

Community Urinary Tract Infection due to ESBL producing *E. coli*: epidemiology and susceptibility to oral antimicrobials including Mecillinam

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ABSTRACT

Background: There is increasing incidence of (Extended spectrum beta lactamases) ESBL producing *E. coli* causing community urinary tract infections (UTI). The primary objective of this study was to study the epidemiological factors associated with ESBL positive community acquired uropathogenic *E. coli* isolates and to determine their susceptibility to newer oral drugs including mecillinam.

Methods: In this prospective study, from total of 140 community isolates of *E. coli* causing UTI, ESBL was detected by Clinical Laboratory Standards Institute criteria. Drug susceptibility was done by Kirby-Bauer method disc diffusion method for various oral antimicrobial agents. Various epidemiological factors associated with ESBL for each patient were recorded on individual forms. This included age, presence of diabetes mellitus, renal calculi, pregnancy, history of urinary instrumentation, recurrent UTI and antibiotics intake.

Results: Out of total of 140 strains of *E. coli*, which were screened for ESBL production, 30 (21.4%) isolates were positive. High-level resistance 94 (70%) was seen for many antimicrobial agents. Only 4.5% of uropathogenic *E. coli* were resistant to Mecillinam. Various epidemiological factors associated with ESBL causing infections were female patients, H/o antimicrobial intake, elderly age > 60 years, renal calculi and H/o recurrent UTI.

Conclusions: The epidemiology of ESBL positive uropathogenic *E. coli* is becoming more multifaceted.

Keywords: Community UTI; *E. coli*; epidemiology; ESBL

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Background:

Community acquired urinary tract infection (UTI) due to *Escherichia coli* is one of the most common form of bacterial infections, affecting people of all ages. Originally ESBL (Extended Spectrum β -lactamases) producing *E. coli* was isolated from hospital setting but lately this organism has begun to disseminate in the community.¹

In India community presence of ESBL producing organisms has been well documented. Various epidemiological factors associated with ESBL producing strains need to be documented. This will allow clinicians to separate patients with community UTI having these factors so that appropriate and timely treatment can be given.² Community UTI when complicated may be potentially life-threatening condition. In addition, for deciding the empirical treatment for

patients with UTI warrants a thorough knowledge of local epidemiology and patient's profile. Therefore, the primary objective of this study was to determine the epidemiological factors associated with ESBL positive community acquired uropathogenic *E. coli* isolates and to determine their susceptibility to newer oral drugs. Mecillinam is a novel β -lactam antibiotics that is active against many Enterobacteriaceae. It binds to PBP2, an enzyme critical for the establishment and maintenance of bacillary cell shape. It is given as a prodrug that is hydrolyzed into active agent. It is well tolerated orally in the treatment of acute cystitis.³

Methods:

This prospective study was conducted in Government Medical College Hospital, Chandigarh, India, which caters to medical needs of the community from North India from Jan 2012- July 2012.

Study group

It included patients diagnosed as having UTI in outpatient clinic or emergency room or patients diagnosed within 48 hrs after hospitalization. These patients were labeled as having community UTI. A diagnosis of symptomatic UTI was made when patient had at least one of the following signs or symptoms with no other recognized cause: fever $\geq 38.8^\circ\text{C}$, urgency, frequency, dysuria or suprapubic tenderness and patient had a positive urine culture i.e. $\geq 10^5$ microorganisms/ml of urine.⁴ Various epidemiological factors for each patient were recorded on individual forms. This included age, presence of diabetes mellitus, renal calculi, pregnancy, history of urinary instrumentation, recurrent UTI (more than 3 UTI episodes in the preceding year) and antibiotics intake (use of β -lactam in the preceding 3 months).²

Patients with H/O previous or recent hospitalizations were excluded from study.

