SENSITIVITY PATTERN OF CEFIXIME AGAINST UROPATHOGENS CAUSING URINARY TRACT INFECTION IN PREGNANT WOMEN

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ABSTRACT

OBJECTIVES

This study aimed to determine the susceptibility pattern of cefixime against uropathogens causing urinary tract infections among pregnant women attending a tertiary care hospital in Peshawar, Pakistan.

METHODOLOGY

A descriptive cross-sectional study was conducted in the Department of Obstetrics and Gynaecology at Khyber Teaching Hospital, Peshawar, with approval from the Institutional Ethical Review Committee. The study was carried out over six months (June 30 2024, to December 31 2024). A total of 197 pregnant women with culture-confirmed UTI were enrolled through consecutive non-probability sampling. Midstream urine specimens were collected aseptically and processed for routine examination, culture, and antibiotic susceptibility testing. Culture and sensitivity testing were performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines (the latest available hospital-level laboratory protocol). Cefixime susceptibility was reported as sensitive or resistant according to the standard zone interpretation used in the institutional microbiology laboratory. Data were analysed using SPSS version 20. Quantitative variables were summarised as means ± standard deviations. The chi-square test was used for subgroup analysis, and binary logistic regression was used to identify predictors of cefixime sensitivity. A p-value ≤ 0.05 was considered statistically significant. Odds ratios (OR) with 95% confidence intervals (CI) were reported.

RESULTS

Among 197 pregnant women with culture-confirmed UTIs, Escherichia coli was the most common uropathogen (83.8%). Overall, 36.5% of isolates were sensitive to cefixime, while 63.5% were resistant. Chi-square analysis demonstrated no significant association between cefixime sensitivity and age, BMI, education, residence, or uropathogen type. Binary logistic regression identified education as the only significant predictor of cefixime sensitivity (OR = 1.89, 95% CI: 1.16-3.08, p = 0.010).

CONCLUSION

A high level of cefixime resistance was observed among uropathogens, particularly E. coli. These findings highlight the importance of urine culture and susceptibility testing before antibiotic selection. However, broader multicenter studies with multiple antibiotics and additional clinical variables are needed before changing empirical treatment policies.

KEYWORDS: *Urinary Tract Infection, Cefixime Sensitivity, Pregnancy, Uropathogens.*

INTRODUCTION

Urinary tract infections (UTIs) are a common worldwide illness that affects over 150 million people annually, with women accounting for most cases. Due to several physiological, structural, and hormonal variations, pregnancy raises the risk of UTI, endangering the health of both the expecting mother and the baby. About 50-60% of pregnant women get a UTI, which is a frequent and serious health problem.[1] Treating UTIs during pregnancy is crucial, and care guidelines have been released globally to help doctors choose the best antibiotic for every individual while considering the safety profile of both the mother and the fetus.[2] Because of things like lower bladder tone, ureter dilatation and elevated bladder capacity, pregnant women are more vulnerable to having a UTI. Preterm childbirth, premature delivery, intrauterine fetal death, chronic renal failure, anaemia, and hypertension are among the consequences that might arise from these physiological changes, including urine retention and

