Original Investigation / *Özgün Araştırma*

DOI: 10.5578/ced.20250205 • *J Pediatr Inf 2025;19(2):e105-e112*

Frequency of Extended Spectrum Beta-Lactamase Positive *Enterobacteriaceae* in Children with Urinary Tract Infection and The Role of Fecal Carriage on The Risk of Urinary Tract Infection

İdrar Yolu Enfeksiyonu Olan Çocuklarda Genişlemiş Spektrumlu Beta-Laktamaz Pozitif *Enterobacteriaceae* Sıklığı ve Dışkı Taşıyıcılığının İdrar Yolu Enfeksiyonu Geçirme Riski Üzerindeki Rolü

Merve Güvenç[1] (İD), Melike Emiroğlu[2] (İD), Harun Peru[3] (İD), Hatice Türk Dağı[4] (İD), Hilmi Uygun[4] (İD)

[1] *Clinic of Pediatrics, Boyabat 75. Yıl State Hospital, Sinop, Türkiye*
[2] *Division of Pediatric Infectious Diseases, Department of Pediatrics, Selçuk University Faculty of Medicine, Konya, Türkiye*
[3] *Division of Pediatric Nephrology, Department of Pediatrics, Selçuk University Faculty of Medicine, Konya, Türkiye*
[4] *Department of Microbiology, Selçuk University Faculty of Medicine, Konya, Türkiye*

Cite this article as: Güvenç M, Emiroğlu M, Peru H, Türk Dağı H, Uygun H. Frequency of extended spectrum beta-lactamase positive *Enterobacteriaceae* in children with urinary tract infection and the role of fecal carriage on the risk of urinary tract infection. J Pediatr Inf 2025;19(2):e105-e112.

**This study is a thesis study of Merve Güvenç under the supervision of Melike Emiroğlu (Thesis Center registration no: 10369064).*

Abstract

Objective: The most common cause of fever in children, following upper respiratory tract infections, is urinary tract infections (UTIs). Inadequately treated UTIs can result in kidney damage. The presence of extended-spectrum beta-lactamase (ESBL)-positive agents significantly affects treatment response and mortality rates. Fecal colonization contributes to the etiology of UTIs. However, the effects of ESBL-positive enteric bacterial carriage on the risk of UTI and its clinical consequences in children remain largely unknown. This study aims to determine the frequency of ESBL-positive *Enterobacteriaceae* in children with UTIs and to assess the role of fecal carriage in these infections.

Material and Methods: Among the patients admitted to the Department of Pediatrics at Selçuk University Faculty of Medicine between 2019 and 2020, 132 children were included in the study upon

Öz

Giriş: Çocuklarda ateşle başvuruların en sık sebebi, üst solunum yolu enfeksiyonlarından sonra idrar yolu enfeksiyonudur (İYE). İyi tedavi edilmeyen İYE, böbrek hasarına yol açabilir. Genişlemiş spektrumlu beta-laktamaz (GSBL) pozitif etken varlığının, tedaviye yanıt ve mortalite üzerinde önemli bir etkisi bulunmaktadır. İdrar yolu enfeksiyonu etiyolojisinde fekal kolonizasyonun rolü büyüktür. Ancak çocuklarda GSBL pozitif enterik bakteri taşıyıcılığının İYE geçirme riski üzerindeki etkileri ve klinik sonuçları tam olarak bilinmemektedir. Bu çalışmanın amacı, İYE geçiren çocuklarda GSBL pozitif *Enterobacteriaceae* sıklığını tespit etmek ve dışkı taşıyıcılığının enfeksiyon etkeni üzerindeki rolünü belirlemektir.

Gereç ve Yöntemler: Selçuk Üniversitesi Tıp Fakültesi, çocuk sağlığı ve hastalıkları polikliniğine 2019-2020 tarihleri arasında başvuran hastalardan 132 çocuk hasta gönüllü olur formu doldurularak çalışmaya alındı.

Correspondence Address/Yazışma Adresi

Melike Emiroğlu

Division of Pediatric Infectious Diseases,
Department of Pediatrics,
Selçuk University Faculty of Medicine,
Konya, Türkiye

E-mail: mkeser17@gmail.com

Received: 02.07.2024 **Accepted:** 03.01.2025
Available Online Date: 27.06.2025

filling out the volunteer consent form. In this prospective study, various data were recorded in a standard form, including the patients' age, sex, admission complaints, diagnosis, results of urine and blood tests, use of prophylaxis, urinary ultrasonography and dimercaptosuccinic acid scintigraphy results, history of hospitalization and antibiotic use in the past three months, yogurt consumption, and probiotic use. Additionally, urine and stool cultures were collected from all patients.

