Original Article

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Pharmacology Section

Changing Spectrum of Antimicrobial Drug Resistance among Uropathogens in Pregnant Women over Three Years at a Tertiary Healthcare Facility: A Retrospective Observational Study

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ABSTRACT

Introduction: Infections caused by uropathogens are common during pregnancy, and empirical treatment with Antimicrobial Agents (AMAs) is also frequently encountered. The emergence of Antimicrobial Drug Resistance (AMR) in uropathogens is a major concern.

Aim: To evaluate the spectrum of AMR among uropathogens in pregnant women in a tertiary healthcare facility.

Materials and Methods: The present retrospective observational study was conducted in Department of Pharmacology in collaboration with the Department of Microbiology of MKCG Medical College and Hospital, Berhampur, Odisha, India, to evaluate all consecutive samples of laboratory confirmed uropathogens of urine culture sensitivity reports of pregnant women during the period of three years (July 2020-July 2023). Data were collected from past records from July 2023 to September 2023 were subsequently analysed in November 2023 to December 2023. A total sample size of 606 was estimated with inclusion or exclusion criteria. The data set included demographic parameters of pregnant subjects, such as age, type of gravida, provisional diagnosis, with its clinicopathological types and resistance pattern were observed from manually maintained case records. The association between selected parameters and AMR was established using Pearson's chi-square test, which was found to be statistically significant (p-value <0.05).

Results: Of the 2,631 cases, 1,326 (50.4%) were culture-positive for uropathogens. Among these, 606 pregnant women were identified. The mean age of pregnant women with AMR was 31±1.81 years. A rising trend of AMR among uropathogens in pregnant women was observed from 86 (14.2%) in 2020 to 262(43.2%) in 2023 out of 606 sample size. A progressive prevalence of Ciprofloxacin (CIP)-Ceftriaxone (CTR)-Cefixime (CIX) 71.6% Multidrug Resistance (MDR) was encountered in *Escherichia coli* (*E.coli*) which accounted for 75.08% of uropathogens in symptomatic bacteriuria among pregnant women with Urinary Tract Infection (UTI).

Conclusion: A rising trend of AMR to different AMAs needs antibiotic use optimisation thereby promoting rational antibiotic use in the management of UTI in pregnant subjects and execution of Antimicrobial Stewardship Program (ASP) for mitigation of MDR as a future prospect. AMR to different AMAs among uropathogens in pregnant women in case of UTI limits the availability of treatment options for healthcare providers.

Keywords: Anti-bacterial agents, Multidrug resistance, Pregnancy, Urinary tract infection

INTRODUCTION

Bacterial infection of the urogenital tract is one of the common causes for seeking clinical service among pregnant women in different settings. Effective management of such conditions basically relies on the type of causative uropathogens that gives rise to disease. Empirical antibiotic administration in pregnant women is a common scenario in clinical practice. This requires timely updating of recommended empiric antibiotic regimens and selecting appropriate AMAs effective against the specific uropathogen [1].

Among the uropathogens, *E.coli* and other Enterobacteriaceae are the most common accounting approximately 75% of the isolates. According to a study, AMR rates among common uropathogens, including *E.coli, Klebsiella species* (sp.), *Proteus mirabilis, Pseudomonas aeruginosa (P. aeruginosa), Staphylococcus* sp. *and Enterococcus* sp. have been increasing. Their susceptibility pattern demonstrates temporal and topographical variation worldwide [2].

Globally accepted guidelines recommend treatment of UTI with cephalosporins, nitrofurantoin, fosfomycin and fluoroquinolones. Rise in AMR can be attributed to regional variation in distribution, different trends of resistance among uropathogens to different AMAs, and overuse of commonly used antibiotics in empirical therapy. This has subsequently given rise to multi-drug resistant uropathogen strains, leading to poor poor clinical outcomes [3].

UTI in pregnancy refers to the invasion and subsequent growth of pathogens in any part of the urinary tract, including the bladder and associated structures. It is due to mechanical factors like a gravid uterus impeding urinary outflow, along with hormonal changes like increased progesterone lead to relaxation of urinary tract smooth muscle, resulting in urinary stasis, allowing uropathogens to ascend from the urethra to the bladder and kidneys. Furthermore, a short urethra and proximity to the anus cause easy contamination of the urinary tract with faecal microbes. Although both males and females may become infected with UTI, an interplay of mechanical and hormonal factors makes pregnant females more likely to develop UTI compared to males [4,5].