enhanced vesicoureteral reflux. To avoid these negative consequences, early identification and treatment of UTIs throughout pregnancy are crucial. A study of 564 pregnant women aged 17-44 showed that 48 (8.50%) had urinary tract infections during pregnancy. The sensitivity of these etiologic agents to antibiotics varied, with Piperacillin-tazobactam having the highest overall sensitivity (89.6%), followed by Meropenem (87.5%), Nitrofurantoin (87.5%), and Cefixime (68.8%).[3] About 8% of pregnant women in the US suffer from lower urinary tract infections (LUTIs), which are among the most common medical conditions. In addition to taking into consideration the impaired breakdown of drugs during pregnancy and possible hazards of teratogenicity or fetal harm related to certain antibiotics, treatment should focus on the most common uropathogens. Escherichia coli is the most common cause of urinary tract infections, accounting for 80–90% of pregnancy-related UTIs.[4,5] One of the main causes of inappropriate antibiotic prescriptions has been identified by clinical signs of UTI without obtaining a urine culture.[6] Antibiotic-resistant UTI infections are becoming more common worldwide, which affects hospitals as well as the community. Treatment sometimes begins experimentally before the results of susceptibility testing and urine cultures are available. Continuous surveillance of resistance trends is crucial to improving empirical antibiotic treatment recommendations, reducing hospital stays, improving patient outcomes, and reducing healthcare costs.[7] The increasing prevalence of antimicrobial resistance has become a major global public health concern. Inappropriate empirical antibiotic use contributes to the emergence of resistant uropathogens, resulting in treatment failure, prolonged illness, increased healthcare costs, and adverse maternal and fetal outcomes. Continuous surveillance of local antimicrobial susceptibility patterns is therefore essential for evidence-based empirical therapy. The significance of this study lies in optimising antibiotic therapy for urinary tract infections (UTIs) during pregnancy by evaluating the susceptibility pattern of cefixime against common uropathogens. The findings may improve empirical treatment, reduce antimicrobial resistance and complications, and support evidence-based clinical guidelines. As cefixime susceptibility varies across regions and local data in Pakistan are limited, the objective of the present study was to determine the susceptibility pattern of cefixime against uropathogens causing UTIs among pregnant women presenting to the Department of Obstetrics and Gynaecology, Khyber Teaching Hospital, Peshawar, Pakistan.

METHODOLOGY

This descriptive analytical cross-sectional study was conducted at the Department of Gynaecology and Obstetrics at KTH, Peshawar, from June 30 to December 31, 2024, after obtaining approval from the research review board. A total of 197 pregnant women in the age range of 18 to 45 years diagnosed with urinary tract infection were enrolled and evaluated for sensitivity to cefixime. The patients were excluded when there was a history of antibiotic use in the last month, patients with urogenital anomalies, malignancy or comorbid conditions like diabetes and immunocompromised patients like those taking steroids. Sample size was 197, calculated using the WHO sample size calculator with a 95% confidence interval, a 7% margin of error, and an anticipated frequency of 40.6% for Cefixime sensitivity.[5] Written informed consent was obtained from participants prior to their inclusion. A structured proforma was used to document demographic information and clinical history. For all patients included in the study, midstream urine samples were collected under sterile conditions and promptly sent to the laboratory for routine analysis and culture. Antibiotic susceptibility testing was performed on isolated uropathogens to determine their sensitivity or resistance to cefixime. Other commonly used antibiotics for UTI treatment, such as Trimethoprim-sulfamethoxazole, nitrofurantoin, and ciprofloxacin, were also included in the testing. All culture and sensitivity testing was done under the supervision of a consultant microbiologist with a minimum of 5 years of experience. Urinary tract infection was confirmed based on urine culture with a bacterial count of >105 colony-forming units (CFU)/ml in a midstream urine sample collected in an air-tight, sterile jar. Antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method, interpreted according to CLSI guidelines, M100-S25, 2024 version (as implemented in the institutional laboratory protocol). Cefixime susceptibility was categorised as sensitive or resistant based on zone diameter interpretation. When cefixime produced an inhibitory zone of 14mm or more for a bacterium at 37 °C, that specific microorganism was said to be sensitive to cefixime and an inhibitory zone of less than 14mm was considered resistant. The obtained data were analysed using SPSS version 20.0. The mean and standard deviation (SD) were calculated for all quantitative variables, such as age and BMI, while the categorical variables, such as education status, residence, and sensitivity to cefixime, were

presented as frequencies and percentages. Effect modifiers such as age, educational status, BMI, and residence were handled through stratification. Chi-square test was used for subgroup analysis. Binary logistic regression was applied to determine predictors of cefixime sensitivity. Odds ratios (OR) with 95% confidence intervals were reported. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