Results: Mean age of the 132 children included in the study was 4.90 ± 4.70 years, and 55 (41.7%) of them were boys. Fifty-three children with UTIs formed the patient group, while 80 children without UTIs comprised the control group. There was no significant difference in age and sex distribution between the two groups. *Escherichia coli* was identified in 66% of urine cultures, and *Klebsiella* species were found in 26.4%. Extended-spectrum beta-lactamase (ESBL)-positive agents were detected in 28.3% of the positive urine cultures. In patients with positive urine cultures, higher blood leukocyte levels, increased rates of hospitalization, and antibiotic use in the past three months were observed. Additionally, these patients had lower yogurt consumption, and urinary system anomalies were detected on ultrasound in 39.1% of them. The rate of ESBL-positive growth in stool cultures was 30.2% in the patient group and 24% in the control group (p= 0.254). No statistically significant relationship was found between ESBL growth status in the stool, the presence or absence of growth in the urine culture, and hospitalization status in the last three months (p= 0.097 and p= 0.542, respectively). ESBL-positive agent was produced in the stool of 30.2% of children with UTI. In patients with positive urine cultures, the rate of ESBL positivity in stool was statistically significantly higher than the rate of ESBL negativity (p= 0.003). However, no statistically significant relationship was found between ESBL-positive growth in urine culture and ESBL-positive growth in stool culture (p= 0.546).

Conclusion: ESBL-positive growth in the stool may pose a risk for UTIs in children.

Keywords: Beta-lactamases, child, fecal carriage, urinary tract infections

Prospektif yapılan bu çalışmada hastanın yaşı, cinsiyeti, başvuru şikayetleri, tanısı, idrar ve kan tetkik sonuçları, profilaksi kullanımı, üriner ultrasonografi ve dimerkaptosüksinik asit sintigrafi sonuçları, son üç ayda hastane yatış ve antibiyotik kullanım öyküsü, yoğurt tüketimi ve probiyotik kullanımı standart veri formuna kaydedildi. Bütün hastalardan idrar ve gaita kültürü alındı.

Bulgular: Çalışmaya dahil edilen 132 çocuğun yaş ortalaması 4.90 ± 4.70 yıl olup 55 (%41.7)'i erkek idi. İdrar yolu enfeksiyonu geçiren 53 çocuk hasta grubunu, geçirmeyen 79 çocuk kontrol grubunu oluşturdu. Her iki grup arasında yaş ve cinsiyet dağılımı arasında anlamlı farklılık saptanmadı. İdrar kültüründe %66 oranında *Escherichia coli*, %26.4 oranında *Klebsiella* spp. üredi. İdrar kültürü üremelerinin %28.3'ünü GSBL pozitif etken oluşturdu. İdrar kültüründe üreme olan hastalarda kanda lökosit değerleri, son üç ayda hastanede yatış ve antibiyotik kullanımı daha yüksek olup, yoğurt tüketimi daha azdı, %39.1'inde ultrasonografide üriner sistem anomalisi gözlendi. Hasta grubunda gaita kültüründe GSBL pozitif üreme oranı %30.2, kontrol grubunda ise %24 saptandı (p= 0.254). Gaitada GSBL üreme durumu ile idrar kültüründe üreme olup olmaması ve son üç ayda hastanede yatış durumu arasında anlamlı bir ilişki bulunamadı (sırasıyla p= 0.097 ve p= 0.542). İdrar kültüründe üreme olan çocukların %30.2'sinin gaitasında GSBL pozitif etken üretilmiştir. İdrar kültüründe üreme olan hastalarda gaitadaki GSBL pozitifliği istatistiksel olarak GSBL negatifliğine kıyasla anlamlı olarak daha fazla orana sahipti (p= 0.003). Ancak, idrar kültüründe GSBL pozitif üreme ile gaita kültüründe GSBL pozitif üreme arasında istatistiksel olarak anlamlı bir ilişki saptanmadı (p= 0.546).

Sonuç: Gaitada GSBL pozitif üreme, çocuklarda İYE için risk faktörü olabilir.

Anahtar Kelimeler: Beta-laktamazlar, çocuk, fekal taşıyıcılık, idrar yolu enfeksiyonları

Introduction

Urinary tract infection (UTI) is a common cause of bacterial infections in infants and young children with fever of unknown origin. UTI can lead to complications such as parenchymal kidney damage and hypertension. Therefore, diagnosis and treatment of UTI and risk factors are important. Periurethral colonization with uropathogenic bacteria is considered an important factor. Mostly pathogens belonging to the intestinal flora are responsible for UTI formation. UTIs are most commonly due to *Enterobacteriaceae*, especially *Escherichia coli* (1).

Extended-spectrum β-lactamases (ESBLs) are a diverse, complex and rapidly evolving group of plasmid-mediated enzymes and are the main cause of β-lactam resistance in gram-negative bacilli. Today, they are responsible for community-acquired infections as well as hospital-acquired infections and cause great difficulties in treatment (2).

Infections due to ESBL positive agents range from uncomplicated UTIs to life-threatening sepsis. Increasing isolation of ESBL-positive *E. coli* and *Klebsiella pneumoniae* causing UTI in children leads to failure in empirical treatment, which may result in serious clinical complications including sepsis, renal scar formation and prolonged hospitalization (3).

Gastrointestinal tract colonization is usually the first stage for infections caused by ESBL positive bacteria (4). While fecal colonization of nosocomial ESBL-positive bacteria was previously mentioned, recently an increase in community-acquired colonization has been reported (5). In people colonized with ESBL-positive *Enterobacteriaceae* spp. in the community, empirical treatment of infections that may occur with these agents may be inadequate and hospitalization may be required (2).

