INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY FUTURISTIC DEVELOPMENT

Multidrug Resistance and ESBL-Producing Uropathogens in Pregnancy: Epidemiology, Susceptibility Patterns, and Risk Stratification

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Article Info

P-ISSN: 3051-3618
E-ISSN: 3051-3626
Impact Factor (RSIF): 8.31
Volume: 07
Issue: 01
Received: 11-01-2026
Accepted: 09-02-2026
Published: 08-03-2026
Page No: 61-66

Abstract

Background: UTI is a common bacterial complication in pregnancy, and has significant morbidity in both the mother and child. The appearance of the antimicrobial resistance (AMR) especially the extended-spectrum beta-lactamase (ESBL) and multidrug resistance (MDR) makes the empirical therapy more complicated. This research was done to establish the prevalence, microbial spectrum, antimicrobial susceptibility, and independent predictors of ESBL-positive UTIs among pregnant women.

Methods: A cross-sectional research study was conducted on 250 pregnant women at Tikrit in Iraq who attended antenatal clinics. Urine samples of the midstream were also cultured and antimicrobial susceptibility testing was done on the isolates. The combination disk method was used to detect ESBL. Multivariate logistic regression was used to predict independent predictors of ESBL-producing Gram-negative infections. The statistical significance was determined at $p<0.05$.

Results: Bacteriuria of significance was observed in (51.6%) participants with the highest rate observed in the second trimester (44.9%). The gram-negative organisms were dominant (70%), with the lead taken by *Escherichia coli* (51.9%) and *Klebsiella pneumoniae* (17.8%). The highest susceptibility (>85%) was retained by nitrofurantoin and ampicillin and TMP-SMX had limited activity. At the species level, *K. pneumoniae* was found to be much less susceptible to both nitrofurantoin and ampicillin than *E. coli* ($p<0.05$). Maternal age ≥ 35 years (adjusted OR 2.86), diabetes mellitus (adjusted OR 2.79), and past UTI history (adjusted OR 2.94) were the independent predictors of ESBL-positive infection. The prevalence rate of overall MDR and ESBL was 34.7% and 23.5%, respectively, and the highest prevalence rate of K. pneumoniae was 47.8% and 34.8% in terms of MDR and ESBL rates, respectively.

Conclusions: MDR and ESBL prevalence are high in this obstetric population of UTIs. Screening and culture-guided therapy based on risks and cultures are suggested, as the optimal way of improving the maternal-fetal outcome and antimicrobial stewardship.

DOI: https://doi.org/10.54660/IJMFD.2026.7.1.61-66

Keywords: Urinary tract infection, Pregnancy, ESBL, Multidrug resistance, antimicrobial susceptibility

Introduction

Urinary tract infections (UTIs) are a significant complication of bacteria in pregnancy that is important in terms of maternal morbidity, and therefore it is preventable (WHO, 2025). The changes of the anatomy, hormone, and immunology such as progesterone-induced ureteral relaxation, urinary stasis, and dysfunctional cell-mediated immunity enable the rising bacterial colonization (CDC, 2026). According to the reports of global surveillance, it is estimated that 8-15 percent of pregnant women develop bacteriuria, and it progresses to a symptomatic infection upon untreated (CDC, 2026). Uropathogenic *Escherichia coli* is the most common causative agent,

and then *Klebsiella pneumoniae* and *Proteus mirabilis*. But UTIs epidemiology is becoming affected more by antimicrobial resistance (AMR), especially ESBL-producing strains, which hydrolyze third-generation cephalosporins that are used in pregnancy (ECDC, 2025). Current surveillance (2025-2026) shows that there is still an increase in the number of community-acquired ESBL-producing Enterobacteriaceae, and the resistance rates are more than 25-35% (CDC, 2026). Failure or late treatment exposes the patient to the risk of developing pyelonephritis, preterm births, low birth weight, and poor neonatal outcomes. The safety restrictions of broad-spectrum agents during pregnancy further limit treatment, and the profiling of local resistance and stewardship is of high importance (WHO, 2025). Risk factors related to the ESBN acquisition, such as previous exposure to antibiotics, frequent UTIs, gestational diabetes, healthcare contact, and maternal advanced age need to be identified to refine empirical therapy and mitigate complications. The purpose of this study was to define the prevalence and microbial spectrum of UTIs, characterize the patterns of antimicrobial susceptibility, and determine independent risk factors of ESBL-producing infections in pregnant women as the current epidemiological evidence on the best approach to combating obstetric infections.