Among 197 pregnant women with culture-positive urinary tract infection, cefixime sensitivity was observed in 72 (36.5%) isolates, while 125 (63.5%) were resistant. Age was categorised into groups, with the highest frequency in the 26-30 years age group (39.1%), followed by the 31–35 years age group (21.3%), while participants aged 41-45 years represented the smallest proportion (7.6%). A BMI more than 24.0kg/m^2 was observed in 91 patients (46.2%). Regarding residence, 112 patients (56.9%) resided in rural areas, as reported in Table 1. Escherichia coli was the most frequently isolated organism (83.8%), followed by Pseudomonas (6.1%) and Klebsiella pneumoniae (5.1%). The least common organisms were Pantoea species and Citrobacter (0.5% each). No statistically significant difference was observed in the distribution of uropathogens (p = 0.066). (Table 2) Overall, cefixime sensitivity was observed in 72 patients (36.5%), while 125 patients (63.5%) were resistant, as shown in Table 3. On stratified analysis using the Chi-square test, cefixime sensitivity did not show a statistically significant association with age (p = 0.958), BMI (p = 0.426), education level (p = 0.052), residence (p = 0.381), or uropathogen type (p = 0.066). To identify independent predictors of cefixime sensitivity, a binary logistic regression analysis was performed (Table 4). Education was the only variable significantly associated with cefixime sensitivity (OR = 1.893, 95% CI: 1.164–3.080, p = 0.010). In contrast, age (OR = 0.739, 95% CI: 0.343-1.591, p = 0.439), BMI (OR = 1.379, 95% CI: 0.865-2.197, p = 0.176), residence (OR = 1.255, 95% CI: 0.680-2.317, p = 0.467), and uropathogen type (OR = 0.817, 95% CI: 0.608-1.097, p = 0.178) were not significantly associated with cefixime sensitivity.

Table 1: Baseline Characteristics of Study Participants (n = 197)

Parameters		Frequency	%age	P-Value
Age (years)	18-25 years	37	18.8	0.958
	26-30 years	77	39.1	
	31-35 years	42	21.3	
	36-40 years	26	13.2	
	41-45 years	15	7.6	
BMI (kg/m^2)	less than 18	23	11.7	0.426
	18-24	83	42.1	
	Greater than 24	91	46.2	
Education	Primary or below	85	43.1	0.052
	Secondary	92	46.7	
	Higher	20	10.2	
Residence	Urban	85	43.1	0.381
	Rural	112	56.9	

Table 2: Distribution of Uropathogens Isolated from Urine cultures (n = 197)

Parameters		Frequency	%age	P-Value
Uropathogen	E coli	165	83.8	0.066
	Pseudomonas	12	6.1	
	Klebsiella pneumoniae	10	5.1	
	proteus	05	2.5	
	Pantoea Spp	01	0.5	
	Enterobacter	03	1.5	
	Citrobacter diversus	01	0.5	

Table 3: Cefixime Sensitivity Pattern among Isolated Uropathogens (n = 197)

		Frequency	%age
Cefixime Sensitivity Pattern	Yes	72	36.5
	No	125	63.5

Table 4: Logistic Regression Analysis to Analyse the Predictors of Cefixime Sensitivity (n = 197)

Variables	B	S.E.	Wald	P-Value	OR	95% C.I.for EXP(B)	
						Lower	Upper
Age (years)	-0.303	0.392	0.598	0.439	0.739	0.343	1.591
BMI(kg/m^2)	0.321	0.238	1.827	0.176	1.379	0.865	2.197
Education	0.638	0.248	6.611	0.010	1.893	1.164	3.080
Residence	0.227	0.313	0.529	0.467	1.255	0.680	2.317
Uropathogen	-0.202	0.150	1.812	0.178	0.817	0.608	1.097
Constant	-0.948	0.872	1.184	0.277	0.387		