Considering the increasing rates of antibiotic-resistant uropathogens worldwide, prevention of infections due to resistant agents, early diagnosis and appropriate treatment in cases where they cannot be prevented will constitute an important step in preventing negative outcomes.

Materials and Methods

A total of 132 children admitted to Selçuk University Faculty of Medicine, Department of Pediatrics between 2019 and 2020 were included in the study on a voluntary basis. The patients were divided into two groups. Group 1 consisted of patients with urine cultures and Group 2 consisted of patients who presented with any complaint but did not have UTI. In this prospective study, a standardized data form was created; age, sex, complaint, diagnosis, urine and blood

test results, prophylaxis use, urinary ultrasonography (USG) and dimercaptosuccinic acid (DMSA) scintigraphy results, if available, hospitalization and antibiotic use history in the last three months, yogurt and probiotic use at least three days a week in the last three months, urine and stool culture growth and the name of the growth agent were recorded.

Urine cultures were obtained by midstream urine in children with established urinary control and by using a urine bag in young children and by urinary catheter or suprapubic aspiration when necessary. A rectal swab or stool sample was obtained voluntarily from each patient. Data were obtained by scanning the patients' urinary USG and DMSA scintigraphies registered in the automation system.

Significant bacteriuria (growth of a single pathogen containing at least 10^4 CFU for catheter samples and at least 10^5 CFU from midstream clean catch samples) was defined as UTI. Stool samples were cultured on ESBL CHROM agar medium to screen for ESBL-positive *E. coli* and *Klebsiella* spp. strains. Plates were incubated at 37°C for 18-24 hours. At the end of the incubation period, pink and blue colonies grown on the medium were passaged onto EMB agar. The indole reaction was identified using conventional methods such as motility, urease test, ability to utilize citrate and reactions on TSI agar. Combined disk diffusion test was performed to detect ESBL production of isolates identified as *E. coli* or *Klebsiella* spp. in accordance with the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Cefotaxime/ceftriaxone (30 µg), cefepime (30 µg), cefotaxime/clavulanic acid (30µg/10µg), cefepime/clavulanic acid (30µg/10µg), cefotaxime (30 µg)+clavulanic acid (10 µg)+cloxacillin (200 µg) discs were used. The zone around the combination disks was considered ESBL positive if it was 5 mm or wider than the zone around the clavulanic acid-free disk. *E. coli* ATCC 25922 and *K. pneumoniae* ATCC 700603 standard strains were used as quality control (6).

In the statistical method, the distribution of the data was analyzed by Shapiro Wilk test. Comparisons between two groups of normally distributed variables were made by independent sample t test, and comparisons between two groups of variables not normally distributed were made by Mann-Whitney U test. The relationship between categorical variables was evaluated by chi-square and McNemar test. Descriptive statistics of the data were expressed as mean ± standard deviation, median (minimum-maximum) and frequency (percentage). All statistical analyses were analyzed and reported in IBM SPSS Statistics 22.0 program at α= 0.05 significance level.

Results

Mean age of the 132 patients included in the study was 4.90 ± 4.70 years, and 55 (41.7%) were males. There was no significant difference in age and sex distribution between the two groups. However, a significant correlation was found between the complaints reported in patients with and without urine culture growth (p< 0.001). It was observed that the most common complaint in those with urine culture growth was burning sensation during urination with 43.4%, while the most common complaint in those without urine culture growth was non-specific with 67.1% (Table 1).

Table 1. Comparison of patients with and without urine culture growth

Variable	Urine Culture		p
	Growth n= 53	No Growth n= 79	
Age (year)	2.50 (0-16)	4.16 (0-18)	0.368[b]
Sex			
Male	18 (34%)	37 (46.8%)	0.141
Female	35 (66%)	42 (53.2%)	
Complaint			
Fever	10 (18.9%)	5 (6.3%)	**p< 0.001**
Burning when urinating	23 (43.4%)	0 (0%)	
Abdominal pain	3 (5.7%)	7 (8.9%)	
Constipation	0 (0%)	14 (17.7%)	
non-Specific complaint	17 (32.1%)	53 (67.1%)	
Leucocyte in blood (x1000/mm^3)	9.80 (0.50-29.50)	8.20 (2.70-22)	**0.005[b]**
CRP (mg/dL)	8 (0-249)	3 (0.40-96)	0.075[b]
Creatinine (mg/dL)	0.33 (0.04-1.49)	0.34 (0.16-0.80)	0.711[b]
Urine density	1015.04 ± 7.77	1015.66 ± 10.38	0.735[a]

Table 1. Comparison of patients with and without urine culture growth (continue)