UTIs are classified as either asymptomatic or symptomatic bacteriuria during pregnancy. The presence of a significant number of bacteria as 10^5 Colony-Forming Unit (CFU)/mL of cultured clean

catch urine in the absence of signs and symptoms of UTI, is known as Asymptomatic Bacteriuria (ABU). ABU occurs 2% to 15% of pregnant women [6]. Guidelines recommend early prenatal ABU screening and timely initiation of antibiotics in the first or second trimester treatment, which reduces chances of progression to complicated UTI by 3% to 4%. Subsequent prompt diagnosis and treatment tend to reduce the incidence of further complications such as pyelonephritis, preterm delivery and Low Birth Weight (LBW) [7]. This was validated from a Cochrane review study featuring antibiotic treatment causing reduction in pyelonephritis (average Risk Ratio (RR)-0.24) along with reduction in preterm birth and LBW babies. There was reduction in persistent bacteriuria during the peripartum period (RR-0.30) [8].

Routine Antimicrobial Susceptibility Tests (AST) are a major challenge in the majority of low-income developing countries as a result of which treatment of infectious disease including UTI in pregnant women, often gets initiated with an empirical antibiotic, further contributes to the emergence of resistant pathogens [9]. In a recent review, the global prevalence of AMR in UTI and ABU in pregnancy ranged from 3 to 35% across 5 continents in countries with preterm birth rates >10% [10]. A systematic review of AMR of uropathogens in the Asia-Pacific region suggested AMR prevalence of *E. coli* to sulfamethoxazole/trimethoprim, ciprofloxacin, and CTR was 33-90%. This was much greater compared to nitrofurantoin resistance which was just 2.7-31.4%, and the resistance rate to fosfomycin was about 1.8% [11]. According to a Mexican study, *Klebsiella pneumoniae (K. pneumoniae)* isolates had greater sensitivity to amikacin and carbapenems, whereas nitrofurantoin had a median resistance of 52%. It has been reported that *K. pneumoniae* (40.4%) showed MDR more frequently than *E. coli* (23.3%) [12]. According to present Indian scenario, AMR prevalence data from different community settings portrayed *E. coli* as predominant uropathogen as 68.3% among all isolates with 51.8% ampicillin resistance whereas nitrofurantoin resistance among *K. pneumoniae* was more prevalent as 14% [13]. Scarce evidence exists to evaluate AMR trend among uropathogens in different healthcare settings due to geographical variation in AMR prevalence [14-16].

The present study aimed to assess the distribution of AMR among various uropathogens and their association with clinicopathological types of UTI, type of gravida and age in years. The primary objective of the study was to analyse the changing trend of AMR among uropathogens in pregnant women, and the secondary objectives were to estimate the prevalence of AMR patterns to different AMAs among various uropathogens in pregnant women.

MATERIALS AND METHODS

The present study was a retrospective observational study conducted by the Department of Pharmacology in collaboration with the Department of Microbiology, MKCG Medical College, Berhampur, Odisha, India, during the study period from July 2020 to November 2023. Data was collected from past records from July 2023 to September 2023 were subsequently analysed in November 2023 to December 2023. The study was approved, and waiver of consent was sought from the Institutional Ethics Committee (IEC) No.1267, Chairman, IEC, MKCG Medical College and Hospital, Berhampur, Odisha, India.

As the study was record-based with no patient interaction, the inclusion of informed consent stands exempted. Patient confidentiality was maintained by coding name initials, thus obscuring identity. Details of case data were accessible only to the principal investigator and the corresponding author.

Sample size: Sample size was not statistically calculated, as this was a time-bound study and all 2631 consecutive samples were encountered during the study where 606 samples satisfying the inclusion criteria were considered for analysis.

Inclusion and exclusion criteria: All consecutive laboratory-confirmed urine culture sensitivity reports showing bacterial isolates with a provisional diagnosis, gravida status, and complete demographic details during the study period were included. Those with incomplete and ambiguous sociodemographic profiles or with no isolate, all cases except pregnant women with a specific urine culture positive uropathogen, non pregnant individuals and males were excluded.

