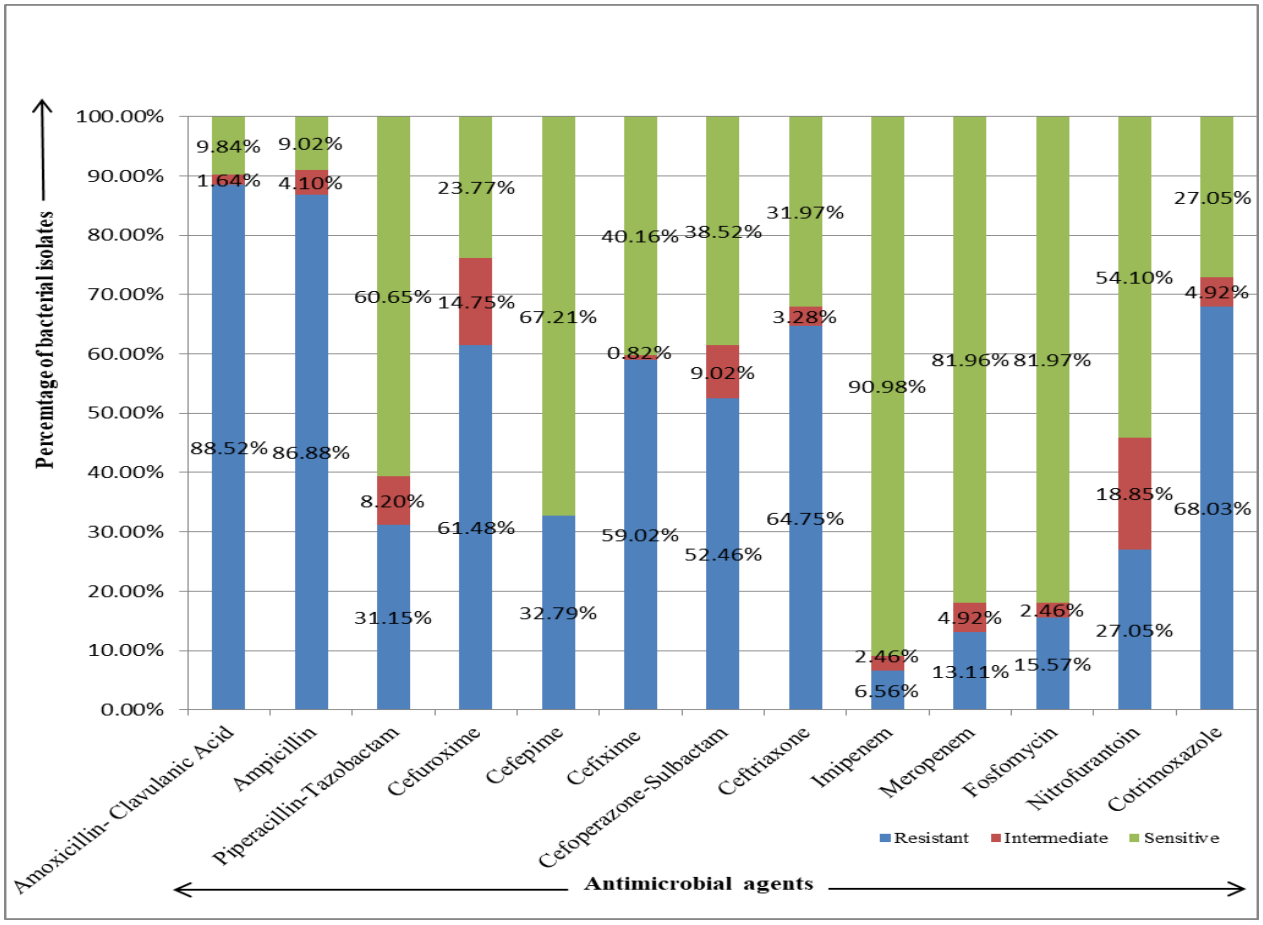

Figure 4: Composite Bar diagram showing overall sensitivity and resistance of isolated and identified bacterial uropathogens to antimicrobial agents in pregnancy

Table 3: Association between socio-demographic and obstetric variables of pregnant women and prevalence of UTI