Variable	Urine Culture		p
	Growth n= 53	No Growth n= 79	
Urine pH	6 (5.50-8)	6 (5-8)	0.445[b]
Leukocytes in urine	68 (0-1108)	0 (0-5)	**p< 0.001[b]**
Leukocyte esterase in urine	38 (77.6%)	0 (%0)	**<0.001**
Nitrite in Urine	20 (40.8%)	1 (1.9%)	**<0.001**
Proteinuria in urine	17 (34.7%)	1 (1.9%)	**<0.001**
Erythrocyturia in urine	29 (59.2%)	13 (24.5%)	**0.001**
Urinary USG	45 (86.5%)	29 (37.7%)	**<0.001**
Anomaly in urinary USG	18 (39.1%)	3 (10.3%)	**0.007**
Scar on DMSA scintigraphy	7 (41.2%)	1 (14.3%)	0.352
Diagnosis			
Pyelonephritis	14 (26.4%)	0 (0%)	N/A
Cystitis	39 (73.6%)	0 (0%)	
The causative agent in urine			
None	0 (0%)	79 (100%)	**<0.001**
ESBL positive *Klebsiella* spp.	6 (11.3%)	0 (0%)	
ESBL negative *Klebsiella* spp.	8 (15.1%)	0 (0%)	
ESBL positive *E. coli*	9 (17%)	0 (0%)	
ESBL negative *E. coli*	26 (49.1%)	0 (0%)	
Enterococcus faecalis	1 (1.9%)	0 (0%)	
Pseudomonas aeroginosa	3 (5.7%)	0 (0%)	
Stool culture growth	19 (35.8%)	19 (24.1%)	0.142
Stool reproduced agent			
ESBL positive *Klebsiella* spp.	5 (26.3%)	4 (21.1%)	0.254
ESBL positive *E. coli*	11 (57.9%)	15 (78.9%)	
ESBL negative *E. coli*	3 (15.8%)	0 (0%)	
Vancomycin resistant *Enterococcus*	0 (0%)	6 (7.6%)	1
Hospitalization in the last three months	18 (34%)	6 (7.6%)	**<0.001**
Antibiotic use in the last three months	42 (79.2%)	48 (60.8%)	**0.025**
Yogurt consumption	10 (18.9%)	33 (41.8%)	**0.006**
Probiotic use	7 (13.2%)	13 (16.5%)	0.610

[a]The p value of the independent sample t test. [b]Mann-Whitney U test p value.
CRP: C-reactive protein, USG: Ultrasonography, DMSA: Dimercaptosuccinic acid, N/A: Not applicable, ESBL: Extended spectrum ß-lactamases, *E. coli*: *Escherichia coli*.

Although there was no difference in C-reactive protein (CRP) and creatinine values between patients with and without urine culture growth (p> 0.05), leukocyte value in blood was found to be higher in patients with urine culture growth (p= 0.005) (Table 2).

There was no difference in urine pH and urine density between patients with and without urine culture growth. However, as expected, urine leukocyte count, presence of leukocyte esterase in urine, nitrite positivity, erythrocyturia and proteinuria were significantly different in patients with UTI. Urinary system anomalies were observed on USG in 39.1% of patients with urine culture growth and in 10.3% of patients without urine culture growth (p= 0.007) (Table 3).

ESBL positive agents were grown in 28.3% of the patients with urine culture growth. While hospitalization and antibiotic use in the last three months were significantly higher in patients with urine culture growth, yogurt consumption was lower in patients without urine culture growth (p values <0.001, 0.025, 0.006, respectively). No correlation was found between stool culture growth, stool agent and probiotic

Table 2. Comparison of patients with and without ESBL positive growth in urine culture

Variable	Growth in Urine Culture		p
	ESBL+ n= 16	ESBL- n= 33	
Age (Year)	4.46 (0-9)	1.83 (0-16)	0.579[b]
Sex (Male/Female)	6/10	9/24	0.520[c]
Leucocyte in blood (x1000/mm^3)	8.30 (5.60-29.50)	9.80 (0.50-22.20)	0.365[b]
CRP (mg/dL)	10.35 (1-79.20)	5.60 (0-249)	0.950[b]
Creatinine (mg/dL)	0.36 (0.04-1.49)	0.30 (0.12-1.46)	0.455[b]
Urine leukocytes	115 (0-569)	43 (0-1108)	0.475[b]
Nitrite in urine	2 (13.3%)	17 (54.8%)	**0.007**
Proteinuria in urine	7 (46.7%)	8 (25.8%)	0.191[c]
Erythrocyturia in urine	10 (66.7%)	18 (58.1%)	0.749[c]
Species in urine culture			
E. coli	9 (56.3%)	25 (75.8%)	**<0.001[c]**
Klebsiella spp.	6 (37.5%)	8 (24.2%)	
Diagnosis			
Pyelonephritis	4 (25%)	9 (27.3%)	1.0[c]
Cystitis	12 (75%)	24 (72.7%)	
Urinary USG anomaly	8 (50%)	8 (30.8%)	0.327[c]
Scar on DMSA scintigraphy	2 (66.7%)	3 (27.3%)	0.505[c]
Antibiotic use in the last three months	14 (87.5%)	24 (72.7%)	0.300[c]
Hospitalization in the last three months	6 (37.5%)	9 (27.3%)	0.520
Yogurt consumption	3 (18.8%)	7 (21.2%)	1.0
Probiotic use	1 (6.3%)	6 (18.2%)	0.402

*Data are expressed as median (minimum-maximum) and frequency (percentage).
[b]Are p values of Mann-Whitney U test. [c]Values are p values of chi-square test.
CRP: C-reactive protein, *E. coli*: *Escherichia coli*, DMSA: Dimercaptosuccinic acid, USG: Ultrasonography.

use and urine culture growth (p> 0.05). When the causative agents were analyzed in the stool cultures, ESBL positive *Klebsiella* spp. was found in 9 (23.7%), ESBL positive *E. coli* in 26 (68.4%) and ESBL negative *E. coli* in 3 (7.9%). Vancomycin-resistant enterococci were found in 4.5% of all children included in the study (Table 1).