Study Procedure

The study was conducted on clean catch Midstream Urine (MSU) samples of pregnant women from the Obstetrics and Gynaecology (O&G) Department reporting for AST at the Department of Microbiology, and showing AMR were considered the defined study population. The results of AST were recorded in year-wise urine culture susceptibility manually designed records in the Bacteriology section, along with other cases from different departments subjected to urine bacterial AST. These records formed the source of retrospective data collection from 2020-2023, from which concerned cases required for the study were pooled after applying inclusion criteria.

Those cases with urine culture-positive uropathogens were screened. Again, from the population of pregnant women having a urine culture positive uropathogen, those cases showing AMR to different AMAs were taken for final analysis and were considered as the defined study population. Details of selected cases were recorded using a manually designed structured case record form validated by pharmacologists and microbiologists of the concerned departments of the Institution.

EUCAST (European Committee on Antimicrobial Susceptibility Testing) guidelines [17] for Antimicrobial Abbreviations 2022 were used in forming patterns of MDR and sensitivity of AMAs. Each AMA was abbreviated by its corresponding first three letters, like

1. AMP: AMPicillin, GEN: GENtamycin and so on.
2. For beta-lactamase inhibitors like AMoxicillin-Clavulanate: two letters of first agent and first letter of the second agent were used.

For cases with resistance to multiple AMAs, repeated analysis analyses were done to consolidate AMR into a single pattern, such as resistance to Ciprofloxacin-Ceftriaxone-Cefixime were presented as CIP-CTR-CIX [18].

Multidrug Resistance (MDR) definition: MDR is commonly defined as non susceptibility to at least one agent in three or more antimicrobial categories, and it is commonly defined as resistance to antimicrobial drugs from more than three classes [19].

Asymptomatic Bacteriuria (ABU): Significant growth of uropathogens (>10^5 bacteria/mL) in the absence of clinical manifestation [20].

Symptomatic UTI: Patients whose urine yields positive cultures (>105 CFU/mL) and who have symptoms referable to urinary tract [21].

Complicated UTI: Any UTI in pregnancy which is a clinical trajectory from simple UTI characterised by MDR bacterial colonisation associated with immunocompromised disease states like diabetes, post chemotherapy or chronic steroid use which may further co-present with recurrent cystitis or ascending pyelonephritis, anatomical abnormalities like urinary tract stones, hydronephrosis or colovesical fistula [22].

STATISTICAL ANALYSIS

Categorical variables were analysed using Pearson's chi-square test in IBM Statistical Package for the Social Sciences (SPSS) Statistics version 17.0, and a p-value of <0.05 was considered statistically significant.

RESULTS

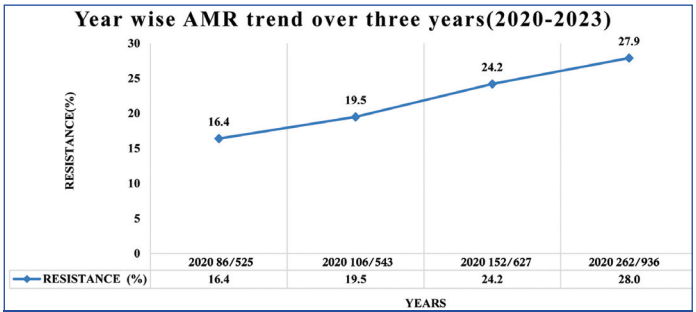
A total of 2631 consecutive cases from records of three years, ranging from 2020 to 2023 were taken for studying the pattern of AMR among uropathogens. Among 2631 cases, year-wise distribution of consecutive cases was 525 (19.9%), 543 (20.6%), 627 (23.8%), 936 (35.5%) in 2020, 2021, 2022, 2023, respectively. About 1,326 (50.4%) pregnant cases demonstrated positivity to one of the uropathogens. Among these 606 pregnant women, 86 (14.2%) in 2020, 106 (17.5%) in 2021, 152 (25.1%) in 2022 and 262 (43.2%) in 2023 were resistant to different AMAs as shown in [Table/Fig-1].