Materials and Methods

Study Design and Setting: A cross-sectional study that was performed between February 2025 and December 2025 in Tikrit Teaching Hospital and other related obstetric clinics, Tikrit, Iraq.

Population of Study: Two hundred and fifty pregnant women, all aged between 18 and 45 years old, were consecutively recruited into the study, at all trimesters. The exclusion criteria were that they could not have had any antibiotic within the last two weeks, structural renal anomalies or did not consent to take part. The data were taken through structured questionnaires in terms of demographic and clinical information.

Specimen Collection and Microbiological Analysis: The midstream urine samples were collected in aseptic conditions. A significant bacteriuria was considered10 ^{5} CFU/mL. MacConkey and blood agar were used to grow cultures, which were incubated at 37°C in 18-24 hours. Identification was done using standard methods of biochemical and API 20E. Susceptibility testing was done according to CLSI 2025 guidelines with the help of the Kirby-Bauer disk diffusion technique. Detection of ESBL was done by use of combination disk technique.

Definitions MDR Resistance to three classes of antimicrobials. ESBL: Production of the extended-spectrum b- lactamase. Considerable bacteriuria: $\geq 10^5$ CFU/mL.

Statistical Analysis: The analysis of the data was conducted with the help of SPSS version 29 (IBM Corp., 2025). The reports of continuous variables were a mean and SD; categorical variables counts and percentages. There were associations that were measured using chi square tests. Multivariate logistic regression was used to determine independent predictors of ESBL infection. The Hosmer Leme show test was used to test model calibration; discrimination by area under the ROC curve. Significance level p<|human|>Significance level was p = 0.05.

Results

Maternal Demographics and Clinical Risk Factor: Two hundred and fifty pregnant women had been enrolled and the mean age was 29.8 +- 5.6 years. The reasons were advanced maternal age ((≥35 years) (33.6%), and multigravidity (60.8%). UTI had been reported in the past in 29.6% of the sample and diabetes mellitus (including gestational diabetes) at 16.4 of the participants (Table 1).

Table 1: Demographic and Obstetric Characteristics (n=250)

Variable	n (%)
Age ≥35 years	84 (33.6)
Mean age (years)	29.8 +- 5.6
Second trimester	112 (44.8)
Multigravidity	152 (60.8)
Previous UTI history	74 (29.6)
Diabetes mellitus	41 (16.4)

Significant bacteriuria at the Gestational Trimester Significant bacteriuria ($\geq 10^5$ CFU/mL) was found in 51.6 percent of the participants. The prevalence was the greatest during the second trimester (44.9%), as physiological changes of the mid-pregnancy, such as progesterone-induced ureteral relaxation and a urinary stasis (Table 2).

Table 2: Significant bacteriuria during gestational trimester.

Trimester	Positive Culture n (%)
First	36 (27.9)
Second	58 (44.9)
Third	35 (27.2)
Total	129 (51.6)

Microbial Etiology of UTIs

Gram-negative bacteria were the most common with about 70 percent of these being isolates. Escherichia coli was most common (51.9%), followed by *K. pneumoniae* (17.8%), whereas *P. mirabilis* was not common (6.2). *Staph. saprophyticus* (14.7) and *E. faecalis* (9.3) were considered gram-positive uropathogens (Table 3, Figure 1).

Table 3: Distribution of uropathogens in pregnant women.

Uropathogen	n (%)
Escherichia coli	67 (51.9)
Klebsiella pneumoniae	23 (17.8)
Staphylococcus saprophyticus	19 (14.7)
Enterococcus faecalis	12 (9.3)
Proteus mirabilis	8 (6.2)