The presence of nitrite was found to be lower in patients with ESBL positive urine cultures compared to negative urine cultures (p= 0.007). There was no statistically significant difference between ESBL positive and negative growth in urine culture and other variables (p> 0.05) (Table 2).

In patients with urine culture growth, no significant correlation was found between the agent grown in stool culture and the use of prophylaxis (p= 1.0).

No significant correlation was found between the presence of growth in stool culture and gender, antibiotic use in the last three months, complaints at presentation, yogurt consumption and probiotic use (p> 0.05).

No significant correlation was found between ESBL positive and negative stool cultures, urine culture growth and hospitalization status in the last three months (p= 0.097 and p= 0.542, respectively).

Table 3. Relationship between growth in urine culture, ESBL positive growth in urine culture and ESBL positive growth in stool culture

	Stool ESBL+	Stool ESBL-	p
Urine culture+	16 (84.2%)	3 (15.8%)	**0.003[€]**
Urine ESBL+	6 (37.5%)	2 (66.7%)	0.546*
Urine ESBL-	10 (62.5%)	1 (33.3%)	

[€]p value is the value of chi-square test. *p value is the value of McNemar test.
ESBL: Extended spectrum ß-lactamases.

ESBL positive agents were found in the stool of 30.2% of children with UTI. In patients with urine culture growth, ESBL positivity in stool was statistically significantly higher than ESBL negativity (p= 0.003). However, no statistically significant correlation was found between ESBL positive growth in urine culture and ESBL positive growth in stool culture (p= 0.546) (Table 3).

Discussion

UTI is the second most common infection among pediatric infections. Since delayed diagnosis and inadequate treatment may result in renal scar formation, hypertension and end-stage renal failure, early diagnosis and appropriate treatment are very important. Gram-negative intestinal bacteria constitute the reservoir from which UTI originates. There is an increase in the prevalence of ESBL positive agents in UTI isolates.

The prevalence of UTIs varies depending on age and gender and is more common in girls, although the reason is not clearly known. However, it is more common in boys under the age of one year (7). In a study by Zaoutis et al. the median age of 664 children aged 2-10 years with UTI was four years, and in a study by Altıncık et al. including 82 children with UTI, the median age of UTI was 5.42 years (1 month-14 years) (8,9). The median age of children with UTI was 2.42 years (0-16).

While fever is usually the most common reason for presentation in UTIs, increased frequency of voiding, abdominal pain/tenderness, feeding difficulties and burning during urination are other common symptoms (8,9,10). The most common presenting symptom in our patients was burning during urination (43.4%), and fever was found in 18.9%.

Since UTI may be the first finding of many congenital anomalies in the urinary system, urinary USG is recommended after the first febrile UTI (11). Dayan et al. have found urinary anomalies in 32% of ESBL-positive and 5% of ESBL-negative children with UTI (12). In a meta-analysis, the prevalence of urinary system anomaly in USG performed after the first febrile UTI in 9170 children has been found to be 22.1%, while the rate of anomaly important enough to change the follow-up of the patient has been reported to be 3.1% (11). While 39.1% of patients with UTI had urinary anomalies on USG, 10.3% of patients without UTI had urinary anomalies on USG (p= 0.007). This rate was 50% in ESBL positive patients and 30.8% in ESBL negative patients (p= 0.327). It has been reported that renal scarring was observed more frequently on DMSA scintigraphy in patients with ESBL positive growth in urine culture and this may be related to inappropriate antibiotherapy in ESBL positive patients and the higher incidence of underlying urinary system diseases in ESBL positive group (13). In our study, no significant difference was found between the two groups in terms of scarring on DMSA (p= 0.505).

Antibiotic use and hospitalization rate in the last three months were found to be significantly higher in those with UTI compared to those without UTI (p values 0.025 and <0.001, respectively). While yogurt consumption was found to be lower in those with UTI (p= 0.006), no association was found between probiotic use and UTI (p= 0.610). While there is no data in the literature on the effect of yogurt consumption on UTI, the effect of probiotics is controversial (14).

In a meta-analysis conducted between 1996 and 2014, including 7374 pediatric patients, the prevalence of UTIs due to ESBL-positive *Enterobacteriaceaen* was found to be 14% worldwide (5% in community-acquired UTIs and 12% in hospital-acquired UTIs). The rates were 76% in Africa, 37% in South East Asia, 12% in Europe, 7% in the Western Pacific, 5% in the Eastern Mediterranean and 2% in the Americas. A non-significant increasing trend was found in UTIs due to ESBL positive *Enterobacteriaceae* over time (15). In Türkiye, the prevalence of UTIs due to ESBL-positive *Enterobacteriaceae* in children was found at similar rates in the studies of Kızılca et al. and Conkar et al. (43% and 44.3%, respectively) (16,17). In our study, this rate was found to be 28.3%.

