

# A Brazilian survey of the antimicrobial susceptibility of 847 *Escherichia coli* isolates from community-acquired urinary tract infections

## Abstract

We describe the antimicrobial susceptibility of *Escherichia coli* isolates from 847 community-acquired urinary tract infections episodes in patients under 15-year-old, diagnosed at the Emergency Department from 2013 to 2017. We found 2.1% extended-spectrum beta-lactamase producing *E. coli*. Low antimicrobial activity was observed for ampicillin (42.9%), cephalothin (51.9%), and trimethoprim-sulfamethoxazole (62.6%). Second and third generation cephalosporins, amoxicillin-clavulanate, and aminoglycosides remain suitable choices for empiric treatment.

**Keywords:** antimicrobial susceptibility, antimicrobial resistance, urinary tract infections, *Escherichia coli*, children, adolescent

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**Abbreviations:** UTI, urinary tract infection; ED, emergency department; ESBL, extended-spectrum beta-lactamase; IQR, interquartile ranges; CFU, colony-forming units

## Introduction

Suspected urinary tract infection (UTI) is often empirically treated at the emergency department (ED) settings. Prompt and effective initiation of antimicrobials is essential to prevent kidney scarring and damage to renal function.<sup>1</sup> Therefore, pediatricians must rely on updated antimicrobial susceptibility patterns of the most common UTI causing agents in their community to guide the empirical antibiotic choice, keeping in mind the increasing incidence of extended-spectrum beta-lactamase (ESBL) producing bacteria reported worldwide.<sup>2,3</sup> *Escherichia coli* is globally described as the most frequent causing agent of UTI, accounting for up to 80% of all community-acquired UTI.<sup>4</sup> Cephalosporins, ampicillin, amoxicillin-clavulanate, and trimethoprim-sulfamethoxazole are common first-line antibiotics prescribed in primary care. However, ESBL-positive microorganisms have recently emerged as a serious medical issue that is associated with poor outcomes, making impracticable the use of some antimicrobials commonly used for empirical treatment of UTI, such as monobactams and cephalosporins.<sup>2,3</sup> Therefore, it is essential to update the local resistance pattern of UTI causing *E. coli*, as well as the prevalence of ESBL-producing strains. Our study aimed to describe the antimicrobial susceptibility pattern and the prevalence of ESBL-positive strains of *E. coli* isolates from community-acquired UTI in a community-university hospital.

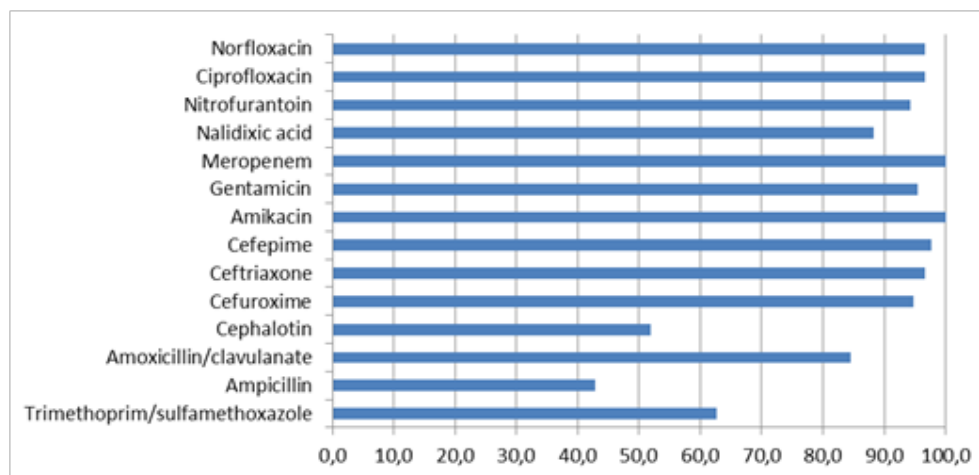
## Methods

We performed a retrospective analysis of all urine cultures obtained from patients under 15 years old at the pediatric ED of the Hospital Universitario da Universidade de Sao Paulo, Brazil, an urban public teaching hospital, from January 2013 to November

2017. UTI was defined as bacteriuria of a single species yielding  $\geq 50,000$  colony-forming units (CFU)/mL in a catheter sample or  $\geq 100,000$  CFU/mL in a midstream urine sample. The protocols for identification and susceptibility testing of the *E. coli* isolates and ESBL-positive determination were performed according to the Clinical and Laboratory Standards Institute recommendations.<sup>5</sup> Data were analyzed by using the SPSS 10.0 statistical package. Summary statistics were reported as frequencies and proportions for categorical data and as medians and interquartile ranges (IQR) for continuous variables. Chi-square or Fisher's exact tests were used to compare categorical data. This study was approved by the local Committee of Ethics on Research.

## Results

During the 5-year study period, a total of 1174 UTI episodes were identified. *E. coli* was the most frequent agent, accounting for 847 (72.1%) of all the community-acquired UTI in our sample. Other microorganisms included *Proteus mirabilis* (193; 16.4%), *Klebsiella pneumoniae* (63; 5.4%) and *Enterococcus faecalis* (16; 1.4%). The analysis of the UTI episodes caused by *E. coli* showed a higher prevalence among females as compared to males (78.4% vs. 21.6%,  $p < 0.0001$ ). The median age was 30.2 months (IQR 10.1–73.9 months). Among the 847 *E. coli* isolates, the prevalence of ESBL-producing strains was 2.1%. High antimicrobial susceptibility ( $>80\%$  of the isolates) was observed for the following antibiotics: amoxicillin-clavulanate (84.5%), second, third and fourth-generation cephalosporins (cefuroxime, 94.8%; ceftriaxone, 96.7%; cefepime, 97.8%), aminoglycosides (gentamicin, 95.4%; amikacin, 100%), meropenem (100%), nalidixic acid (88.3%), nitrofurantoin (94.2%), and quinolones (ciprofloxacin, 96.6%; norfloxacin, 96.6%). Low antimicrobial susceptibility of the *E. coli* isolates was observed for ampicillin (42.9%), cephalothin (51.9%), and trimethoprim-sulfamethoxazole (62.6%). The antimicrobial susceptibility profile of the 847 *E. coli* isolates is shown in Figure 1.