Socio-demographic variables	***Number of pregnant women diagnosed with UTI (n_1 = 122)***	***Number of pregnant women not diagnosed with UTI (n_2 = 280)***	***Total number of pregnant women (Total=402)***	***Comments***
Age (in years) :				
20 - 25	52 (42.62%)	31 (11.07%)	83 (20.65%)	$\chi2$ = 52.4214
26 - 30	32 (26.23%)	102 (36.43%)	134 (33.33%)	df = 3
31 - 35	18 (14.75%)	79 (28.21%)	97 (24.13%)	**p value < 0.00001***
36 - 40	20 (16.39%)	68 (24.29%)	88 (21.89%)	
Occupation :				$\chi2$ = 0.1086
Service	28 (22.95%)	62 (22.14%)	90 (22.39%)	df = 2
Business	26 (21.31%)	57 (20.36%)	83 (20.64%)	p value = 0.947153
Homemaker	68 (55.74%)	161 (57.5%)	229 (56.97%)	
Literacy Status:				$\chi2$ = 75.6171
Literate	37 (30.33%)	213 (76.07%)	250 (62.19%)	df = 1
Illiterate	85 (69.67%)	67 (23.93%)	152 (37.81%)	**p value < 0.00001***
Residential Area:				$\chi2$ = 11.4556
Rural	82 (67.21%)	137 (48.93%)	219 (54.48%)	df = 1
Urban	40 (32.79%)	143 (51.07%)	183 (45.52%)	**p value = 0.000713***
Obstetric variables	*Number of pregnant women diagnosed with UTI (n_1=122)*	*Number of pregnant women not diagnosed with UTI (n_2=280)*	*Total number of pregnant women (Total=402)*	*Comments*
Gestational Period (in trimester) :				$\chi2$ = 11.8134
First	39 (20.49%)	101 (36.07%)	140 (34.83%)	df = 2
Second	25 (31.97%)	93 (33.21%)	118 (29.35%)	**p value = 0.002721***
Third	58 (47.54%)	86 (30.72%)	144 (35.82%)	
Gravida:				$\chi2$ = 10.4083
Primigravida	34 (27.87%)	126 (45%)	160 (39.8%)	df = 1
Multigravida	88 (72.31%)	154 (55%)	242 (60.2%)	**p value = 0.001254***
Parity:				$\chi2$ = 13.4496
Nulliparous	34 (27.87%)	126 (45%)	160 (39.8%)	df = 2
Primiparous	26 (21.31%)	62 (22.14%)	88 (21.89%)	**p value = 0.001201***
Multiparous	62 (50.82%)	92 (32.86%)	154 (38.31%)	

Values obtained as per Chi Square ($\chi2$) Test. df = degrees of freedom, *p values<0.05 were taken as statistically significant, as per standard convention.

Table 4: Antibiogram of different species of isolated and identified Gram negative bacterial uropathogens in pregnancy

Antimicrobial Agent	*Escherichia coli* (n = 83)			*Klebsiella pneumoniae* (n = 23)			*Proteus vulgaris* (n = 4)			*Pseudomonas aeruginosa* (n = 5)		
	R (%)	I (%)	S (%)	R (%)	I (%)	S (%)	R (%)	I (%)	S (%)	R (%)	I (%)	S (%)
Amoxicillin-clavulanic acid	91.57	1.2	7.23	82.61	4.35	13.04	75	-	25	100	-	-
Ampicillin	86.75	4.82	8.43	91.3	4.35	4.35	100	-	-	80	-	20
Cefuroxime	57.83	16.87	25.3	73.91	4.35	21.74	50	25	25	100	-	-
Cefepime	33.73	-	66.27	21.74	-	78.26	100	-	-	20	-	80
Cefixime	44.58	-	55.42	91.3	4.35	4.35	75	-	25	100	-	-
Cefoperazone-sulbactam	51.81	9.64	38.55	60.87	13.04	26.09	-	-	100	20	-	80
Ceftriaxone	63.86	3.61	32.53	73.91	-	26.09	50	-	50	40	20	40
Fosfomycin	6.02	-	93.98	26.09	13.04	60.87	25	-	75	80	-	20
Imipenem	4.82	2.41	92.77	13.04	4.35	82.61	25	-	75	-	-	100
Meropenem	12.05	7.23	80.72	17.39	-	82.61	-	-	100	20	-	80
Nitrofurantoin	13.25	26.51	60.24	82.61	-	17.39	25	-	75	20	20	60
Piperacillin-tazobactam	33.74	8.43	57.83	39.13	13.04	47.83	-	-	100	20	-	80
Cotrimoxazole	66.27	4.82	28.91	60.87	8.69	30.44	100	-	-	100	-	-