In studies of children with community-acquired UTIs, *E. coli* was the most common causative agent in those with ESBL positive or negative growth, whereas the rate of *Klebsiella* was found to be higher in the ESBL positive group (3,12,18). Kızılca et al. found ESBL negative growth in 57% and ESBL positive growth in 43% of 344 patients with community-acquired UTI. While *E. coli* was the most common agent in both groups, ESBL was detected in 53.2% of *Klebsiella* strains and 41.4% of *E. coli* strains (16). In our study, *E. coli* was the most common pathogen in both groups. In addition, we found that 25.7% of *E. coli* and 42.8% of *Klebsiella* spp. were ESBL positive. When all growths were considered, we found ESBL positivity at a rate of 28.3%.

It has been shown that nitrite positivity and leukocyte count in urine are not different in UTIs developing with ESBL positive bacteria compared to ESBL negative UTIs (12). In our study, similarly, no significant difference was found in the number of leukocytes in urine in patients with ESBL-positive growth in urine culture (p= 0.475), while the presence of nitrite in urine was observed less (p= 0.007). Antibiotic use in the last three months in patients with ESBL positive UTIs was found to be significantly higher in both pediatric and adult patients (18,19). We found a history of antibiotic use in the last three months in 87.5% of ESBL positive UTI patients and 72.7% of ESBL negative UTI patients (p= 0.300). Hospitalization in the last three months has been reported as a risk factor for ESBL positive UTI, but no significant relationship was found in our study (p= 0.520) (12,18). In our study, no significant relationship was found between yogurt and probiotic use and presence of ESBL in urine. There is no related study in the literature.

The frequency of fecal colonization with ESBL positive microorganisms varies between geographical regions. This dif-

ference varies according to the antibiotic use policies of the regions and whether the study was conducted in hospital outbreak situations (4,20). There is an increase in infections caused by ESBL positive microorganisms all over the world. It was reported that the rate of fecal carriage of ESBL positive *Interobacteriaceae* in Spain increased from 0.6% in 1991 to 7.0% in 2003 (5). In Bolivia and Peru, the prevalence of fecal carriage in children was 0.1% in 2001 and 1.7% in 2005 (21). In a study conducted by Ünver et al. in İstanbul in 2006, 15.2% of 250 stool samples were positive for ESBL positive *Enterobacteriaceae*, while this rate was 22% in hospitalized patients and 14.4% in outpatients. Of the 38 ESBL positive bacteria, 76.3% were *E. coli* and 18.4% were *K. pneumoniae* (22). In the study of the same center in 2008, ESBL positive *Enterobacteriaceae* were found in 21.3% of 150 individuals who had not been hospitalized in the last three months and had not received antibiotic treatment. Of the 32 ESBL positive bacteria, 84.4% were *E. coli* and 12.5% were *K. pneumoniae* (23). In Türkiye, there are very few publications on fecal carriage of ESBL-positive bacteria in the community in childhood and these are generally related to inpatients. Kiremitçi et al. showed ESBL positive microorganisms in stool samples of 24% of hospitalized children and 7.2% of outpatients. While *K. pneumoniae* was predominantly found in inpatients (59%), *E. coli* was found at a higher rate in outpatients (71.4%) (24). Söğütlü et al. detected ESBL positive bacteria in the stool of 33% of 454 pediatric outpatients, 92.2% of which were *E. coli* (25). In our study, ESBL positive fecal carriage rate was found to be 26.5% in children admitted to the outpatient clinic. Among the patients with ESBL positive fecal carriage, 25.7% had ESBL positive *Klebsiella* spp. and 74.3% had ESBL positive *E. coli.*

Birgy et al. showed that the use of third generation cephalosporins in children increased the fecal carriage of ESBL positive bacteria (26). Kiremitçi et al. reported that the use of second- or third-generation cephalosporins caused a 2.4-fold increase in fecal carriage in children admitted to outpatient clinics (24). Azap et al. reported antibiotic use in the last 90 days as the only independent risk factor for fecal colonization in patients admitted to outpatient clinics and found a statistically significant relationship between ESBL positivity and beta-lactam and quinolone use. No relationship was found between fecal colonization and hospitalization in the last three months (27). Söğütlü et al. found no significant correlation between age, gender, educational status, antibiotic use in the last three months, UTI in the last six months, hospitalization, surgery, underlying disease status and ESBL positivity in stool (25). The antibiotic use in our patients could not be determined; however, antibiotic use in the last three months was found in 73.7% of those with stool culture growth and 66% of those without stool culture growth (p= 0.388). In our study, no significant relationship was found between age, gender, hospitalization in the last three months and fecal colonization (p> 0.05).

In 310 women from four southern European countries who presented to outpatient clinics with symptoms suggestive of UTI, fecal carriage of ESBL positive *E. coli* was found in 20.3%, while UTI due to ESBL positive *E. coli* was observed in 12.3% of women. Fecal carriage of ESBL positive *E. coli* was 18 times higher in UTIs due to ESBL positive *E. coli*. Fecal colonization due to the same clone was observed in 63.2% of 38 women with UTIs due to ESBL positive *E. coli* (28). ESBL positive *E. coli* was found in 66.3% of the stool of 86 patients with UTI (29). The clinical outcomes of ESBL positive enteric bacteria carriage in children are not fully known. ESBL positive agents were found in the stool of 30.2% of our patients who had UTI. In our pediatric patients with urine culture growth, the rate of ESBL positivity in stool was higher than ESBL negativity (p= 0.003). The rate of ESBL positive growth in urine and ESBL positive growth in stool was 37.5% (p= 0.546). This suggests that the presence of ESBL positive agents in the stool may be a risk factor for ESBL positive UTI.