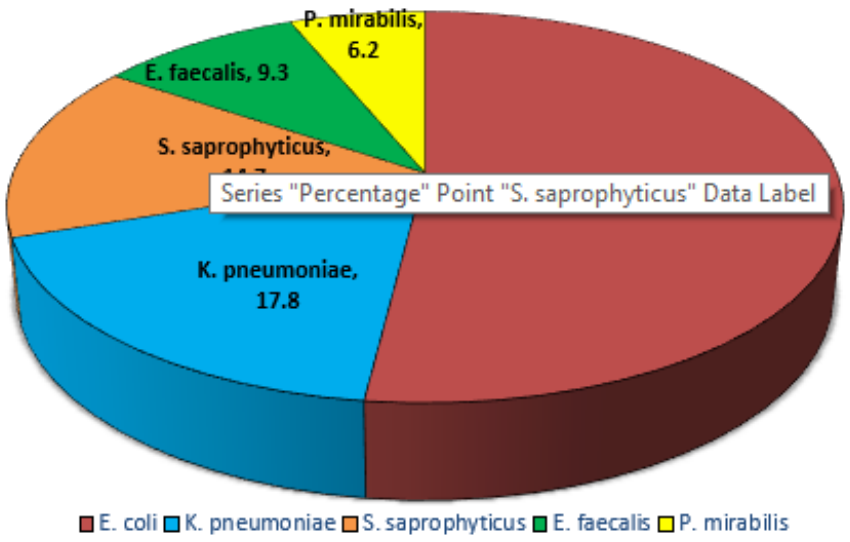

Fig 1: Uropathogens distribution during Pregnancy (Pie chart)

Antimicrobial Susceptibility Patterns

Nitrofurantoin had the greatest overall activity (>85) both in Gram-negative and Gram-positive isolates. The Gram-negative pathogens were not significantly active to ampicillin and trimethoprim-sulfamethoxazole. Ceftriaxone and gentamicin had no loss of activity, and could still be used as a parenteral therapy (Table 4, Figure 2).

Table 4: Antimicrobial susceptibility of bacterial isolates.

Antibiotic	Gram negative (%)	Gram positive (%)
Nitrofurantoin	85.7	90.3
Ceftriaxone	79.6	87.1
Gentamicin	74.5	83.9
Ciprofloxacin	68.4	71.0
Amoxicillin-clavulanate	60.2	77.4
TMP-SMX	44.9	58.1
Ampicillin	28.6	45.2

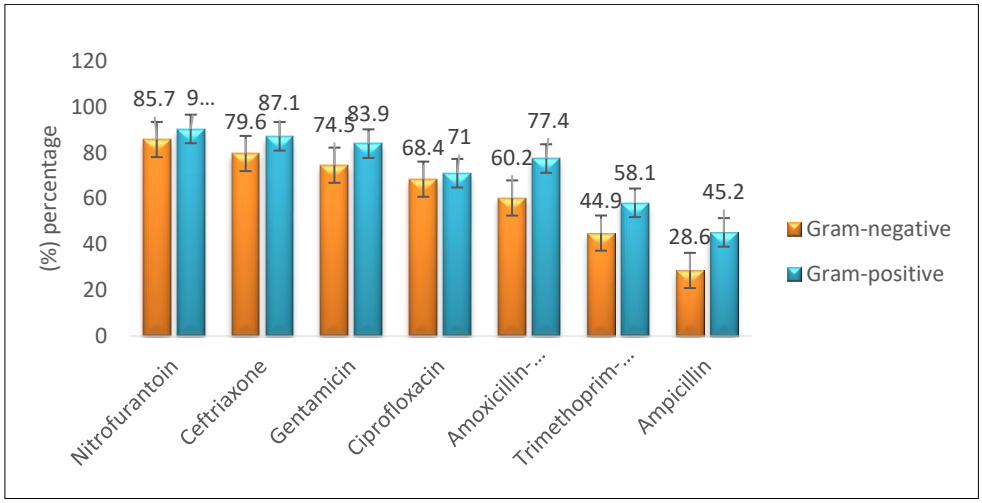

Fig 2: Antimicrobial susceptibility profiles of gram-Negative and gram-positive isolates (Clustered Bar Chart).

Species-Specific Susceptibility

E. coli exhibited important higher susceptibility to nitrofurantoin (88.1% vs 69.6%; p=0.031) and ampicillin (32.8% vs 13.0%; p=0.018) than K. pneumoniae, which is indicative of inherent and acquired susceptibility to the medication (Table 5).

Table 5: Percentage of species-specific antimicrobial susceptibility.

Antibiotic	*E. coli* (%)	*K. pneumoniae* (%)	P-value
Nitrofurantoin	88.1	69.6	0.031
Ampicillin	32.8	13.0	0.018
Ceftriaxone	82.1	73.9	0.276
Gentamicin	76.1	69.6	0.412

Independent predictors of ESBL-producing infections

Multivariate logistic regression revealed that advanced maternal age (≥35 years; OR 2.86), diabetes mellitus (OR 2.79) and prior UTI (OR 2.94) were significant independent predictors of ESBL-positive infection. Multigravidity could not be significant on its own (Table 6, Figure 3).

