

RESEARCH ARTICLE

Risk Factors in Cases of ESBL-Positive *E. coli* Isolated from Urine Cultures in Community-Acquired Urinary Tract Infections in Children

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Abstract

Article Info

Received Date: 11.09.2025

Revision Date : 29.09.2025

Accepted Date: 29.09.2025

Keywords:

ESBL-Positive *E. coli*,
Urine Cultures,
Urinary Tract Infections

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Introduction: Extended-spectrum β -lactamase (ESBL)-producing *Escherichia (E.) coli* has become an increasing concern in pediatric community-acquired urinary tract infections (UTIs). The primary aim of this study is to investigate and identify the clinical, demographic, and medical history-related risk factors associated with ESBL-producing *E. coli* strains isolated from urine cultures of pediatric patients diagnosed with community-acquired UTIs.

Methods: : We retrospectively reviewed 100 pediatric patients with ESBL-positive *E. coli* UTIs hospitalized between 2008–2012, all of whom received meropenem therapy. Risk factors, clinical manifestations, urine collection methods, comorbidities, and prior antibiotic exposure were collected.

Results: ESBL-positive *E. coli* UTIs were more frequent in boys during the neonatal period but became predominant in girls thereafter, with the highest prevalence under two years of age. Clinical manifestations vary with age, ranging from nonspecific symptoms such as fever and vomiting in infants to typical complaints like abdominal pain and dysuria in older children. *E. coli* was identified as the leading pathogen, while high resistance rates to commonly used antibiotics (ampicillin, amoxicillin/clavulanate, TMP-SMX) were observed. Carbapenems remained the most effective agents, though their use should be reserved due to cost and hospitalization requirements. Underlying urinary tract abnormalities, vesicoureteral reflux, recurrent infections, and recent antibiotic exposure were major risk factors for ESBL (+) UTIs.

Conclusion: Our results highlight the clinical significance of ESBL-producing *E. coli* in pediatric UTIs. Early recognition of risk factors, careful diagnostic evaluation, and rational antibiotic selection are crucial for optimal management.

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Introduction

Urinary tract infections (UTIs) are among the most frequently encountered bacterial infections in the pediatric population.^{1,2} They occur in approximately 3–5% of girls and 1% of boys.³ In developing countries, including Türkiye, UTIs in children are of particular concern due to their potential to cause long-term renal damage.⁴ Pyelonephritis, especially when recurrent and associated with vesicoureteral reflux (VUR), is recognized as a major cause of secondary hypertension and chronic kidney disease (CKD) in childhood.^{5,6} For this reason, early diagnosis, appropriate empirical treatment, and identification of risk factors play a vital role in minimizing both acute complications and chronic sequelae.

The emergence of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* strains has significantly changed the epidemiology and treatment approach to UTIs.^{7,8} ESBL enzymes, first described in *Klebsiella pneumoniae* isolates from nosocomial infections in the 1980s, have since been detected in *E. coli* and other Enterobacteriaceae.⁹ These enzymes confer resistance to penicillins, third-generation cephalosporins, and monobactams, complicating the selection of effective empirical antibiotics. Although carbapenems and cephamycins are generally effective against ESBL-producing organisms, their use is often reserved for severe infections to avoid further resistance development.^{10,11} According to the Clinical and Laboratory Standards Institute (CLSI), ESBL-producing strains should be reported as resistant to all penicillins and cephalosporins (excluding cephamycins), even if in vitro susceptibility is observed.¹²

ESBL-producing organisms were initially associated with hospital-acquired infections. However, their increasing prevalence in community-acquired infections, particularly UTIs in children, has raised serious concerns.¹³ Risk factors for colonization or infection with these resistant strains include prior hospitalization, recent antibiotic exposure (especially broad-spectrum beta-lactams), underlying urinary tract anomalies, invasive procedures, and prolonged catheterization.^{14,15} Given the growing incidence of ESBL-positive *E. coli* in outpatient settings, especially in pediatric patients, appropriate surveillance and identification of high-risk groups have become essential.¹⁶ Despite the clinical significance of ESBL-producing *E. coli*, most of the existing literature focuses on adult populations, and pediatric data remain limited.¹⁷ Moreover, current treatment guidelines do

not always address the distinct epidemiological and clinical features observed in children.