Ethics Committe Approval: This study was approved by the Ethics Committee of the Local Ethics Committee of the Rectorate of Selçuk University (Decision no: 2019/151, Date: 12.06.2019).

Author Contributions: Concept - MG, ME, HP; Design - MG, ME, HP, HTD; Supervision - MG, ME, HP, HTD; Resource - All of authors; Data collection and/or processing - MG, ME, HTD, HU; Analysis and/or interpretation - MG, ME, HTD, HU; Literature search - MG, ME, HP, HTD; Writing - All of authors; Critical reviews - All of authors.

Conflict of Interest: All authors declare that they have no conflict of interest.

Financial Disclosure: This research was supported by Selçuk University Scientific Research Projects Coordinatorship with 19102048 project number.

References

1. *Leung AKC, Wong AHC, Leung AAM, Hon KL. Urinary tract infection in children. Recent Pat Inflamm Allergy Drug Discov 2019;13(1):2-18. https://doi.org/10.2174/1872213X13666181228154940*
2. *El Aila NA, Al Laham NA, Ayesh BM. Prevalence of extended spectrum beta lactamase and molecular detection of blaTEM, blaSHV and blaCTX-M genotypes among gram negative bacilli isolates from pediatric patient population in Gaza strip. BMC Infect Dis 2023;23(1):99. https://doi.org/10.1186/s12879-023-08017-1*
3. *Vachvanichsanong P, McNeil EB, Dissaneewate P. Extended-spectrum beta-lactamase Escherichia coli and Klebsiella pneumoniae urinary tract infections. Epidemiol Infect 2020;149:e12. https://doi.org/10.1017/S0950268820003015*
4. *Kader AA, Kumar A, Kamath KA. Fecal carriage of extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae in patients and asymptomatic healthy individuals. Infect Control Hosp Epidemiol 2007;28(9):1114-6. https://doi.org/10.1086/519865*
5. *Valverde A, Coque TM, Sánchez-Moreno MP, Rollán A, Baquero F, Cantón R. Dramatic increase in prevalence of fecal carriage of extended-spectrum beta-lactamase-producing Enterobacteriaceae during nonoutbreak situations in Spain. J Clin Microbiol 2004;42(10):4769-75. https://doi.org/10.1128/JCM.42.10.4769-4775.2004*