Table 6: Autonomous maternal risk factors of ESBL-producing Uropathogens.

Variable	ESBL+ n (%)	ESBL− n (%)	Adjusted OR	95% CI	p-value
Age ≥35 years	11 (47.8)	18 (24.0)	2.86	1.08-7.52	0.034
Diabetes mellitus	9 (39.1)	14 (18.7)	2.79	1.01-7.68	0.047
Previous UTI	14 (60.9)	26 (34.7)	2.94	1.15-7.49	0.024
Multigravidity	15 (65.2)	41 (54.7)	1.55	0.57-4.18	0.392

OR: Odds ratio, Adjusted OR: Adjusted odds ratio, 95%CI: 95% confidence interval.

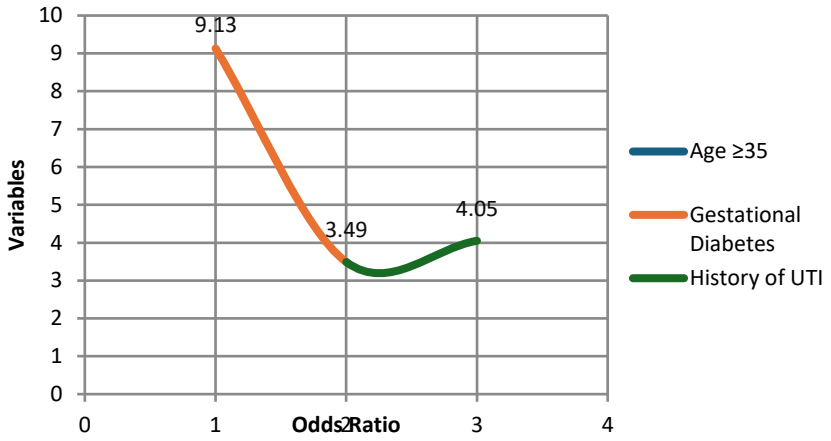

Fig 3: The adjusted odds ratio and 95% CI.

Multidrug Resistance and ESBL Prevalence

Of the Gram-negative isolates, there was a 34.7 and 23.5 MDR and ESBL prevalence, respectively. The highest MDR (47.8) and ESBL (34.8) rates were demonstrated by *K. pneumoniae* (Table 7).

Table 7: MDR and ESBL prevalence of gram-negative isolates.

Uropathogens	MDR (%)	ESBL (%)
E. coli	31.3	20.9
K. pneumoniae	47.8	34.8
P. mirabilis	25.0	12.5
Overall	34.7	23.5

Discussion

Urinary tract infections (UTIs) have continued to be a serious cause of maternal morbidity in pregnancy, and their implications on the health of mothers and fetuses, as well as on antimicrobial stewardship initiatives, are immense. The significant bacteriuria prevalence was 51.6 in the current cohort, which is significantly greater than the global estimates of 8-15 percent in modern surveillance, and is an indication of local epidemiological pressures and possibly the minimal compliance with standard screening protocols in resource-limited practice (Hatamleh *et al.*, 2025) [7]. The clinical significance of these infections is that untreated or carelessly treated UTIs are linked with such consequences as preterm birth, low birth weight, and neonatal morbidity (American College of Obstetricians and Gynecologists, 2023). As we have illustrated in the analysis, the prevalence of bacteriuria was highest in the second trimester which is in line with physiological changes that occur during mid pregnancy such as progesterone-induced relaxation of the ureters, decreased bladder tone, and mechanical compression