Parameters	2020	2021	2022	2023
Total number of cases (N=2631)	525(19.9%)	543(20.6%)	627(23.8%)	936(35.5%)
No uropathogens isolated (n=1056)	233(22.06%)	184(17.4%)	268(25.4%)	371(35.1%)
No uropathogens isolated in pregnant women (n=223)	74(33.2%)	63(28.3%)	78(34.9%)	8(3.6%)
Uropathogens isolated in other cases (n=249)	67(26.9%)	22(8.8%)	79(31.7%)	81(32.5%)
Uropathogens isolated in pregnant women (n=1326)	263(19.8%)	365(27.5%)	413(31.1%)	285(21.5%)
AMR among uropathogens in pregnant women (n=606)	86(14.2%)	106(17.5%)	152(25.1%)	262(43.2%)

[Table/Fig-1]: Trends of AMR and uropathogens among pregnant and non-pregnant subjects over three year period.

A period prevalence of AMR among uropathogens in pregnant women over a three-year period (2020-2023) was found 23.03% as 606 pregnant women out of 2631 demonstrated AMR. A rising AMR trend observed from 2020 to 2023. A progressive prevalence of CIP CTR CIX (42.3%), MDR in E.coli (57.3%) in symptomatic bacteriuria among pregnant women with UTI was encountered. Different resistant cases of pregnant women among consecutive cases were observed for each year, starting with 86/525 (16.4%), 106/543 (19.5%), 152/627 (24.2%), 262/936 (28.0%) in 2020, 2021, 2022, 2023, respectively. Hence, a trend line chart demonstrating these respective year wise resistance rates as point prevalence was plotted as shown in [Table/Fig-2].

Age was normally distributed had Gaussian distribution depicted by equal mean, median and mode 31, hence mean±Standard Deviation (SD) was 31±1.81 years computed using descriptive statistics in SPSS version 17.0 as shown in [Table/Fig-3].



[Table/Fig-2]: Trend chart showing AMR point prevalence over a period of three years (2020-2023).

Age (years)	Count n (%)	Mean±SD	Kurtosis	Skewness
26	4 (0.6%)	31±1.81	-0.16	-0.43
27	23 (3.8%)			
28	43 (7.09%)			
29	53 (8.74%)			
30	64 (10.5%)			
31	161 (26.5%)			
32	157 (25.9%)			
33	40 (6.6%)			
34	61(10.06%)			

[Table/Fig-3]: Age-wise distribution of pregnant women exhibiting AMR in uropathogens.

Major isolate contributing to relevance of uropathogen AMR was *E.coli* 455(75%) with CIP-CTR-CIX resistance prevalence as 326(71.6%). Subsequent descending counts of isolates out of 606 were *P. aeruginosa* 66(10.8%), *Klebsiella* sp. 43(7.1%), *Enterococcus* sp.41 (6.8%), *Staphylococcus aureus*, 1(0.2%). AMR prevalence pattern distribution of Piperacillin-Tazobactam (PIT)-CEP-CTR-AMP among uropathogen out of their respective counts were *Klebsiella* sp. 28/43(65.1%), *Enterococcus* sp. 13/41(31.7%), *E.coli* 55/455(12%) was second highest followed by MDR pattern PIT-GEN-LEV having an uniform percentage distribution among *P. aeruginosa* 17/66(25.7%), *Enterococcus* sp. 6/41(14.6%), *E.coli* 58/455(12.7%), *Klebsiella* sp. 2/43(5%). Ceftazidime (CTZ) mono resistance had a greater prevalence in *P. aeruginosa* 18/66 (27.3%) as demonstrated in [Table/Fig-4].

Among 606 pregnant women, 505/606(83.3%) were primigravida and 101/606 (16.7%) were multigravida. CIP-CTR-CIX was found to have the highest prevalence with count and percentage as 365/606(60.2%). CIP-CTR-CIX resistance among primigravida women and multigravida women were 313/505(60.8%) and 52/101(51.4%) respectively. PIT-CEP-CTR-AMP was second highest prevalence of AMR pattern with count and percentage as 96/606(15.8%) and percentage distribution among pregnant women as 82/505(16.2%) and 14/101(13.8%) in primigravida and multigravida respectively. Other AMR pattern prevalence includes Piperacillin-tazobactam-Gentamicin-Levofloxacin (PIT-GEN-LEV), Ampicillin-Levofloxacin-Fosfomycin (AMP-LEV-FOS), Gentamicin-Levofloxacin (GEN-LEV), Pituitary-Ceftriaxone-Ampicillin-Nitrofurantoin (PIT-CTR-AMP-NIT), Pituitary-Meropenem-Ampicillin-Nitrofurantoin (PIT-MRP-AMP-NIT) with count (%) with respect to gravida as 83/606 (13.7%), 19/606 (3.1%), 18/606 (2.9%), 11/606 (1.8%), 10/606 (1.6%), 2/606 (0.3%), respectively as shown in [Table/Fig-5].