DISCUSSION

This study demonstrates a high level of cefixime resistance among uropathogens in pregnant women, particularly *E. coli*. The predominance of *E. coli* is consistent with global literature. The significant prevalence among women with an elevated body mass index (BMI) is consistent with recent findings that relate an elevated BMI prior to pregnancy to a greater likelihood of UTIs.[8,9] The study's applicability across a variety of community contexts, where the availability of diagnostics and antibiotic use may differ, is highlighted

by the distribution pattern among urban and rural residents. E. coli was the most common urinary tract pathogen, accounting for a large percentage of infections, in line with local and worldwide statistics on both community-wide and pregnancy-related UTIs.[10,11] It is consistent with previous studies. While the uncommon discovery of Pantoea species and Citrobacter diversus highlights that unusual infectious agents are sometimes identified, potentially in situations involving repeated infection or concurrent host illnesses, the segregation of other organisms, such as Pseudomonas aeruginosa and Klebsiella pneumoniae, conforms to anticipated trends.[12] The strikingly low overall sensitivity to cefixime is the study's most notable finding. This suggests a significant degree of resistance that seriously compromises the medication's effectiveness as an oral first-line treatment. Although this incidence is significantly lower than some previous findings, it supports a growing body of recent data showing that Gram-negative uropathogens are becoming increasingly resistant to third-generation cephalosporins, especially in low- and middle-income countries.[13,14] Increasing antimicrobial resistance among Gram-negative uropathogens has been widely reported, particularly in low- and middle-income countries.[15] Cefixime sensitivity did not significantly correlate with patient age, BMI, or place of residence in subgroup analyses. The slightly increased sensitivity observed in patients over 30 years of age compared with those with a normal body mass index (BMI) was not statistically significant, indicating that resistance is common and not limited to certain demographic groups within the pregnant community. There was a trend toward a substantial correlation with educational attainment, with highly educated individuals exhibiting the least sensitivity. This unexpected result calls for further research, but it may be linked to differences in healthcare availability, self-treatment, or past antibiotic exposure patterns across socioeconomic groups.[16] Important insights were obtained from analysis by pathogen kind. The variation in sensitivity patterns across uropathogens was only marginally significant, despite E. coli showing the greatest degree of resistance. Interestingly, Pseudomonas isolates showed a comparatively high sensitivity rate; however, this finding should be interpreted cautiously, as it is based on a limited sample. On the other hand, Enterobacteriaceae other than E. coli have also shown significant resistance. Given its prevalence, the elevated resistance in E. coli is particularly worrisome, as it means cefixime would be ineffective against a significant number of the most prevalent illnesses. Our results on cefixime sensitivity are especially striking when compared to current research. Significant regional diversity was reported in a comprehensive study of antibiotic resistance in pregnancy-related UTIs, although South Asia had particularly high cephalosporin resistance rates.[17] Cefixime sensitivity in E. coli was shown to be poor in another study conducted in a similar setting, strongly supporting our findings and suggesting a regional issue.[18] This highlights the rapid development of resistance compared with earlier research or studies from areas with more stringent antibiotic regulations, where higher susceptibility rates were nevertheless documented 10 years ago.[19]

LIMITATIONS

Its single-centre design restricts generalizability due to potential regional variation in antimicrobial resistance patterns. Only cefixime was evaluated, limiting comparison with other commonly used antibiotics in pregnancy and reducing clinical interpretability. Although susceptibility testing was performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines as implemented in the institutional laboratory, the absence of details on CLSI version, quality control strains, disk potency, and ESBL confirmation limits methodological reproducibility. Furthermore, obstetric variables such as gestational age, trimester, parity or pregnancy outcomes were not routinely collected in the original study protocol. Finally, the relatively small number of non-*Escherichia coli* isolates reduced the statistical power of subgroup analyses and limits confidence in organism-specific comparisons. Collectively, these limitations constrain the generalizability of the findings and underscore the need for larger, multicenter studies with comprehensive microbiological and clinical characterisation.

CONCLUSIONS

The present study demonstrates that E. coli is the predominant uropathogen among pregnant women with urinary tract infection and that a substantial proportion of isolates were resistant to cefixime. These findings emphasise the importance of obtaining urine culture and antimicrobial susceptibility results whenever possible to guide appropriate antibiotic therapy. Given the single-centre design and evaluation of only one antimicrobial agent, further multicenter prospective studies incorporating multiple antibiotics and comprehensive clinical variables are warranted to inform empirical treatment recommendations.

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AUTHORS CONTRIBUTION

Syeda Maria Shah *- Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Final Approval*

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The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.