6. *Testing ECoAS. EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance. EUCAST, Basel, Switzerland: Available from: http://www.eucast org/clinical_breakpoints 2013. (Available date: 01.01.2019).*
7. *Pouladfar G, Basiratnia M, Anvarinejad M, Abbasi P, Amirmoezi F, Zare S. The antibiotic susceptibility patterns of uropathogens among children with urinary tract infection in Shiraz. Medicine (Baltimore) 2017;96(37):e7834. https://doi.org/10.1097/MD.0000000000007834*
8. *Zaoutis T, Shaikh N, Fisher BT, Coffin SE, Bhatnagar S, Downes KJ, et al. Short-course therapy for urinary tract infections in children: The SCOUT randomized clinical trial. JAMA Pediatr 2024;178(6):630.*
9. *Altıncık A. Çocuklarda idrar yolu enfeksiyonu ile hiperkalsiüri ilişkisi. Tıpta Uzmanlık Tezi. Adnan Menderes Üniversitesi, Tıp Fakültesi; 2008.*
10. *Kanellopoulos TA, Salakos C, Spiliopoulou I, Ellina A, Nikolakopoulou NM, Papanastasiou DA. First urinary tract infection in neonates, infants and young children: A comparative study. Pediatr Nephrol 2006;21(8):1131-7. https://doi.org/10.1007/s00467-006-0158-7*
11. *Yang S, Gill PJ, Anwar MR, Nurse K, Mahood Q, Borkhoff CM, et al. Kidney ultrasonography after first febrile urinary tract infection in children: A systematic review and meta-analysis. JAMA Pediatr 2023;177(8):764-73. https://doi.org/10.1001/jamapediatrics.2023.1387*
12. *Dayan N, Dabbah H, Weissman I, Aga I, Even L, Glikman D. Urinary tract infections caused by community-acquired extended-spectrum β-lactamase-producing and nonproducing bacteria: A comparative study. J Pediatr 2013;163(5):1417-21.. https://doi.org/10.1016/j.jpeds.2013.06.078*
13. *Dotis J, Printza N, Marneri A, Gidaris D, Papachristou F. Urinary tract infections caused by extended-spectrum betalactamase-producing bacteria in children: A matched case control study. Turk J Pediatr 2013;55(6):571-4.*
14. *Canales J, Rada G. Are probiotics effective in preventing urinary tract infection? Medwave 2018;18(2):e7186. https://doi.org/10.5867/medwave.2018.02.7185*
15. *Flokas ME, Detsis M, Alevizakos M, Mylonakis E. Prevalence of ESBL-producing Enterobacteriaceae in paediatric urinary tract infections: A systematic review and meta-analysis. J Infect 2016;73(6):547-57. https://doi.org/10.1016/j.jinf.2016.07.014*
16. *Kizilca O, Siraneci R, Yilmaz A, Hatipoglu N, Ozturk E, Kiyak A, et al. Risk factors for community-acquired urinary tract infection caused by ESBL-producing bacteria in children. Pediatr Int 2012;54(6):858-62. https://doi.org/10.1111/j.1442-200X.2012.03709.x*
17. *Conkar S, Demirkaya S. Çocuklarda idrar örneklerinden saptanan toplum kaynaklı gram negatif mikroorganizmaların dağılımı ve 2013 yılı antibiyotik dirençleri. Dicle Tıp Dergisi 2015;42 (2):181-5 . https://doi.org/10.5798/diclemedj.0921.2015.02.0555*
18. *Topaloglu R, Er I, Dogan BG, Bilginer Y, Ozaltin F, Besbas N, et al. Risk factors in community-acquired urinary tract infections caused by ESBL-producing bacteria in children. Pediatr Nephrol 2010;25:919-25. https://doi.org/10.1007/s00467-009-1431-3*
19. *Kung CH, Ku WW, Lee CH, Fung CP, Kuo SC, Chen TL, et al. Epidemiology and risk factors of community-onset urinary tract infection caused by extended-spectrum β-lactamase-producing Enterobacteriaceae in a medical center in Taiwan: A prospective cohort study. J Microbiol Immunol Infect 2015;48(2):168-74. https://doi.org/10.1016/j.jmii.2013.08.006*
20. *Rodríguez-Baño J, López-Cerero L, Navarro MD, Díaz de Alba P, Pascual A. Faecal carriage of extended-spectrum beta-lactamase-producing Escherichia coli: Prevalence, risk factors and molecular epidemiology. J Antimicrob Chemother 2008;62(5):1142-9. https://doi.org/10.1093/jac/dkn293*
21. *Pallecchi L, Bartoloni A, Fiorelli C, Mantella A, Di Maggio T, Gamboa H, et al. Rapid dissemination and diversity of CTX-M extended-spectrum beta-lactamase genes in commensal Escherichia coli isolates from healthy children from low-resource settings in Latin America. Antimicrob Agents Chemother 2007;51(8):2720-5. https://doi.org/10.1128/AAC.00026-07*
22. *Ünver D, Küçükbasmacı Ö. Salgın dışı durumlarda dışkıda genişlemiş spektrumlu beta-Laktamaz üreten Enterobacteriaceae üyelerinin prevalansının saptanması. Türk Mikrobiyol Cem Derg 2008;38:126-31.*
23. *Küçükbasmacı Ö. Dışkıda genişlemiş spektrumlu beta-laktamaz üreten Enterobacteriaceae üyelerinin prevalansının araştırılması. Türk Mikrobiyol Cem Derg 2009;39:85-8.*
24. *Kiremitçi A, Dinleyici EÇ, Yargıç ZA, Durmaz G, Tekin N, Aybey AD, et al. Prevalence and risk factors of fecal carriage of extended-spectrum β-lactamase (ESBL) -producing enterobacteriaceae in hospitalized and ambulatory children. J Pediatr Inf 2011;5:54-8. https://doi.org/10.5152/ced.2011.22*
25. *Söğütlü N, Cömert F, Pişkin İE, Aktaş E, Köktürk F, Külah C. Zonguldak ilindeki çocuklarda, genişlemiş spektrumlu beta-laktamaz (GSBL) üreten Escherichia coli ve Klebsiella spp.'nin fekal taşıyıcılığı. Flora 2019;24:236-43. https://doi.org/10.5578/flora.67966*
26. *Birgy A, Cohen R, Levy C, Bidet P, Courroux C, Benani M, et al. Community faecal carriage of extended-spectrum beta-lactamase-producing Enterobacteriaceae in French children. BMC Infect Dis 2012;12:315. https://doi.org/10.1186/1471-2334-12-315*
27. *Azap OK, Arslan H, Karaman SO, Togan T. Risk factors for fecal carriage of extended-spectrum beta-lactamase producing Escherichia coli and Klebsiella spp. in the community. Turk J Med Sci 2007;37:31-8.*
28. *Ruppé E, Lixandru B, Cojocaru R, Büke C, Paramythiotou E, Angebault C, et al. Relative fecal abundance of extended-spectrum-β-lactamase-producing Escherichia coli strains and their occurrence in urinary tract infections in women. Antimicrob Agents Chemother 2013;57(9):4512-7. https://doi.org/10.1128/AAC.00238-13*
29. *Djuikoue IC, Woerther PL, Toukam M, Burdet C, Ruppé E, Gonsu KH, et al. Intestinal carriage of extended spectrum beta-lactamase producing E. coli in women with urinary tract infections, Cameroon. J Infect Dev Ctries 2016;10(10):1135-9. https://doi.org/10.3855/jidc.7616*