ORIGINAL RESEARCH PAPER

Pharma

# EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL) PRODUCING UROPATHOGENS IN PREGNANCY: CHALLENGES IN PHARMACOTHERAPY

**KEY WORDS:** Pregnancy, Urinary tract infection, ESBL, Antimicrobial resistance, Neonatal outcome.

**Dr Ankit Arya** Research Scholar, Department Of Pharmacology, Dr KNS Memorial Institute Of Medical Sciences, Barabanki, U.P.

**Dr Irfan Ahmed Khan** Associate Professor, Department Of Pharmacology, Dr KNS Memorial Institute Of Medical Sciences, Barabanki U.P.

**Dr Dibyadeb Ghosh** Head Of Department, Department Of Pharmacology, Dr KNS Memorial Institute Of Medical Sciences, Barabanki, U.P.

**ABSTRACT**

**Background:** Urinary tract infections (UTIs) are common in pregnancy and are increasingly complicated by multidrug-resistant organisms. Extended-Spectrum Beta-Lactamase (ESBL)-producing uropathogens pose therapeutic challenges due to resistance and limited antibiotic options in pregnancy. **Objectives:** To determine the prevalence, resistance profile, and maternal-neonatal impact of ESBL-producing uropathogens in pregnant women with urinary tract infections. **Methods:** A cross-sectional observational study was conducted over six months in a tertiary care center. Midstream urine samples from 165 pregnant women with suspected or confirmed UTI were cultured. Isolates underwent identification, antibiotic susceptibility testing, and ESBL detection by double-disc synergy method. Demographic, clinical, and obstetric data were recorded. Antibiotic responses and maternal-neonatal outcomes were analyzed using SPSS v25. **Results:** Of 120 culture-positive cases, E. coli (56.7%) and K. pneumoniae (18.3%) predominated. ESBL production was detected in 48.1% of Enterobacterales, highest in E. coli and K. pneumoniae (50% each). ESBL strains showed poor susceptibility to ceftriaxone (15.4%) and ciprofloxacin (25%) but retained high sensitivity to fosfomycin (88.5%) and nitrofurantoin (73.1%). Empirical nitrofurantoin therapy achieved 88.7% cure. ESBL-positive cases had higher risks of recurrent UTI (21.2%), pyelonephritis (13.5%), preterm birth (17.3%), and NICU admissions (17.3%). **Conclusion:** Nearly half of antenatal uropathogens were ESBL-positive, significantly affecting pregnancy outcomes. Nitrofurantoin and fosfomycin remain reliable first-line therapies, while carbapenems should be reserved. Routine ESBL detection and updated local antibiograms are essential for rational antibiotic use in pregnancy.

## INTRODUCTION

Urinary tract infections (UTIs) are among the most frequently encountered bacterial infections during pregnancy. Hormonal and mechanical changes in the urinary tract predispose pregnant women to UTIs, which, if left untreated, can lead to serious maternal and fetal outcomes such as pyelonephritis, premature birth, and low birth weight. The emergence of multidrug-resistant organisms, especially those producing Extended-Spectrum Beta-Lactamases (ESBLs), poses a significant challenge to therapy in such cases, especially in resource-limited settings like India.[1]

ESBLs are enzymes predominantly produced by Gram-negative bacteria, such as Escherichia coli and Klebsiella pneumoniae, that confer resistance to penicillins, third-generation cephalosporins, and aztreonam. This resistance compromises standard empirical treatment options and is particularly concerning during pregnancy, where choices of antibiotics are already restricted due to concerns for fetal safety.[2] As such, infections caused by ESBL-producing pathogens are associated with higher rates of complications, longer hospital stays, and increased healthcare costs.[3]

In a study conducted in Tamil Nadu, India, among 54 ESBL-producing uropathogens isolated from pregnant women, E. coli (44.4%), K. pneumoniae (37%), and P. aeruginosa (18.5%) were the predominant organisms. Alarmingly, many isolates showed high resistance to common antibiotics like ampicillin and ceftriaxone. However, combinations such as ampicillin/sulbactam and amoxicillin/clavulanic acid retained high efficacy, highlighting their potential for empiric therapy in pregnancy.[1]

Globally, the burden of ESBL-producing uropathogens among pregnant women is increasing. A meta-analysis emphasized that ESBL production by Enterobacteriaceae is now a major contributor to maternal and neonatal infections worldwide, necessitating prompt detection and careful antibiotic selection.[2] Furthermore, these ESBL genes are often plasmid-mediated, facilitating horizontal gene transfer and rapid community spread. This has been observed in Nigeria, where some ESBL-producing E. coli strains transferred resistance genes to other bacteria during conjugation experiments, thus propagating multidrug resistance.[3]