Three clinicopathological types of UTI was ABU 142/606(23.4%), symptomatic uncomplicated UTI 403/606(66.5%) and complicated UTI 61/606(10%) presented with cystitis, pyelonephritis and comorbidities such as type II diabetes mellitus and hypertension or coronary artery disease. Prevalence of AMR were maximum for CIP-CTR-CIX in symptomatic uncomplicated UTI as 278(68.9%) followed by 74(52.1%) in ABU but least prevalent in complicated UTI 5(8.2%). Second highest distribution was found with PIT-CEP-CTR-AMP in ABU, symptomatic uncomplicated and complicated UTI as 27(19%), 58(14.4%) and 2(3.3%) as depicted in [Table/Fig-6].

Statistical significant association existed between parameters of clinicopathological types, isolates and state of gravida with AMR which was demonstrated by computing Pearson's chi-square 335.9, 302.7, 754.2 respectively with p-value=0.001 in [Table/Fig-7].

DISCUSSION

Study depicts a rise in AMR trend among uropathogens in pregnant subjects retrospectively over a period of three years (2020-2023)

Uropathogens (606)	AMP-LEV-FOS (19/606) (3.1%)	CTZ (18/606) (2.9%)	CIP-CTR-CIX (365/606) (60.2%)	CIX-NIT -COT-LEV (2/606) (0.3%)	GEN-LEV (11/606) (1.8%)	PIT-CEP-CTR-AMP (96/606) (15.8%)	PIT-CTR-AMP -NIT (10/606) (1.6%)	PIT-GEN-LEV (83/606) (13.6%)	PIT-MRP -AMP -NIT (2/606)(0.3%)
E.coli (455)	9/455 (1.9%)	*	326/455 (71.6%)	*	*	55/455 (12.08%)	6/455 (1.3%)	58/455 (12.7%)	1/455 (0.2%)
Enterococcus (41)	*	*	21/41 (51.2%)	*	*	13/41 (31.7%)	1/41 (2.4%)	6/41 (14.6%)	*
Klebsiella (43)	6/43 (14.0%)	*	3/43 (6.9%)	*	*	28/43 (65.1%)	3/43 (6.9%)	2/43 (4.6%)	1/43 (2.3%)
P.aeruginosa (66)	4/66 (6.1%)	18/66 (27.3%)	15/66 (22.7%)	1/66 (1.5%)	11/66 (16.7%)	*	*	17/66 (25.7%)	*
S.aureus (1)	*	*	*	1/1 (100%)	*	*	*	*	*

[Table/Fig-4]: Antimicrobial Drug Resistance (AMR) distribution among uropathogens.
AMP: Ampicillin, CEP: Cefepime; CIP: Ciprofloxacin; CIX: Cefixime; COT: Cotrimoxazole; CTR: Ceftriaxone; CTZ: Ceftazidime; FOS: Fosfomycin; GEN: Gentamycin; LEV: Levofloxacin; MRP: Meropenem; NIT: Nitrofurantoin; PIT: Piperacillin-tazobactam; *signifies no drug resistance found

Gravida (606)	AMP-LEV-FOS (19/606) (3.1%)	CTZ (18/606) (2.9%)	CIP-CTR-CIX (365/606) (60.2%)	CIX-NIT -COT-LEV (2/606) (0.3%)	GEN-LEV (11/606) (1.8%)	PIT-CEP-CTR-AMP (96/606) (15.8%)	PIT-CTR-AMP -NIT (10/606) (1.6%)	PIT-GEN-LEV (83/606) (13.6%)	PIT-MRP -AMP -NIT (2/606) (0.3%)
Primigravida	4/505 (0.8%)	12/505 (2.3%)	313/505 (61.9%)	1/505 (0.2%)	4/505 (0.8%)	82/505 (16.2%)	10/505 (1.98%)	78/505 (15.5%)	1/505 (0.2%)
Multigravida (101)	15/101 (14.8%)	6/101 (5.9%)	52/101 (51.5%)	1/101 (0.9%)	7/101 (6.9%)	14/101 (13.8%)	*	5/101 (4.9%)	1/101 (0.9%)