(n= number of isolates, R= Resistant, I= Intermediate, S= Sensitive)

Table 5: Antibiogram of different species of isolated and identified Gram positive bacterial uropathogens in pregnancy

Antimicrobial Agent	***St. saprophyticus* (3)**			***St. Aureus* (2)**			***Ent. faecalis*(2)**		
	R (%)	**I (%)**	**S (%)**	**R (%)**	**I (%)**	**S (%)**	**R (%)**	**I (%)**	**S (%)**
Amoxicillin-clavulanic acid	100	-	-	100	-	-	-	-	100
Ampicillin	100	-	-	100	-	-	-	-	100
Cefuroxime	-	66.67	33.33	50	-	50	100	-	-
Cefepime	33.33	-	66.67	-	-	100	50	-	50
Cefixime	100	-	-	100	-	-	50	-	50
Cefoperazone-sulbactam	66.67	-	33.33	100	-	-	100	-	-
Ceftriaxone	66.67	-	33.33	50	-	50	100	-	-
Fosfomycin	33.33	-	66.67	50	-	50	50	-	50
Imipenem	-	-	100	-	-	100	-	-	100
Meropenem	-	-	66.67	-	-	100	50	-	50
Nitrofurantoin	33.33	-	66.67	-	-	100	-	-	100
Piperacillin-tazobactam	-	-	100	-	-	100	-	-	100
Cotrimoxazole	33.33	-	66.67	100	-	-	100	-	-

(R= Resistant, I= Intermediate, S= Sensitive)

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DISCUSSION

We observed a prevalence of UTI in pregnant women of 30.35% (Table 2),which was comparable with the prevalence rates reported in studies in Bangladesh (30%) and Egypt (31.3%)**[17, 18]** and higher compared to the findings of *Gour et al*. (20.27%) and *Kant et al.* (3.3%) in North India, and *Thomas et al*. (25%) in South India, respectively **[2, 3, 13]**.However, *Sibi G et al.* (46.6%) in South India and *Rizvi et al.* (51.2%) in North India reported a higher prevalence of UTI **[10, 14]**.

The prevalence of asymptomatic UTI (21.39%) among pregnant women was found to be higher than the prevalence of symptomatic UTI (8.96%) in pregnant women in our study (Figure 2) like *Thomas et al.* and *Rizvi et al.* **[13, 14]** However, *Kant et al.* and *Vaijanathrao et al.* found a higher prevalence of symptomatic UTI compared to asymptomatic UTI, which was opposing our study findings **[3, 19]** .The higher prevalence of asymptomatic bacteriuria in our study was alarming since asymptomatic bacteriuria might not be detected early due to lack of symptoms and may rapidly progress to acute pyelonephritis causing significant morbidity for mother and fetus **[9]**.The high prevalence of UTI in general and asymptomatic bacteriuria in particular in pregnant population as observed in our study lead us to suggest that compulsory screening for UTI in pregnancy be continued in the current study setting and be started in other health centers in India and across the developing World.

In our study, 42.62% of pregnant women diagnosed with UTI belonged to the age-group of 20 - 25 years followed by 26.23% who were of the age group of 26 - 30 years, which together amounted to 68.85% of total cases of UTI (Table 4). Similar patterns were also reported by *Thomas et al., Ahmed et al*. and *Elazayat et al.* **[13, 15, 20].**This led us to conclude that pregnant women in the age range of 20 - 30 years constitute a high-risk group for UTI **[13, 15]**.The reasons for high prevalence of UTI in young age group can be attributed to early sexual activity, early child bearing and early marriage **[9]** as concluded by *Jalali et al.* in their study on more vulnerable pregnant population **[21]**. Our study found the association between maternal age and prevalence of UTI to be statistically significant (p value < 0.00001) (**Table 4**), like studies by *Laari et al*. and *Al Kashif et al*. **[19, 22]** However, some other studies did not find significant association between maternal age and risk of UTI **[18, 28].**

In our study, 55.74% of pregnant women suffering from UTI were homemakers (Table 3). This finding is contradictory to the findings of *Al-Kashif* et al. who found pregnant females with UTI employed in work (57.4%) were more than homemakers **[22]**. The study findings by *Multani et al*. in North India were also in disagreement with our results **[23].** In our study, it was observed that working women could possibly might not be able to attend the antenatal clinic regularly due to work constraints resulting in lower numbers being reported **[24]**.With regard to literacy, the prevalence of UTI was found to be higher in illiterate females (69.67%) than among literate females (30.33%) (Table 3) with a p value < 0.00001 which was similar to most other studies **[18, 25, 26];** This could probably be attributed to lack of awareness and knowledge among illiterate pregnant women on hygienic practices related to urination.