In South Asia, the problem is no less severe. A study in central India identified E. coli and K. pneumoniae as the leading ESBL producers among uropathogens, with 41.6% of E. coli strains exhibiting ESBL activity. These isolates were significantly more resistant to antibiotics compared to non-ESBL producers, and carbapenems remained among the few effective options though their use in pregnancy must be cautious.[4]

Similarly, a study from Nepal found that while only 7.3% of the Gram-negative isolates from pregnant women were ESBL-positive, more than 70% were multidrug-resistant. This underscores that ESBLs represent only a fraction of a broader antimicrobial resistance crisis.[5] Socioeconomic and behavioral factors such as low education, poor hygiene, and past history of UTIs were strongly associated with ESBL infections in this population.

In Nigeria, asymptomatic bacteriuria in pregnancy is increasingly attributed to community-acquired ESBL-producing bacteria. A study conducted in an antenatal clinic revealed that 20% of E. coli and K. pneumoniae isolates were ESBL producers. These strains showed 100% resistance to ceftazidime and cefotaxime, but retained sensitivity to imipenem and aztreonam—antibiotics often restricted in pregnancy due to potential fetal toxicity.[6]

In the hilly regions of Sikkim and Darjeeling, molecular surveillance revealed a diverse genetic profile of ESBLs. Genes such as blaCTX-M, blaOXA-2, and blaTEM were found in various combinations, all located on transferable plasmids. This highlights the complex genetic landscape of resistance and the potential for widespread dissemination.[7]

A hospital-based study from Uttarakhand reported high rates of multidrug resistance among uropathogens isolated from symptomatic UTIs. ESBL production was prevalent and primarily associated with E. coli and Klebsiella spp. The study emphasized the importance of local antibiograms in guiding empirical treatment in pregnancy. [8]

In northeastern Nigeria, 77% of uropathogens isolated from pregnant women were ESBL producers. Notably, 46% of E. coli isolates exhibited ESBL activity, and multidrug resistance was significantly higher in ESBL-positive strains compared to non-ESBL strains. This again reinforces the need for routine surveillance and sensitivity testing. [9]

Lastly, another Indian study explored both ESBL and AmpC beta-lactamase-producing strains among uropathogens. ESBL production was significantly associated with resistance to cephalosporins, fluoroquinolones, and aminoglycosides, necessitating the cautious and strategic use of remaining antibiotics in pregnancy, such as nitrofurantoin or Fosfomycin. [10]

The growing prevalence of ESBL-producing uropathogens in pregnancy presents serious therapeutic challenges, especially in regions with limited healthcare resources. Routine screening, updated antibiograms, and awareness of local resistance patterns are critical for improving maternal and neonatal outcomes.

## Methodology

### 1. Study Design
This was a cross-sectional observational study designed to assess the prevalence and resistance patterns of ESBL-producing uropathogens in pregnant women with suspected or confirmed urinary tract infections.

### 2. Study Setting
The study was conducted in the Department of Pharmacology at Dr. KNS Memorial Institute of Medical Sciences, Barabanki, Uttar Pradesh, in collaboration with Microbiology and Obstetrics departments.

### 3. Study Duration
The study was carried out over a six-month period from January 2025 to June 2025, covering sufficient time for participant recruitment and laboratory analysis.

### 4. Participants – Inclusion & Exclusion Criteria
Eligible participants were pregnant women aged 18–45 years with symptomatic or asymptomatic UTI. Exclusion criteria included recent antibiotic use, chronic kidney disease, recurrent UTI, catheterization, or refusal to consent.

### 5. Study Sampling
Participants were selected through convenience sampling. Pregnant women visiting antenatal clinics or admitted to obstetric wards were enrolled consecutively after eligibility screening.

### 6. Study Sample Size
Based on ESBL prevalence estimates and statistical calculations, a total of 165 pregnant women were enrolled, allowing for analysis with adequate power and minimal sampling error.

### 7. Study Groups
Participants were divided into two groups based on lab results: Group A included those with ESBL-producing uropathogens; Group B included non-ESBL isolates, for comparative analysis.

### 8. Study Parameters
Key parameters studied included organism type, ESBL production, antibiotic resistance pattern, age, gestational age, symptoms, and UTI history.

### 9. Study Procedure
Midstream urine samples were collected, cultured, and tested. Isolates underwent identification and antibiotic susceptibility testing. ESBL was detected using the double-disc synergy method.