The primary aim of this study is to investigate and identify the clinical, demographic, and medical history-related risk factors associated with ESBL-producing *E. coli* strains isolated from urine cultures of pediatric patients diagnosed with community-acquired UTIs.

Material and Methods

Study Design and Ethical Approval

This retrospective study was conducted at the Department of Child Health And Diseases, Zeynep Kamil Women And Children Diseases Training And Research Hospital. The study protocol was reviewed and approved by the institutional Ethics Committee (Date: 12.09.2012, Decision No. 17780). All procedures were performed in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice.

Study Population

Patients hospitalized in the Department of Child Health and Diseases between January 2008 and December 2012 were retrospectively evaluated. One hundred pediatric patients who were hospitalized during the study period and whose cultures showed growth of ESBL-producing *E. coli* were included in the study. Exclusions included concomitant infections at other sites, receipt of antibiotic therapy for indications known malignancy or rheumatologic disease, use of immunosuppressive treatment for any reason, and acute or chronic liver or renal failure. Additionally, patients who had not received meropenem therapy were excluded from the statistical analyses.

Data Collection

Demographic, clinical, laboratory, and imaging data were retrospectively obtained from patient medical records. Urine culture results, ultrasonographic findings, and prior antibiotic use were reviewed and systematically documented. Prolonged antibiotic use was defined as ≥ 14 days of continuous therapy.

Statistical Analysis

The data of the study were evaluated using the Statistical Package for the Social Sciences (SPSS) version 15.0. In addition to descriptive statistical methods, Chi-square and Fisher's exact tests were used for the analysis of categorical variables between groups. The results were assessed at a 95% confidence interval, and a p-value < 0.05 was considered statistically significant.

Results

A total of 100 patients were included in the study, of whom 66% were female and 34% were male. The age distribution of the patients was as follows: 27% were aged 0-11 months, 36% were 12-59 months, and 37% were 60 months and older (Table 1 and Figure 1). When analyzed by age groups, the proportion of females was 33.3% (n=9) in the 0-11 months group, increasing to 61.1% in the 12-59 months group, and reaching 94.6% (n=35) in the 60 months and older group. Symptomatic presentation was observed in 64% of the patients, while 36% were asymptomatic. Females were significantly more likely to be symptomatic compared to males (71.2% vs. 50%; $p=0.036$). When evaluated by age, the proportion of symptomatic patients was 59.3% (n=16) in the 0-11 months group, 61.1% (n=22) in the 12-59 months group, and 70.3% (n=26) in those aged 60 months and above. The most common presenting symptom was fever (43%), followed by vomiting (23%), abdominal pain (21%), dysuria (14%), irritability (10%), decreased appetite (4%), and enuresis (2%). Multiple symptoms were reported in 38 patients.

Table 1. Clinical Characteristics Related to Antibiotic Use, Infection, and Hospitalization History in the Last 3 Months

Variables	n	%
Prolonged antibiotic use (over 14 days)	10	10.0
Prolonged hospital stay (over 14 days)	4	4.0
Antibiotic use in the last 3 months	51	51.0
Cephalosporin	25	25.0
Penicillin	39	39.0
Quinolone	0	0.0
Carbamazepine	5	5.0
Aminoglycoside	3	3.0
Combined therapy	20	20.0
Infection history in the last 3 months	58	58.0
Urinary tract infection (UTI)	47	47.0
Cystitis	7	7.0
Upper respiratory tract infection (URTI)	18	18.0
Hospitalization history in the last 3 months	27	27.0
Due to UTI	23	23.0
Other reasons	9	9.0

Gender-specific analysis revealed that dysuria (19.7% vs. 2.9%; $p=0.031$) and abdominal pain (30.3% vs. 2.9%; $p=0.001$) were significantly more frequent in females than males. No statistically significant dif-

ferences were found between genders for other symptoms. Regarding age groups, fever (40.7%), irritability (29.6%), and vomiting (25.9%) were predominant in the 0-11 months group, whereas abdominal pain, dysuria, enuresis, and decreased appetite were absent. In the 12-59 months group, fever (44.4%), vomiting (22.2%), abdominal pain (22.2%), dysuria (11.1%), decreased appetite (8.3%), and irritability (5.6%) were reported; enuresis was not observed. Among children aged 60 months and above, fever (43.2%), abdominal pain (35.1%), dysuria (27%), vomiting (21.6%), enuresis (5.4%), and decreased appetite (2.7%) were reported; irritability was absent in this group. Only 34% of patients presented with positive urine cultures. The rate of positive cultures was significantly higher in males compared to females (50% vs. 25.8%; $p=0.015$).