[Table/Fig-5]: Uropathogen Antimicrobial Drug Resistance (AMR) according to type of gravida.
AMP: Ampicillin, CEP: Cefepime; CIP: Ciprofloxacin; CIX: Cefixime; COT: Cotrimoxazole; CTR: Ceftriaxone; CTZ: Ceftazidime; FOS: Fosfomycin; GEN: Gentamycin; LEV: Levofloxacin; MRP: Meropenem; NIT: Nitrofurantoin; PIT: Piperacillin-tazobactam; *signifies no drug resistance found

Clinicopathological types (606)	AMP-LEV-FOS (19/606) (3.1%)	CTZ (18/606) (2.9%)	CIP-CTR-CIX (365/606) (60.2%)	CIX-NIT -COT-LEV (2/606) (0.3%)	GEN-LEV (11/606) (1.8%)	PIT-CEP-CTR-AMP (96/606) (15.8%)	PIT-CTR-AMP -NIT (10/606) (1.6%)	PIT-GEN-LEV (83/606) (13.6%)	PIT-MRP -AMP -NIT (2/606) (0.3%)
Asymptomatic Bacteriuria (ABU)	17/142 (11.9%)	1/142 (0.7%)	74/142 (52.1%)	*	11/142 (7.75%)	27/142 (19%)	1/142 (0.7%)	10/142 (7.04%)	1/142 (0.7%)
Symptomatic UTI	2/403 (0.4%)	12/403 (2.9%)	278/403 (68.9%)	1/403 (0.2%)	*	58/403 (14.4%)	2/403 (0.4%)	49/403 (12.1%)	1/403 (0.2%)
Complicated UTI (61)	*	5/61 (8.1%)	5/61 (8.1%)	1/61 (1.6%)	*	2/61 (3.2%)	7/61 (11.4%)	41/61 (67.2%)	*

[Table/Fig-6]: Uropathogen Antimicrobial Drug Resistance (AMR) in various clinicopathological types of UTI.
AMP: Ampicillin; CEP: Cefepime; CIP: Ciprofloxacin; CIX: Cefixime; COT: Cotrimoxazole; CTR: Ceftriaxone; CTZ: Ceftazidime; FOS: Fosfomycin; GEN: Gentamycin; LEV: Levofloxacin; MRP: Meropenem; NIT: Nitrofurantoin; PIT: Piperacillin-tazobactam; *signifies no drug resistance found

Variables	AMR prevalence in pregnant subjects n (%) (total count = 606)	Positivity rate n (%) (total count = 1326)	Chi-square (p-value)
Uropathogens			
Eischerichia coli	455 (75.08)	810 (61.08)	302.7 (0.001)
Enterococcus sp.	41 (6.76)	106 (7.99)	
Klebsiella sp.	43 (7.09)	202 (15.23)	
Pseudomonas aeruginosa	66 (10.89)	123 (9.27)	
Staphylococcus aureus	1 (0.16)	85 (6.4)	
Gravida			
Primigravida	505 (84.8)	646 (48.71)	754.2 (<0.001)
Multigravida	101 (15.18)	680 (51.28)	
Clinico pathological types			
Asymptomatic Bacteriuria (ABU)	142 (23.59)	634 (47.81)	335.9 (0.001)
Symptomatic UTI	403 (66.33)	191 (14.40)	
Complicated UTI	61 (10.06)	501 (37.78)	

[Table/Fig-7]: AMR prevalence and positivity rate with respective factors association using descriptive statistics.

from 16.4% in 2020 to 27.9% in 2023. A rise in the number of reported cases and resistance rates was observed in the post-Coronavirus Disease (COVID) period after 2021. However, the underlying reasons for this increase could not be established from the current dataset. This was quite similar to a study carried out by *Shawkat ND et al.,* which depicted AMR as a silent epidemic gathered during the pandemic due to overconsumption of antibiotics which resulted in highest resistance rates among most frequently encountered uropathogen *E.coli* (88.8%) to ampicillin and amoxicillin-clavulanic acid [22].