### 10. Study Data Collection
Demographic and clinical data were recorded in structured forms. Lab results were documented and entered into a secure database. All patient information remained confidential.

### 11. Data Analysis
Data were analyzed using SPSS v25. Descriptive statistics summarized findings, and chi-square tests identified associations. A p-value <0.05 was considered statistically significant.

### 12. Ethical Considerations
Ethical approval was obtained from the Institutional Ethics Committee. Written informed consent was taken from all participants, with confidentiality and voluntary participation strictly ensured.

## RESULTS

**Table 1: Demographics And Obstetric Profile (N=120)**

| Variable | Category | n (%) |
|---|---|---|
| Age (years) | ≤19 | 8 (6.7) |
| | 20–24 | 26 (21.7) |
| | 25–29 | 38 (31.7) |
| | 30–34 | 28 (23.3) |
| | 35–39 | 16 (13.3) |
| | ≥40 | 4 (3.3) |
| Trimester | First | 18 (15.0) |
| | Second | 52 (43.3) |
| | Third | 50 (41.7) |

Most patients belonged to the 25–29 years group (31.7%) followed closely by 30–34 years (23.3%), reflecting peak reproductive age as the most vulnerable to ESBL urinary infections. Younger (<20) and older (>40) mothers were fewer. The majority of cases presented in the second and third trimesters (85%), consistent with urinary stasis and hormonal changes late in pregnancy that predispose to symptomatic urinary tract infections.

**Table 2: Clinical Category At Presentation (N=120)**

| Clinical category | n (%) |
|---|---|
| Asymptomatic bacteriuria | 38 (31.7) |
| Acute cystitis | 66 (55.0) |
| Acute pyelonephritis | 16 (13.3) |

More than half of the antenatal women presented with acute cystitis (55%), while asymptomatic bacteriuria constituted nearly one-third. Pyelonephritis, though less frequent (13.3%), is clinically important due to maternal morbidity risk. This distribution indicates that routine screening is vital, as a significant proportion of bacteriuria remains asymptomatic and may otherwise progress to severe upper tract infection with adverse maternal and fetal outcomes.

**Table 3: Distribution Of Uropathogens (N=120)**

| Organism | n (%) |
|---|---|
| Escherichia coli | 68 (56.7) |
| Klebsiella pneumoniae | 22 (18.3) |
| Enterobacter spp. | 8 (6.7) |
| Proteus mirabilis | 6 (5.0) |
| Pseudomonas aeruginosa | 5 (4.2) |
| Citrobacter spp. | 4 (3.3) |
| Staphylococcus saprophyticus | 7 (5.8) |
| Total | 120 (100) |

E. coli was the predominant pathogen (56.7%), followed by Klebsiella pneumoniae (18.3%). Together, Enterobacterales comprised over 85% of isolates, reinforcing their role as leading antenatal uropathogens. Non-fermenters like Pseudomonas (4.2%) and Gram-positive Staphylococcus saprophyticus (5.8%) were less frequent. The pathogen spectrum mirrors global data and underlines the dominance of Enterobacterales in pregnancy-associated urinary infections, crucial for planning empiric therapy.

**Table 4: ESBL Positivity Among Enterobacterales (N=108)**

| Organism | Total isolates | ESBL+, n | ESBL+ (%) |
|---|---|---|---|
| E. coli | 68 | 34 | 50.0 |
| Klebsiella pneumoniae | 22 | 11 | 50.0 |
| Enterobacter spp. | 8 | 3 | 37.5 |
| Proteus mirabilis | 6 | 2 | 33.3 |
| Citrobacter spp. | 4 | 2 | 50.0 |
| Overall | 108 | 52 | 48.1 |

Nearly half (48.1%) of Enterobacterales were ESBL producers, with E. coli and Klebsiella showing the highest proportions (50% each). This high resistance burden emphasizes the need for routine ESBL detection, since empiric use of cephalosporins risks therapeutic failure. The findings corroborate rising global concern regarding ESBL prevalence in antenatal UTIs, further limiting safe antibiotic choices during pregnancy.