The majority of patients (78%) had underlying conditions, with nine patients presenting multiple comorbidities. Urinary system disorders were the most prevalent underlying diseases (69%), with recurrent urinary tract infections (UTIs) being the most common (33%). Vesicoureteral reflux (VUR) was the second most frequent urinary pathology (15%), followed by urinary tract anomalies such as urethral strictures and duplicated collecting systems (14%). Two patients had multiple concurrent urinary system abnormalities. Beyond urinary disorders, cardiological diseases accounted for 6% of cases, while gastrointestinal diseases and sepsis each represented 4%. Prolonged antibiotic use, defined as usage exceeding 14 days, was observed in 10% of patients, and extended hospital stays (>14 days) in 4%. Among the 27 patients hospitalized within the past three months, 23 admissions were related to UTIs, with five patients having multiple hospitalization causes. Antibiotic use within the last three months was documented in 51% of patients; penicillins were the most commonly prescribed (39%), followed by cephalosporins (25%) and combination therapies (20%). Usage of carbamazepine and aminoglycosides was reported in 5% and 3% of patients, respectively, while no patients had a history of quinolone use. A history of infection within the previous three months was noted in 58% of patients, predominantly UTIs (47%), followed by upper respiratory tract infections (18%) and cystitis (7%). Fourteen patients experienced multiple infections during this period (Table 1).

None of the patients had received immunosuppressive therapy. However, a history of urinary catheterization was present in 3 patients, invasive procedu-

res in 2 patients, blood and blood product transfusions in 2 patients, neutropenia in 2 patients, central venous catheter use in 2 patients, and total parenteral nutrition (TPN) administration in 1 patient. All patients underwent urinary ultrasonography (USG), with abnormalities detected in 34% of cases. Among these, 17% exhibited renal shape, size, or localization anomalies, 7% showed parenchymal damage, and 10% had combined findings. Urine samples for culture were obtained via midstream catch in 53% of patients, catheterization in 34%, urine bag collection in 9%, and suprapubic aspiration in 3%.

When comparing patients presenting with positive urine cultures to those presenting with symptoms, no statistically significant difference was observed in age distribution ($p > 0.05$). However, symptomatic presentation was significantly more frequent in females compared to culture-positive cases ($p < 0.05$). Underlying diseases were significantly more prevalent in culture-positive patients than symptomatic patients ($p < 0.05$); specifically, urinary system disorders were significantly higher in the culture-positive group ($p < 0.01$), while no significant differences were found regarding the types of urinary diseases or other systemic conditions ($p > 0.05$). No statistically significant differences were detected between the two groups concerning prolonged antibiotic use or extended hospitalization ($p > 0.05$).

Culture-positive patients showed significantly higher rates of antibiotic use within the last three months, infection history in the same period, and hospital admissions within the past three months compared to symptomatic patients ($p < 0.01$). Moreover, penicillin treatment ($p < 0.01$), combined antibiotic therapy ($p < 0.01$), history of urinary tract infections ($p < 0.01$), and hospitalization due to UTIs ($p < 0.001$) in the last three months were all significantly more frequent in culture-positive patients. No statistically significant differences were found between the groups regarding TPN, central venous catheter use, urinary catheterization, invasive procedures, blood transfusions, neutropenia, or USG findings ($p > 0.05$) (Table 2).

