

Extended spectrum beta lactamase positive uropathogenic E. coli - Epidemiological Factors and Resistance

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Abstract

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

Materials & Method: In this prospective study, from total of 140 community isolates of E. coli causing UTI, ESBL was detected by CLSI 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: ESBL, Community UTI, E.coli, epidemiology

Abbreviations: ESBL - Extended spectrum beta lactamases, UTI - Urinary tract infection

Introduction

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. However, various epidemiological factors associated with ESBL producing strains need to be documented. This will allow clinicians to separate patients with community UTI with these factors so that appropriate and timely treatment can be given.² A community UTI when complicated may be a potentially life-threatening condition. In addition, for deciding the empirical treatment for patients with a UTI a thorough knowledge of local epidemiology is required. 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 antibiotic that is active against many members of family Enterobacteriaceae. It binds to penicillin binding protein (PBP 2), 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

Material and Methods

This prospective study was conducted, from Jan 2012- July 2012, in our tertiary care hospital, which caters to medical needs of the community in North India.

Study Group:

The study group included patients diagnosed as having a UTI in outpatient clinic, or the emergency room or patients diagnosed within 48 hrs after of hospitalization. These patients and were labeled as patients having a 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 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 a history of previous or recent hospitalization were excluded from study.

Antibiotic susceptibility testing was carried out following Clinical Laboratory Standards Institute (CLSI) guidelines using the Kirby-Bauer disc diffusion method.⁵ The antibiotics, which

were tested included Amoxyclav (30/10µg), Norfloxacin (10µg), Ciprofloxacin (5µg), Tetracycline (30µg), Nitrofurantoin (300µg), Trimethoprim-sulfamethoxazole (23.75/1.25µg), Cephalexin (30µg), Cefaclor (30µg), Cefuroxime (30µg), Mecillinam (10µg) (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 <22mm and for Cefotaxime < 21mm is presumptively taken to indicate ESBL production.

Confirmatory test - As per CLSI guidelines, ESBLs were confirmed by placing a disc of Cefotaxime and Ceftazidime at a distance of 20mm from a disc of Cefotaxime /Clavulanic acid (30/10µg) and Ceftazidime/Clavulanic acid (30/10µg) 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 was a ≥5mm increase in zone diameter for either antimicrobial agent tested in combination with Clavulanic acid versus its zone when tested alone

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 found to be positive. High-level resistance was seen for many antimicrobial agents like Cephalexin (92.8%), Cefaclor (90%), Amoxycloxacillin (88.57%), Cefuroxime (75.7%), Sulfamethoxazole-trimethoprim (72.8%), Norfloxacin (75.71%) and Ciprofloxacin (70%). Sensitivity to Nitrofurantoin was found to be 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%), history of antimicrobial intake (n = 17,57 %), elderly age >60 years (n =16 53%), renal calculi (n =15, 50%), history of recurrent UTI (n =11, 37 %), pregnancy (n = 11,37%), diabetes mellitus (n = 7, 23%) and history of 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 with treatment failure, delayed clinical response, higher morbidity and mortality. These

organisms are multi-resistant to other antimicrobials like Aminoglycosides, Quinolones and Co-trimoxazole. Therefore, empirical therapy with Cephalosporins and Fluoroquinolones often fail in patients with community UTI.⁷

The rate of ESBL producers in our study is 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 UTIs from a community setting.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 authors like Mahesh et al. and Mandal J et al.^{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%).³ Auer S et al. reported that Mecillinam can be a good oral treatment options in patients with infections due to ESBL organisms.⁷

A limitation 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. In our study female patients, elderly, patients with a history of antimicrobial intake, renal calculi and history of recurrent UTI were important factors for infection due to ESBL producers. These findings are similar to risk factors studied by other authors.² In conclusion; this study confirms that ESBL-producing E. coli strains are a notable cause of community onset infections especially in predisposed patients. The widespread and rapid dissemination of ESBL-producing E. coli seems to be an emerging issue worldwide. Further clinical studies are needed to guide clinicians in the management of community onset infections caused by E. coli.

Competing Interests

None declared

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REFERENCES

- Rodríguez BJ, Alcalá CJ, Cisneros MJ, Grill F, Oliver A, Juan P et al. Community Infections Caused by Extended-Spectrum β-Lactamase-Producing Escherichia coli. Arch Intern Med. 2008; 168: 1897-1902.
- Azap OK, Arslan H, Serefhanoglu K, Colakoglu S, Erdogan H, Timurkaynak F et al. Risk factors for extended-spectrum β-lactamase positivity in uropathogenic Escherichia coli isolated from community-acquired urinary tract infections. Clin Microbiol Infect. 2010;16: 147-51.

3. Wootton M, Walsh TM, Macfarlane L, Howe R. Activity of mecillinam against *Escherichia coli* resistant to third-generation cephalosporins. *J Antimicrob Chemother.* 2010; 65: 79-81.
 4. Dong SL, Chung BL, Seung-JL. Prevalence and Risk Factors for Extended Spectrum Beta-Lactamase-Producing Uropathogens in Patients with Urinary Tract Infection. *Korean J Urology.* 2010; 51:492-7.
 5. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: Twenty First Informational Supplement M100-S21. CLSI, Wayne, PA, USA, 2011.
 6. Neshet L, Novack V, Riesenber F, Schlaeffer F. Regional community-acquired urinary tracts in Israel; diagnosis, pathogens, and antibiotics guidelines adherence: A prospective study. *International J Infect Dis* 2007; 11:245-50.
 7. Auer S, Wojna A, Hell M. Oral Treatment Options for Ambulatory Patients with Urinary Tract Infections Caused by Extended-Spectrum beta-Lactamase-Producing *Escherichia coli*. *Antimicro Agents Chemo.* 2010;54: 4006-8.
 8. Mahesh E, Ramesh D, Indumathi VA, Khan MW, Kumar PS, Punith K. Risk Factors for Community Acquired Urinary Tract Infection caused by ESBL-producing Bacteria. *J Indian acad clinl med.* 2010; 11:271-6.
 9. Taneja N, Rao P, Arora J, Dogra A. Occurrence of ESBL & Amp-C β -lactamases & susceptibility to newer antimicrobial agents in complicated UTI. *Indian J Med Res* 2008; 127: 85-8.
 10. Taneja N, Singh G, Singh M, Madhup S, Pahil S, Sharma M. High occurrence of bla CMY-1 Amp C lactamase producing *Escherichia coli* in cases of complicated urinary tract infection (UTI) from a tertiary health care centre in north India. *Indian J Med Res* 2012; 136: 289-91.
 11. Mandal J, Acharya NS, Buddapriya D, Parija SC. Antibiotic resistance pattern among common bacterial uropathogens with a special reference to ciprofloxacin resistant *Escherichia coli*. *Indian J Med Res* 2012; 136: 842-9.
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