Our investigations revealed that UTI cases in rural population significantly surpassed urban population, with a p value = 0.000713 (**Table 3**). This was in concordance with the study by Multani et al. in Haryana, India **[23].**The reason for higher prevalence of UTI in rural population might have been due to non-compliance to hygienic sanitary conditions in villages, lack of awareness and lower concern for personal and environmental hygiene in rural population which increased the risk for UTI **[21].**This necessitates need for better outreach programs on hygiene and increasing accessibility of antenatal services in rural areas of all developing nations.

The maximum number of cases of UTI were found in the 3rd trimester of pregnancy (47.54%) followed by 2nd trimester (31.97%) and 1st trimester (20.49%) respectively with a p value = 0.002721 **(Table 3).** The observed trend in our study thus shows that prevalence of UTI increases with increase in gestational age like *Kant et al*. and *Sibi G et al.* in their studies in North India and South India respectively **[3, 10].** *Gour et al*. and *Johnson et al*. also reported highest proportion of females with UTI in the 3rd trimester of pregnancy **[7, 27].** The enlarging uterus in later trimesters exerts more pressure on the urinary bladder causing increase in the intra-vesicular pressure and consequent vesico-ureteric

reflux culminating in retention of urine which acts as a suitable environment for bacterial growth **[9].** We suggest that screening for bacteriuria be done in the first antenatal visit, regardless of gestational age.

Our study reported a high proportion of pregnant women with UTI were multiparous with a p value =0.001201 (Table 3) similar to findings of *Haider et al*. **[25]** Multiparity is a known risk factor for UTI in pregnancy as it causes widening of orifice of urethra and descent of organs of pelvic cavity which aids in ascent and colonization of urinary tract by microbial pathogens**[20]**.Likewise, the prevalence of UTI was higher in multigravida accounting for 72.31% of total cases of UTI with a **p value =** 0.001254 (Table 3) which was in agreement of findings in studies by *Al-Kashif and Mohamed et al*.**[22, 28].**

Escherichia coli was the most common causative microorganism responsible for UTI in our study with a prevalence rate of 68.03% (Figure 3) which was similar to majority study findings in India and abroad **[2, 5, 7, 10]** .Urinary stasis in pregnancy is regarded as the most crucial factor predisposing to colonization of the urinary tract by *Escherichia coli* **[29]**.The proportion of cases of UTI caused by *Escherichia coli* as reported in our study was found to be close to the findings by *Sabharwal* (63.3%)**[5]** whereas *Jyoti Jojan et al*. reported *Staphylococcus aureus* (82.6%) to be the most predominant uropathogen **[30]**, which was not in agreement with our findings. *Ansari et al*. reported that *Klebsiella pneumoniae* (28.57%) and *Staphylococcus aureus* (28.57%) were responsible for maximum number of cases of UTI in pregnancy **[31]** whereas our study reported *Klebsiella pneumoniae* as the second most common uropathogen *(18.85%)* followed by *Pseudomonas aeruginosa* (*4.1%) and Proteus vulgaris (3.28%)* respectively *(*Figure 2*). Gour et al*. also reported *Klebsiella pneumoniae* to be the second most predominant (13.33%) in concordance with our study [7]. Sibi *G et al*. found a different species of *Klebsiella* namely *Klebsiella oxytoca* to be the second most common followed by *Klebsiella pneumoniae* in their study **[10]**. The *study by* **Shailja et al.** and ***Thomas et al.*** however found Coagulase negative *Staphylococcus* (17.1%) and *Pseudomonas aeruginosa* (25%) to be the second most common uropathogens respectively **[2, 13]**.