Table 2: Comparison Between Patients With Positive Urine Culture and Those Presenting With Symptoms

Variables	Positive Urine Culture		Symptomatic Presentation		Chi-Square	p
	n	%	n	%		
Age Group						
0-11 months	9	26.5	18	27.3	1.750	0.417
12-59 months	15	44.1	21	31.8		
≥60 months	10	29.4	27	40.9		
Gender						
Female	17	50.0	49	74.2	5.877	0.015*
Male	17	50.0	17	25.8		
Comorbidity						
Absent	3	8.8	19	28.8	5.212	0.022*
Present	31	91.2	47	71.2		
Urinary System Disorders (Total)	31	91.2	38	57.6	11.844	0.001**
Anatomical anomalies	8	23.5	6	9.1	-	0.068
VUR	8	23.5	7	10.6	2.939	0.086
Functional abnormalities	2	5.9	4	6.1	-	0.999
Recurrent UTI	15	44.1	18	27.3	2.880	0.090
Other (nephrolithiasis, etc.)	0	0.0	3	4.5	-	0.549
Cardiological diseases	2	5.9	4	6.1	-	0.999
Neurological diseases	0	0.0	1	1.5	-	0.999
GI diseases	1	2.9	3	4.5	-	0.999
Respiratory system diseases	0	0.0	2	3.0	-	0.547
Endocrinological diseases	0	0.0	2	3.0	-	0.547
Hematological diseases	0	0.0	1	1.5	-	0.999
Sepsis	0	0.0	4	6.1	-	0.296
Prolonged antibiotic use	3	8.8	7	10.6	-	0.999
Prolonged hospitalization (over 14 days)	2	5.9	2	3.0	-	0.603

Table 2: Comparison Between Patients With Positive Urine Culture and Those Presenting With Symptoms (Continue)

Variables	Positive Urine Culture		Symptomatic Presentation		Chi-Square	p
	n	%	n	%		
Prolonged antibiotic use	3	8.8	7	10.6	-	0.999
Prolonged hospitalization (over 14 days)	2	5.9	2	3.0	-	0.603
EU use in the last 3 months	24	70.6	27	40.9	7.910	0.005**
Cephalosporin	11	32.4	14	21.2	1.485	0.223
Penicillin	20	58.8	19	28.8	8.509	0.004**
Carbamazepine	3	8.8	2	3.0	-	0.334
Aminoglycoside	2	5.9	1	1.5	-	0.266
Combined	12	35.3	8	12.1	7.531	0.006**
History of infection in the last 3 months	27	79.4	31	47.0	9.695	0.002**
UTI	24	70.6	23	34.8	11.507	0.001**
Smoking	3	8.8	4	6.1	-	0.687
URTI	5	14.7	13	19.7	0.379	0.538
Hospitalization in the last 3 months	15	44.1	12	18.2	7.658	0.006**
UTI-related	15	44.1	8	12.1	12.972	0.0001**
Other causes	2	5.9	7	10.6	-	0.714
TPN use	0	0.0	1	1.5	-	0.999
Central venous catheter	1	2.9	1	1.5	-	0.999
Urinary catheter	1	2.9	2	3.0	-	0.999
Invasive intervention (surgery, etc.)	1	2.9	1	1.5	-	0.999
Blood and blood product transfusion	1	2.9	1	1.5	-	0.999
Neutropenia	1	2.9	1	1.5	-	0.999
Abnormalities in urinary ultrasound	14	41.2	20	30.3	1.182	0.277
Parenchymal damage	3	8.8	4	6.1	-	0.687
Renal shape, size, and location anomalies	7	20.6	10	15.2	0.470	0.493
Combined	3	8.8	4	6.1	-	0.687

Discussion

In this study, we evaluated urinary UTIs caused by extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* in pediatric patients, focusing on risk factors, clinical manifestations, and therapeutic outcomes. Our findings confirm that ESBL-positive *E. coli* UTIs represent a clinically important subgroup of pediatric infections. While these infections can also contribute to complications such as renal scarring and chronic kidney disease, the present study was limited to ESBL-positive cases and should be interpreted in this context.

Urinary tract infections (UTIs) are among the most common childhood infections and may cause serious complications such as renal scarring and chronic kidney disease if not properly managed. In recent years, the increasing prevalence of extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* has significantly complicated treatment due to high levels of antimicrobial resistance.¹⁸ In our ESBL-positive *E. coli* cohort, infections were more frequent in boys during the neonatal period but became predominant in girls thereafter. These results should be interpreted as specific to ESBL-positive UTIs, not all pediatric UTIs. Clinical manifestations vary with age, ranging from nonspecific symptoms such as fever and vomiting in infants to typical complaints like abdominal pain and dysuria in older children. *E. coli* was identified as the leading pathogen, while high resistance rates to commonly used antibiotics (ampicillin, amoxicillin/clavulanate, TMP-SMX) were observed. Carbapenems remained the most effective agents, though their use should be reserved due to cost and hospitalization requirements. Underlying urinary tract abnormalities, vesicoureteral reflux, recurrent infections, and recent antibiotic exposure were major risk factors for ESBL (+) UTIs. These results emphasize the importance of early recognition, rational antibiotic use, and careful follow-up to prevent long-term complications.