**Figure 1** Antimicrobial susceptibility of 847 *Escherichia coli* isolates from community-acquired urinary tract infection in Brazil.

## Discussion

This study provides an updated report of the antimicrobial susceptibility profile of a large number of UTI episodes caused by *E. coli* and reveals a 2.1% prevalence of ESBL-producing *E. coli* among patients under 15 years old attending a community-university hospital in Sao Paulo, Brazil. These data may help the clinicians to guide empiric antibiotic treatment of community-acquired UTI while monitoring the frequency of ESBL-producing UTI in Brazil. The antibiotic susceptibility profile of the *E. coli* isolates observed in this study is similar to several other reports from different continents, which have shown low *E. coli* antimicrobial susceptibility (<80% of the isolates) to commonly prescribed antimicrobials in primary care, such as ampicillin, first-generation cephalosporins, and trimethoprim-sulfamethoxazole.<sup>3,4,6,7</sup> In comparison with previous Brazilian studies, we found a notable decrease in the susceptibility to the first-generation cephalosporins (which are frequently prescribed as a first-line empiric antibiotic in community-acquired UTIs in Brazilian healthcare settings) in the last decade.<sup>8,9</sup> In a study published in 2008, Guidone et al.<sup>8</sup> observed that only 13% *E. coli* isolates from UTI in children and adolescents were resistant to the first-generation cephalosporins.<sup>8</sup> Similarly, a previous study conducted by our group in 2010 reported a 70.4% susceptibility to cephalothin among the *E. coli* strains.<sup>9</sup> In contrast, the current study observed that the antimicrobial susceptibility of *E. coli* to cephalothin (51.9%) was even lower than the observed for trimethoprim-sulfamethoxazole (62.6%).

Despite the excellent antimicrobial activity against *E. coli* observed for nitrofurantoin and nalidixic acid, these antibiotics fail to achieve therapeutic blood concentrations and, as a result, cannot be recommended for the treatment of febrile UTI with suspected pyelonephritis. Likewise, quinolones, which have also shown excellent antimicrobial activity against *E. coli* in this study, cannot be considered first-line therapy for UTI in children according to the Food and Drug Administration (FDA) recommendations. As previously reported, our study shows that aminoglycosides remain an effective monotherapy for the first-line treatment of febrile UTI in situations when parenteral treatment is required.<sup>10</sup> Other antimicrobials such as amoxicillin-clavulanate, second and third-generation cephalosporins also remain a suitable choice for empiric treatment of UTI caused by *E. coli* in our community.

Resistance rates of ESBL-producing *E. coli* vary among different studies but are increasingly described worldwide.<sup>2,3,7</sup> Recently, Lee et al.<sup>7</sup> analyzed the prevalence of ESBL-producing *E. coli* worldwide, comparing the periods before and after 2010.<sup>3</sup> The lowest rates were reported in France, where the prevalence increased from 1.1% to 3.3% in both periods. Similarly, in South Asia, where the highest rates were reported, the prevalence of ESBL-producing strains increased from 21.7% before 2010 to 33.2% after then.<sup>3</sup> Therefore, our prevalence of ESBL-producing *E. coli* (2.1%) is relatively low, but continuous surveillance and antimicrobial stewardship programs are necessary to prevent increasing rates of ESBL-producing *E. coli*.

A primary limitation of this study relates to the retrospective design, precluding the analysis of risk factors associated with antimicrobial resistance and the occurrence of ESBL-producing *E. coli*. Previous studies have suggested a correlation between antimicrobial resistance and the emergence of ESBL-producing *E. coli* to recent antibiotic exposure, the presence of any underlying disease, hospital admission within a previous three-month period, age under one-year-old, recurrent UTI and the presence of genitourinary anomalies.<sup>2,3,7</sup> Also, this is a single center study, and it must be kept in mind that the antimicrobial susceptibility profile may vary among different regions. Nevertheless, our hospital is a major secondary healthcare center that serves a population of nearly 500,000 inhabitants, making our sample representative of community-acquired UTI in Sao Paulo.

## Conclusion

In conclusion, in this sample of patients under 15 years-old with confirmed UTI attending a community hospital in Sao Paulo, *E. coli* isolates showed low antimicrobial susceptibility to ampicillin, first-generation cephalosporins, and sulfamethoxazole-trimethoprim. Aminoglycosides, amoxicillin-clavulanic acid, second and third-generation cephalosporins are still suitable for empiric treatment of febrile UTI, while nalidixic acid and nitrofurantoin may be used for cystitis. Quinolones, despite its excellent antimicrobial activity, cannot be used as a first-line antibiotic for children. Adequate empiric treatment of UTI, as guided by local antimicrobial susceptibility profile, may help to prevent the emergence of ESBL-producing strains, which accounted for 2.1% of the *E. coli* isolates in this study.

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## Conflicts of interest

The authors have no conflicts of interest or funding to disclose.

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