Among the Penicillin group of β lactam antibiotics, a high overall resistance to amoxicillin-clavulanic acid (88.52%) and ampicillin (86.88%) was shown by uropathogens **(Figure 4**) like most other studies **[5, 15]**. The high resistance to these drugs can be attributed to rampant spread of beta-lactamase producing strains of bacteria **[10]** Most Gram-positive bacteria were highly resistant to both drugs in our study with the sole exception of *Enterococcus faecalis* which was fully sensitive to both the antibiotics. The high resistance of *Staphylococcus* species to ampicillin and amoxicillin-clavulanic acid in our study agreed with many other studies **[7, 15, 32, 33]**. However, both *Samaga and Sadhvi et al*. reported *Enterococcus isolates* to be 100% resistant Amoxycillin-Clavulanic acid and Ampicillin **[32, 33]**. Among Gram-negative bacteria, *Escherichia coli* isolates showed an alarmingly high resistance to amoxicillin-clavulanic acid (91.57%) and ampicillin (86.75%) respectively like several other studies. **[7, 15, 32, 33]** *Klebsiella pneumoniae* also showed high resistance to ampicillin and amoxicillin-clavulanic acid in our study comparable to findings of *Ahmed et al. and Samaga et al*. **[15, 32]**. Indiscriminate use of these antibiotics resulting in alarming drug resistance has made these unsuitable to be included in empirical treatment despite being traditionally safe drugs in pregnancy. The only effective drug from this group is piperacillin-tazobactam which showed an overall high sensitivity of 60.65% in our study. *Staphylococcus aureus* and Coagulase negative *Staphylococcus* had 100% sensitivity to piperacillin-tazobactam which contradicted study findings of *Sadhvi et al* **[33].** The sensitivity rates of *Escherichia coli* (57.83%) and *Klebsiella pneumoniae* (47.83%) in our study were however lower than that reported by ***Kaushal et al.*** **[4]**

Apart from cefepime, bacterial uropathies were found to be moderately resistant to all other cephalosporins with resistance rates ranging between 50% and 65% (**Figure 4**). This might be due to extended spectrum beta lactamase (ESBL) producing organisms. Cefuroxime had an overall sensitivity of 23.77% in our study which was lower than that reported by ***Shamim et al.*** **[34].** The overall sensitivity of ceftriaxone in our study is 31.97% which was comparable to the findings of ***Sabharwal et al.*** but lower than that found by ***Sibi G et al.*** **[5, 10]** Cefoperazone-sulbactam showed an overall sensitivity of 38.52% which was similar to study findings of **Sabharwal *et al.*** **[5]**

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Klebsiella pneumoniae reported a sensitivity of 21.74% to cefuroxime which was similar to the finding of ***Sadhvi et al.*** **[33]**. The percentage sensitivity of uropathogens against Ceftriaxone was as following: *Escherichia coli* (32.53%), *Klebsiella pneumoniae* (26.09%), *Pseudomonas aeruginosa* (40%), *Staphylococcus aureus* (50%) and *Staphylococcus saprophyticus* (33.33%) which was lower than that noted by ***Ali et al***. **[35]**

In our study, the bacterial uropathogens demonstrated a very high sensitivity to Carbapenems: imipenem and meropenem with a total sensitivity rate of 90.98% and 81.96% respectively (**Figure 4**) similar to findings of ***Sabharwal et al*** **[5]**. High sensitivity towards imipenem was observed among *Escherichia coli* (92.77%) in our study, similar to several other observers **[7, 14, 32.** *Klebsiella pneumoniae* also showed high sensitivity to imipenem in our study (82.61%) comparable to other studies. **[7, 27,36]** The sensitivity rates of meropenem to *Escherichia coli* (80.72%) and *Klebsiella pneumoniae* (82.61%) in our study which was lower than that reported by ***Kaushal et al.*** **[4]** Imipenem was 100% sensitive to all Gram-positive isolates in our study **(Table 5).** ***Sadhvi et al.*** reported 100% sensitivity of *Enterococcus* spp. to imipenem which was in agreement with our findings **[33].**

Our study reported an overall high resistance of 68.03% to co-trimoxazole (**Figure 4**) like ***Sabharwal*** and ***Sibi G et al.*** [**5, 10].** *Escherichia coli* demonstrated high resistance to co-trimoxazole of 66.27% (**Table 4**), which was in disagreement with a study by ***Patnaik et al.*** who reported 100% sensitivity of *Escherichia coli* to cotrimoxazole **[37]**. *Pseudomonas aeruginosa* showed very high resistance to cotrimoxazole in our study (**Table 4**), this finding was similar to observations of ***Derese et al.*** in Ethiopia **[40].** Unlike most Gram-positive bacterial isolates in our studies, Coagulase negative *Staphylococcus* showed high sensitivity (66.67%) to co-trimoxazole (**Table 8**) similar to study findings by ***Rohini et al***. **[36].** The results of our study together suggest that co-trimoxazole is less effective in treating UTI in pregnancy, a view corroborated by ***Sibi G et al*** **[10].**