Antibiotic susceptibility testing was carried out following Clinical Laboratory Standards Institute (CLSI) guidelines using Kirby-Bauer method.⁵ The antibiotics which were tested included amoxyclav (30/10 μg), norfloxacin (10 μg), ciprofloxacin (5 μg), tetracycline (30 μg), nitrofurantoin (300 μg), trimethoprim-sulfamethoxazole (23.75/1.25 μg), cephalexin (30 μg), cefaclor (30 μg), Cefuroxime (30 μg), Mecillinam (10 μg) (Hi-Media, Mumbai, India)

Detection of ESBL

ESBL detection was done for all isolates according to latest CLSI criteria.⁵

Screening test- According to latest CLSI guidelines, zone diameter of *E. coli* strain for ceftazidime $<22\text{mm}$ and for

cefotaxime $< 21\text{mm}$ is presumptively taken to indicate ESBL production.

Confirmatory test- As per CLSI guidelines, ESBLs were confirmed by placing disc of cefotaxime and ceftazidime at a distance of 20mm from a disc of cefotaxime /clavulanic acid (30/10 μg) and ceftazidime/ clavulanic acid (30/10 μg) respectively on a lawn culture of test strain (0.5 McFarland inoculum size) on Mueller-Hinton agar. After overnight incubation at 37°C , ESBL production was confirmed if there $\geq 5\text{mm}$ increase in zone diameter for either antimicrobial agent tested in combination with clavulanic acid versus its zone when tested alone.⁵

Control strain - Standard strain of *Klebsiella pneumonia* ATCC 700603 was used as ESBL positive control and *Escherichia coli* ATCC 25922 was used as ESBL negative control.

Results:

Out of total of 140 strains of *E. coli*, which were screened for ESBL production, 30 (21.4 %) isolates were positive. High-level resistance was seen for many antimicrobial agents like cephalexin (92.8%), cefaclor (90%), amoxy-clavulanate (88.57%), cefuroxime (75.7%), sulfamethoxazole-trimethoprim (72.8%), norfloxacin (75.71%) and ciprofloxacin (70%). Whereas, sensitivity for nitrofurantoin was high (90%). Only 4.5% of uropathogenic *E. coli* were resistant to Mecillinam.

Various epidemiological factors seen in ESBL producers include female patients (n =24, 80%), H/o antimicrobial intake (n = 17,57 %), elderly age > 60 years (n =16 53%), renal calculi (n =15, 50%), H/o recurrent UTI (n =11, 37 %), pregnancy (n = 11,37%), diabetes mellitus (n = 7, 23%) and H/O urogenital instrumentation (n = 7, 23%).

Discussion:

The epidemiology of ESBL positive uropathogenic *E. coli* is becoming more multifaceted, with increasingly indistinct boundaries between the community and hospital [6]. In addition, infection with an ESBL producing organisms causing community UTI is associated to treatment failure, delayed clinical response, higher morbidity and mortality. These organisms are mutiresistant to other antimicrobials like aminoglycosides, quinolones and co-trimoxazole. Therefore, empirical therapy with cephalosporins and fluoroquinolones often fail in these patients with community UTI.⁷

The rate of ESBL producers in our study are lower than that described by other authors. In a similar study Mahesh E et al reported higher rate (56.2%) of ESBL positivity from *E. coli*, which were causing UTI from community setting

respectively.⁸ Additionally Taneja N et al described a higher rate (36.5%) of ESBL positivity in uropathogens.^{9,10}

A high rate of resistance was seen to almost all antimicrobial agents. This is in agreement with other studies.^{8,11} Mecillinam showed very good results with only 4.5% resistance. Wootton M et al reported similar high activity of mecillinam against *E. coli* (93.5%).¹² Auer S et al reported that mecillinam can be a good oral treatment options in patients with infections due to ESBL organisms.⁷

Limitations of our study was that being a developing country with limited resources, molecular typing and determination of antimicrobial resistance profiles of the isolates was not done. Since description of ESBL types may have be of some interest for epidemiological purposes.

In our study female patients, elderly, patients with H/o antimicrobial intake, renal calculi and H/o recurrent UTI were important epidemiological factors for infections due to ESBL producers. This is similar to risk factors studied by Azap OK et al. In conclusion, the prevalence of ESBL producers causing community UTI is less and mecillinam is a good treatment option.

Conflict of interest: none

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