The study depicted prevalence of CIP-CTR-CIX AMR with an overall prevalence of 365 out of 606 (60.2%). *E.coli* was the predominant uropathogen isolated among 606 cases accounting for 455(75%). Distribution of the most prevalent pattern of resistance among *E.coli* also stood highest which were 326 out of 455 (71.6%). Chelkeba L et al., documents a higher Amoxicillin monoresistance pattern in *E.coli* was 81% in significant bacteriuria. But the lowest prevalence of Nitrofurantoin monoresistance accounts for 19% which was higher than current study [23]. This study found the percentage of resistance of nitrofurantoin in 0.3% each of CIX-COT-NIT-LEV and PIT-MRP-AMP-NIT as well as fosfomycin in AMP-LEV-FOS 19(3.1%) in *E.coli* ABU in multigravida women. van der Putten BCL et al., depicted mechanisms of Ciprofloxacin resistance in *E.coli* isolates attributed to genetic mutations altering DNA gyrase and topoisomerase IV drug targets, efflux pumps decreasing cellular drug concentration and enzymatic inactivation of Ciprofloxacin [24,25].

E. coli is the predominant uropathogenic bacteria because of several virulence factors related to invasion and colonisation of the urinary epithelium. According to Mohapatra S et al., AMR pattern in ASB confirmed pregnant women conducted by Indian Council of Medical Research (ICMR) identified high resistance rates to ampicillin (60.8%) followed by ciprofloxacin (54.9%) but a lower degree of resistance to fosfomycin (0.0%) and PIT-NIT (29.4%) [25]. This observation was in line with the study findings where ciprofloxacin resistance was found to be highest with a

slow rising pattern of nitrofurantoin, as PIT-CTR-AMP-NIT 1.5% in *E.coli* was observed.

According to Adhikari S et al., in a study about knowledge of UTI in primigravida women, the mean age was about 23.5 years with a range 22-25 [27]. In contrast, the current study showed a uniform Gaussian age distribution at 31 years with SD±1.8 years. This may be due to more marriages and shift in childbearing age from below 25 years to above 25 years in the locality.

In a study done to assess the effect and outcome of UTI in pregnancy, UTI was found to be in 67% primigravida as compared to 28% in multigravida and 2 (3.3%) in grand multigravida. This is quite consistent with the current study, where 514 (84.8%) primigravida women have a greater proportion in distribution compared to 92 (15.1%) multigravida. AMR CIP+CTR+CIX pattern has the highest prevalence in primigravida women pertaining to 60.8% compared to multigravida 56.5% prevalence. This study has not encountered any grand multi-subject so far [28]. Greater prevalence of ABU in pregnancy accounting for 73% of cases was found in a study expressing antimicrobial susceptibility pattern of uropathogens of pregnant women in Ethiopia which was not in agreement with our study where we had greater MDR resistance pattern CIP+CTR +CIX 68.9% as well as proportion distribution of symptomatic uncomplicated UTI in pregnant women which was 66.5% [28,29].

Clinical implications of the study exhibited an ascending trend in uropathogen MDR in pregnancy summons the need for optimisation of antibiotic use, upgradation of local policies. Generation of awareness and implementation of ASP as well as for an integrated management of high soaring AMR in future is important.

Limitation(s)

The current study showed few research gaps and limitations that need to be addressed. Firstly, being a record-based study due to which some parameters like socioeconomic status, previous history of abortions, foetal history and maternal co-morbidities and history of medications could not be elicited with lack of patient Point Of Contact (POC). Secondly, maternal and foetal outcomes such as LBW, Premature Rupture Of Membrane (PROM) could not be perceived especially in cases with complicated UTI. Thirdly, the screening of antibiotics like norfloxacin, clindamycin and novel AMAs like streptogramins quinupristin/dalfopristin used for resistant cases of UTI in pregnancy were not taken into account for AST.

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CONCLUSION(S)

The UTIs in pregnancy were linked to higher rates of adverse outcomes including preterm births, preterm PROMs and neonatal respiratory distress. Due to significant regional variations in resistance patterns, relying on local antibiograms is critical for choosing the right antibiotic. The present study provides insight towards encouraging the rational use of AMAs in pregnant women while treating UTI.

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