Our study found out that the uropathogens demonstrated an overall sensitivity rate of 54.10% to nitrofurantoin (**Figure 4**), which was lower than that reported in rest of India and Uganda. **[5, 27]**. *Staphylococcus aureus* showed high sensitivity to nitrofurantoin (**Table 5**), like some studies in India and abroad **[2, 27].** Although ***Shailja et al.*** and ***Thomas et al***. reported 33.3% and 25% resistance to nitrofurantoin for *Enterococcus faecalis* respectively, while our study reported no resistance (**Table 5**). Sensitivity rates showed that nitrofurantoin was effective against *Escherichia coli* (60.24%) and *Proteus vulgaris* (75%) in agreement with ***Johnson et al.*** **[27]** However, *Klebsiella pneumoniae* differed from other Gram- negative isolates in our study since it showed resistance of 82.61% to nitrofurantoin. High resistance of *Klebsiella pneumoniae* to nitrofurantoin had also been reported in a study in Ethiopia **[38].**

Fosfomycin was found to have an overall sensitivity of 81.97% (**Figure 4**) in our study which was comparable to the study by ***Souza et al.*** in Brazil **[39]**. Fosfomycin was found to be highly effective against most Gram-negative and Gram-positive uropathogens in our study except for *Pseudomonas aeruginosa* which was reported to have only 20% sensitivity. High sensitivity of Fosfomycin to both Gram-positive and Gram-negative pathogens was also reported by ***Rosana et al.*** **[40]** Among the Gram-negative uropathogens, *Escherichia coli* and *Proteus vulgaris* were most sensitive with sensitivity rates of 93.98% and 75% respectively (**Table 4**). Half of the isolates of *Staphylococcus aureus* and *Enterococcus faecalis* were sensitive while 66.67% of the isolates of *Staphylococcus saprophyticus* were sensitive (**Table 5**). Our findings on sensitivity of *Enterococcus fecalis* against Fosfomycin were in disagreement with that of ***Rohini et al.*** which reported 100% sensitivity **[36]**. The overall high sensitivity and wide spectrum of action of Fosfomycin leads us to suggest its use in empirical treatment. Similar to us, ***Souza et al.*** and ***Rosana et al***. have also recommended use of Fosfomycin in empirical treatment of UTI in pregnancy **[39, 40]**. This is also in accordance with the recommendations of the Indian Council of Medical Research **[11].**

CONCLUSION

The high prevalence of UTI in our study leads us to conclude that regular screening of UTI in pregnancy is essential to avert maternal and foetal complications. The sensitivity patterns of

bacterial uropathogens to different antimicrobials in our study lead us to suggest use of carbapenems and Fosfomycin in empirical treatment of UTIs in pregnancy.

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Ethical approval: The study was conducted after it was ethically reviewed and approved by the Institutional Ethics Committee (IEC) of our apex teaching hospital.

Availability of data and materials:

Author contribution: We declare that all listed authors have made substantial contributions to all of the following three parts of the manuscript:

- Research design, or acquisition, analysis or interpretation of data;

- Drafting the paper or revising it critically;

- Approving the submitted version.

We also declare that no-one who qualifies for authorship has been excluded from the list of authors.

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HIGHLIGHTS

- The high prevalence of UTI in general and asymptomatic bacteriuria in particular in pregnant population as observed in our study lead us to suggest that compulsory screening for UTI in pregnancy be continued in the current study setting and be started in other health centers across the developing World and which when diagnosed early can eventually reduce fetal and maternal morbidity and mortality.
- Multidisciplinary awareness and inter-disciplinary communication regarding the uropathogens and antimicrobial susceptibility pattern are necessary in successful treatment and controlling the rising trends of antimicrobial resistance (AMR) more so in vulnerable population like pregnant mothers.
- The rising trends of drug resistance in uropathogens against commonly prescribed antimicrobials like Penicillin, co-trimoxazole etc. raises conflicting and ambiguous scenario in the choice of antimicrobial therapy. An antibiotic policy based on local data and involving all sections of the population is the only answer to this ‘global headache’ of drug resistance.

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