Consistent with previous reports,¹⁹⁻²¹ the emergence of ESBL-producing organisms poses a major therapeutic challenge due to multidrug resistance, particularly against penicillins and cephalosporins. In our cohort, UTI prevalence showed a clear sex- and age-related distribution: during the neonatal period, infections were more common in males, whereas beyond the first month of life, females were disproport-

tionately affected. These findings are in agreement with previous studies.²²⁻²⁴ Moreover, UTI prevalence decreased with age, with the highest rates observed in children under two years, in line with prior evidence.²⁴⁻²⁶

Clinical presentations were age-dependent. While older children more frequently presented with classical symptoms such as abdominal pain and dysuria, younger children, especially infants, exhibited non-specific features such as fever, irritability, and vomiting. Fever was the most frequent symptom, corroborating earlier reports.^{27,28} Importantly, 36% of our patients were asymptomatic, underlining the potential for silent progression of UTIs in pediatric populations and emphasizing the need for vigilance in early diagnostic evaluation.

Regarding microbiology, *E. coli* was the most commonly isolated pathogen, consistent with both national and international data.²⁹ High resistance rates to ampicillin, amoxicillin/clavulanate, and trimethoprim-sulfamethoxazole were observed, which is in accordance with other studies from Turkey and abroad.³⁰⁻³² Particularly concerning was the near-universal resistance to cephalosporins among ESBL-producing isolates. Although carbapenems remained highly effective, their limitations—including cost, intravenous administration, and the need for hospitalization—necessitate judicious use. These findings further support the urgent need for rational antibiotic stewardship to prevent further resistance development.

Radiological evaluation revealed urinary tract abnormalities in approximately one-third of patients, most frequently renal parenchymal changes and structural anomalies. This aligns with previous studies,³³ which demonstrated that ultrasound alone may be insufficient to detect vesicoureteral reflux (VUR) or renal scarring. Therefore, complementary investigations such as voiding cystourethrography (VCUG) and dimercaptosuccinic acid (DMSA) scintigraphy are warranted in selected cases to ensure accurate diagnosis and follow-up.

Our study also confirmed the strong association between UTIs, VUR, and renal scarring, as reported in prior literature.³⁴ Children with underlying urinary tract anomalies, recurrent infections, or recent antibiotic exposure were found to be at significantly higher risk for ESBL (+) UTIs. These findings are in line with data from Hacettepe University³⁵ and inter-

national adult studies,³⁶ which identified comorbidities, prior hospitalizations, and antibiotic use as major predictors of ESBL infections.

This study has several limitations that should be acknowledged. First, only patients with ESBL-positive *E. coli* infections who received meropenem therapy were included, which may have introduced selection bias and limits the generalizability of the findings to all ESBL-positive UTIs. Second, due to the relatively small sample size, we were unable to perform multivariate regression analyses to clearly determine independent risk factors, restricting our ability to control for potential confounding variables. Third, the lack of a control group of ESBL-negative UTI patients precluded direct comparative analyses, which would have strengthened the conclusions. Finally, the data were collected between 2008 and 2012, and thus may not fully reflect the current antimicrobial resistance patterns. Despite our findings provide important information on risk factors such as recurrent UTIs, vesicoureteral reflux, and prior antibiotic exposure, which can guide empirical antibiotic selection and patient follow-up. Future large-scale, prospective studies are needed to validate these observations and to optimize diagnostic and therapeutic strategies in pediatric practice.

In conclusion, our results highlight the clinical significance of ESBL-producing *E. coli* in pediatric UTIs. Early recognition of risk factors, careful diagnostic evaluation, and rational antibiotic selection are crucial for optimal management. Given the high prevalence of antimicrobial resistance, local epidemiological surveillance is essential to guide empirical therapy and prevent treatment failures. Furthermore, our study contributes to the limited pediatric literature on ESBL (+) UTIs, offering valuable insights for both clinical practice and future research.

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