of the urinary tract by the gravid uterus (ACOG, 2025). The findings demonstrate the importance of early and repeated screening based on the current obstetric guidelines especially those having high-risk epidemiological profiles. Enhanced maternal age (≥35 years), diabetes mellitus and a record of previous UTIs were found to be independent predictors of infection with ESBL-producing uropathogens. The correlation to the maternal age corresponds with the established immunosenescence, which disables neutrophil chemotaxis and phagocytic activity, and hence promoting colonization by resistant organisms (Jones & Patel, 2026) [9]. A risk nearly three times higher was observed in diabetes mellitus, which is in line with the fact that hyperglycemia facilitates glycosuria, bacterial growth, and biofilm formation, and at the same time removes the ability of the innate immune defense (Al-Mously *et al*., 2025) [2]. The pre-UTIs were also strongly correlated with ESBL positivity, which probably mirrors the repeated exposure to antimicrobials and continuous colonization of the urogenital tract, which recent studies have shown is a selective pressure in favor of resistant Enterobacteriaceae (Nguyen, 2025) [10]. Although it was found that most of the women in the study were milligravity, it was not independently associated with ESBL infection, indicating that even in cases where metabolic and antimicrobial exposures were adjusted, parity alone may not have a selective effect (Tadesse *et al*., 2026) [11]. Gram-negative bacteria were the dominant in the uropathogens spectrum, the main organism was *E. coli*, and it was followed by *K. pneumoniae*, and *P. mirabilis*. The distribution is reflective of that of the rest of the world, with uropathogenic E. coli (UPEC) continuing to dominate the field by virtue of virulence factors such as P fimbriae, siderophores, and biofilm-forming ability. Clinical importance of the high K. pneumoniae proportion is because it causes UTIs in the community and often carries plasmid-mediated resistance determinants, which play a major role in the spread of ESBLs (WHO, 2025). The overall susceptibility to nitrofurantoin (more than 85 percent in Gram-negative and Gram-positive isolates) continues, which justifies its future use as a first-line agent in uncomplicated cystitis in pregnancy, as per the current IDSA guidelines (IDSA, 2026). Ceftriaxone and gentamicin showed also good activity especially in severe or complicated infections, but ampicillin and trimethoprim-sulfamethoxazole show significantly lower activity which is a manifestation of extensive b-lactamase-mediated resistance (CDC, 2026). Species-specific examination revealed less susceptibility of K. pneumoniae compared to E. coli to nitrofurantoin and ampicillin indicating inherent and acquired resistance related to efflux pumps, chromosomal b-lactamases, and ESBL-carrying plasmid genes. Gram-fnegative isolates were found to be multidrug-resistant (MDR) (34.7), ESBL-prevalent (23.5). It is interesting to note that almost half of the isolates of K. pneumoniae were MDR and over one-third of them produced ESBL, which highlights the significance of the species as a reservoir of resistance. E. coli also had high levels of MDR (31.3) and ESBL (20.9). These findings align with the recent local and global statistics that reflect the overlap of ESBL production and MDR as a significant limitation of empirical therapy, especially in pregnancy during which the fluoroquinolones, as well as some newer b-lactam, are contraindicated (Ahmed *et al*., 2025) [1]. The common co-location of bla CTX-M with aminoglycoside and sulfonamide resistance determinants is probably the root cause of observed MDR phenotype, where horizontal gene transfer and dissemination in the community and healthcare facility are facilitated. All in all, these results highlight a pressing necessity of screening with risk stratification, culture-based therapy, and the inclusion of obstetric cohorts into the frameworks of national surveillance of antimicrobial resistance so that the effectiveness of treatment could be maximized and prevent the spread of antimicrobial-resistant uropathogens.

Acknowledgments

The authors would like to highly acknowledge the participants who participated voluntarily in this research and without whom, this study would not have been done. We also want to thank the medical staff and nursing personnel of Tikrit Teaching Hospital, Tikrit, Iraq, who provided us with priceless assistance in the recruitment of patients and in collecting their specimens.

Funding

No particular funds were allocated to this study.

Conclusions

It is important to note that the reason behind the high incidence of high levels of bacteriuria in this group is the urgent requirement of uniform culture-directed screening procedures and the adoption of personalized empirical treatment regimens in the course of pregnancy. Since this population has limited access to safe antimicrobials, it is necessary to include pregnant women in national systems of antimicrobial resistance surveillance to empower empiric treatment and reduce the risks of treatment failure. The obtained results are consistent with the recent meta-analytical data revealing the increasing tendency of antimicrobial resistance in pregnant women with UTI and the significance of stewardship measures that focus on narrow-spectrum drugs without antimicrobial resistance issues to protect maternal and infant outcomes.

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How to Cite This Article

Al-Hayali WRY. Multidrug resistance and ESBL-producing uropathogens in pregnancy: Epidemiology, susceptibility patterns, and risk stratification. Int J Multidiscip Futur Dev. 2026;7(1):61–66. doi:10.54660/IJMFD.2026.7.1.61-66

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