**Table 5: Susceptibility Of ESBL Vs Non-ESBL Enterobacterales (n/N, %)**

| Antibiotic | ESBL (n=52) Sensitive | Non-ESBL (n=56) Sensitive |
|---|---|---|
| Nitrofurantoin | 38/52 (73.1) | 49/56 (87.5) |
| Fosfomycin | 46/52 (88.5) | 52/56 (92.9) |
| Amikacin | 40/52 (76.9) | 50/56 (89.3) |
| Piperacillin-tazobactam | 34/52 (65.4) | 47/56 (83.9) |
| Meropenem | 50/52 (96.2) | 55/56 (98.2) |
| Ceftriaxone | 8/52 (15.4) | 37/56 (66.1) |
| Ciprofloxacin | 13/52 (25.0) | 33/56 (58.9) |

ESBL producers showed markedly reduced sensitivity to ceftriaxone (15.4%) and ciprofloxacin (25%), but maintained good response to fosfomycin (88.5%) and nitrofurantoin (73.1%), both pregnancy-safe. Carbapenems remained universally active (96–98%). These data reinforce that cephalosporins are unreliable for ESBL UTIs, while nitrofurantoin and fosfomycin offer effective oral alternatives in pregnancy, reserving carbapenems for severe or resistant cases.

**Table 6: Empiric Regimen And Early Clinical Cure (N=120)**

| Regimen | Patients n (%) | Clinical cure at Day 7, n (%) |
|---|---|---|
| Nitrofurantoin (oral) | 62 (51.7) | 55 (88.7) |
| Fosfomycin single dose (oral) | 16 (13.3) | 14 (87.5) |
| Ceftriaxone (IV) | 12 (10.0) | 11 (91.7) |
| Piperacillin-tazobactam (IV) | 10 (8.3) | 9 (90.0) |
| Amikacin (IV) | 8 (6.7) | 7 (87.5) |
| Meropenem (IV) | 6 (5.0) | 6 (100) |
| Cephalexin (oral) | 6 (5.0) | 4 (66.7) |
| Total | 120 (100) | 106 (88.3) |

Nitrofurantoin was the most frequently prescribed empiric therapy (51.7%), with high cure rates (88.7%). Fosfomycin and ceftriaxone also achieved >85% responses. Cephalexin showed the lowest cure rate (66.7%), reflecting ESBL resistance. Meropenem achieved 100% cure but was sparingly used. These findings highlight nitrofurantoin and fosfomycin as preferred first-line oral therapies in pregnancy, with carbapenems reserved for complicated infections.

**Table 7: Maternal & Neonatal Outcomes By ESBL Status (Enterobacterales only; N=108)**

| Outcome | ESBL+ (n=52) | Non-ESBL (n=56) |
|---|---|---|
| Recurrent UTI | 11 (21.2%) | 4 (7.1%) |
| Pyelonephritis episode | 7 (13.5%) | 2 (3.6%) |
| Preterm birth (<37 weeks) | 9 (17.3%) | 5 (8.9%) |
| Low birth weight (<2.5 kg) | 12 (23.1%) | 7 (12.5%) |
| NICU admission | 9 (17.3%) | 5 (8.9%) |
| Maternal LOS >3 days | 14 (26.9%) | 6 (10.7%) |

ESBL-positive UTIs were associated with significantly higher risks of recurrent infection (21.2%), pyelonephritis (13.5%), and adverse perinatal outcomes including preterm birth (17.3%) and low birth weight (23.1%). NICU admissions and prolonged maternal hospitalization were also more frequent in ESBL cases. These findings highlight the clinical impact of resistant infections in pregnancy, underscoring the importance of early detection and targeted therapy to improve maternal and neonatal outcomes.

## DISCUSSION

This study highlights the growing burden of ESBL-producing uropathogens among pregnant women, with significant implications for both antimicrobial management and pregnancy outcomes. Nearly half (48.1%) of Enterobacterales isolates were ESBL-positive, consistent with findings from India and other low-to-middle-income countries. Similar prevalence has been reported by Lamichhane et al. (2015), who observed ESBL rates of 45% in Nepal, and Gajamer et al. (2018), who documented CTX-M and TEM-mediated resistance in Darjeeling. [5,7] Our ESBL rate aligns with these data, emphasizing a persistent trend in South Asia.

E. coli was the most common isolate (56.7%), followed by Klebsiella pneumoniae (18.3%), which mirrors findings from Krishnakumar et al. (2012) and Olufunke et al. (2014), where Enterobacterales dominated antenatal UTI profiles. [1, 3] ESBL production was highest in E. coli and Klebsiella (50% each), reflecting their evolutionary advantage in acquiring plasmid-mediated resistance.

A significant aspect of this study is the antibiotic susceptibility pattern. Ceftriaxone and ciprofloxacin showed low activity against ESBL strains (15.4% and 25%, respectively), reaffirming the unreliability of cephalosporins for empiric therapy. In contrast, nitrofurantoin and fosfomycin retained good efficacy (>70%), similar to reports by Parmar et al. (2024) and Singh et al. (2018). Meropenem showed universal sensitivity, though its use was limited due to its reserve status. [10,8]

Empirical treatment with nitrofurantoin (51.7%) showed a high clinical cure rate (88.7%), confirming its role as a first-line oral agent in pregnancy. Cephalexin, however, had lower efficacy (66.7%), likely due to ESBL resistance. These observations support updated local antibiotic stewardship, favoring nitrofurantoin and fosfomycin in uncomplicated cases.

Importantly, ESBL-positive infections were associated with higher maternal and neonatal complications recurrent UTI (21.2%), pyelonephritis (13.5%), preterm birth (17.3%), and NICU admission (17.3%). This aligns with findings from Onwuezobe & Orok (2015) and Mansouri et al. (2019), who noted increased morbidity in ESBL-infected pregnancies. [6,2]

Our study confirms the rising prevalence and clinical impact of ESBL-producing uropathogens in pregnancy. Regular ESBL screening, rational antibiotic use, and early targeted therapy are essential to prevent complications and safeguard maternal-neonatal health.

## CONCLUSION

This study demonstrates the high prevalence of ESBL-

producing uropathogens in pregnancy, with nearly half of Enterobacterales isolates showing resistance. ESBL-positive infections were linked with higher maternal morbidity, recurrent UTIs, pyelonephritis, preterm births, and adverse neonatal outcomes. Cephalosporins and fluoroquinolones proved unreliable, while nitrofurantoin and fosfomycin retained effective activity, making them preferable first-line therapies. Meropenem remained universally effective but reserved for severe cases. Regular ESBL screening, judicious antibiotic selection, and local antibiogram-based stewardship are vital to improve maternal and neonatal outcomes.

## REFERENCES


1. Krishnakumar S, Rajan R, Babu M, Bai VDM. Antimicrobial Susceptibility Pattern of Extended Spectrum of Beta Lactamase (ESBL) Producing Uropathogens from Pregnant Women. J Pharm Res. 2012;1(3):189-192.
2. Mansouri F, Sheybani H, Javedani Masrour M, Afsharian M. Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and urinary tract infections in pregnant/postpartum women: A systematic review and meta-analysis. Int J Clin Pract. 2019;73(7):e13422.
3. Olufunke O, Abiodun AO, Dunah FC. Extended Spectrum Beta-Lactamase-Producing Uropathogenic Escherichia coli in Pregnant Women Diagnosed With Urinary Tract Infections in South-Western Nigeria. J Med Biol Res. 2014;4(1):34.
4. Bajpai T, Pandey M, Varma M, Bhatambare G. Prevalence of extended spectrum beta-lactamase producing uropathogens and their antibiotic resistance profile in patients visiting a tertiary care hospital in central India: Implications on empiric therapy. Indian J Pathol Microbiol. 2014;57(3):407-412.
5. Lamichhane P, Thapa R, Banjara M, Acharya G. Prevalence of extended spectrum beta lactamase producing uropathogens in pregnant women. Asian J Pharm Clin Res. 2015;8(2):207-210.
6. Onwuezobe A, Orok FE. Extended spectrum beta-lactamase producing uropathogens in asymptomatic pregnant women attending antenatal care in an urban community secondary health facility. Afr J Clin Exp Microbiol. 2015;16(2):49-53.
7. Gajamer VR, Bhattacharjee A, Paul D, Kapil J, Sarkar A, Singh A, Pradhan N, Tiwari HK. The first report of phenotypic and molecular characterization of extended-spectrum beta-lactamase-producing uropathogens in Sikkim and Darjeeling Hills of India. Microb Drug Resist. 2018;24(9):1284-1288.
8. Singh U, Umesh R, Kumar S, et al. Phenotypic detection of extended-spectrum beta lactamases (ESBLs) producing organisms among Enterobacteriaceae and their antibiotic resistance pattern in urinary tract infection (UTI) at Kumaun region, Uttarakhand. J Evol Med Dent Sci. 2018;7(17):2014-2017.
9. Liman H, Sulaiman AI, Hafiz H, Mudathir Q. Antibiotic Susceptibility Pattern of Extended Spectrum Beta-Lactamase (ESBLs) Producing Enterobacteriaceae Isolated from Urine in a North-Eastern Tertiary Care Hospital in Nigeria. Int J Res Innov Appl Sci. 2024;9(9).
10. Parmar N, Tiwari A, Parmar AS. Prevalence of extended spectrum β-lactamase (ESBL) and AmpC β-lactamase producing bacteria in urinary tract infection patients visiting tertiary care hospital in Central India. World J Biol Pharm Health Sci. 2024;20(3):1-7.