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Original research article

Evaluation of antibiotic resistance among uropathogenic *Escherichia coli* from a tertiary care hospital

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Abstract

This study at Mahatma Gandhi Memorial Medical College, Indore, investigates antibiotic resistance in under-five children with pneumonia, sepsis, and meningitis symptoms, focusing on Extended-Spectrum Beta-Lactamase (ESBL)-producing Uropathogenic *Escherichia coli* (UPEC). Analyzing 99 ESBL-positive UPEC strains from 1500 urine specimens, significant resistance was observed, notably against Piperacillin (100%), Ciprofloxacin (93%), and Norfloxacin (92%). Carbapenems (Imipenem, Meropenem) showed lower resistance (2%, 4%), indicating efficacy. Nitrofurantoin (6%) and Amikacin (16%) exhibited moderate resistance. The study provides critical insights into pediatric UTI management, emphasizing judicious antibiotic use, infection control, and ongoing research to address evolving challenges posed by antibiotic-resistant uropathogens in children.

Keywords: Urinary tract infections, *Escherichia coli*, extended-spectrum beta-lactamase, antibiotic resistance, uropathogenic strains, antibiotic susceptibility, empirical therapies, resistance patterns, esbl-producing strains, infection control measures

Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections [1]. With varied clinical spectrum of severity ranging from asymptomatic bacteriuria to cystitis and pyelonephritis to septic shock with multi organsystem failure. UTIs are challenging, not only because of the large number of infections that occur each year, but also because the diagnosis of UTI is not always straight forward. Physicians must distinguish UTI from other diseases that have a similar clinical presentation, some UTIs are asymptomatic or present with atypical signs and symptoms [2]. *Escherichia coli (E. coli)* is the most common cause of both community-acquired and nosocomially transmitted UTIs [3, 4]. In community-acquired illnesses, between 70% and 90% of all UTIs are caused by *E. coli* and is also responsible for 85% of asymptomatic bacteriuria (ABU) and for more than 60% of recurrent cystitis [5]. Antimicrobial resistance has been recognized as an emerging worldwide problem both in developed and developing countries [6].

In *Enterobacteriaceae* antimicrobial resistance in *E. coli* is of particular concern because it is the most common Gram negative pathogen causing infections in humans beings, particularly urinary tract infections (UTIs). In addition, resistant *E. coli* strains have the ability to transfer antibiotic resistance determinants not only to other strains of *E. coli* but also to other bacteria within the gastrointestinal tract. Antimicrobial drug resistance is on the rise worldwide with regional differences in the frequency of occurrence [7].

The most common cause of bacterial resistance to β-lactam antibiotics is the production of enzyme β-lactamases The latest in the series of these enzymes is the evolution of Extended Spectrum β-Lactamases (ESBLs) due to extensive use of 3rd generation Cephalosporins (3GCs). ESBLs are enzymes that mediate resistance to extended spectrum e.g., third generation Cephalosporins as well as monobactams such as Aztreonam (8). Initially ESBL producing organisms were isolated from nosocomial infections but these organisms are now also being isolated from community [9]. This study aim to evaluate antimicrobial resistance among ESBL producing *Escherichia coli*.

Objective: The study was planned to evaluate antibiotic resistance pattern of ESBL producing Uropathogenic *Escherichia coli.*

Materials and Methods

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Study design: Descriptive type cross sectional study.

Place of study: Department of Microbiology, Mahatma Gandhi Memorial Medical College, Indore.

Period of study: The study was carried out form July 2015 to June 2016.

Study population: Study includes all consecutive non-repetitive isolates of *Escherichia coli,* isolated in our laboratory from urine specimens received from both inpatients and outpatients department.

Ethical consideration: Study and data collection done after approval from the institutonal ethics committee.

Procedure: We have included 1500 consecutive non-repeating urine specimens from patients attending inpatient and outpatient Department of tertiary care hospital with clinical symptoms of urinary tract infections. Samples were received in the Department of Microbiology. Semi quantitative culture with a calibrated loop was done on Blood agar, MacConkey agar and HiCrome UTI Agar plates, Inoculated agar plates were incubated aerobically at 37 °C for 24 hours. Colony count of $\geq 10^5$ cfu/ml was considered significant. The *Escherichia coli* strains identified on the basis of colony colour on HiCrome UTI agar, colony morphology, staining characters, motility and other relevant biochemical tests [6]. Antimicrobial susceptibility testing done by Kirby-Bauer disc diffusion method for following antibiotics: Amoxycillin-clavulanic acid (20/10 µg), Piperacillin (100 µg), Piperacillin-tazobactam (100/10 µg), Cefotaxime (30 µg), Ceftriaxone (30 µg), Ceftazidime (30 µg), Cefpodoxime (10 µg), Cefipime (30 µg), Gentamicin (10 µg), Amikacin (30 µg), Tetracycline (30 µg), Ciprofloxacin (5 µg), Levofloxacin (5 µg), Imipenem (10 µg), Meropenem (10 µg), Trimethoprim-sulphamethoxazole (1.25/23.75 µg), Norfloxacin (10 µg) and Nitrofurantoin (300 µg). (87) *E. coli* ATCC 25922 was used as the control strain.

Screening and Confirmation test for ESBLs: Screening of ESBLs producing isolates carried out by standard disc diffusion criteria using four discs of 3rd generation cephalosporin namely cefotaxime (CTX), ceftazidime (CAZ), ceftriaxone (CTR) and cefpodoxime (CPD) and Phenotypic confirmation of ESBL producers were done using Combined disc method as per CLSI guidelines We used *E. coli* ATCC 25922 as an ESBL-negative reference strain and *Klebsiella pneumoniae* ATCC 700603 as an ESBL-positive reference strain.

Result and discussion

Development of bacterial resistance against newer antibiotics makes the main focus of research. Since the 2000s, ESBL-EC have been considered as serious pathogens both in nosocomial and community infections around the world, and their virulence varies by region. In this study we have obtained 171 isolates of *E. coli* from 1500 specimens (Table-1) processed during study period. We have grown 200 *E. coli* during study period; 106 from 856 and 94 from 644 urine specimens of inpatient and outpatient department respectively (Table-2). Out of 200 *E. coli* isolated, 171 were found to be screen positive for ESBL. Among the screen positive *E. coli* 99 (46 from inpatients and 53 from outpatients) were confirmed by phenotypic combined disk method (CDM) and considered as ESBL producer (Table3-4). Antimicrobial resistance of these 99 strains of *E. coli* was evaluated in this study.

The reports presented by different authors clearly indicate that the prevalence of ESBL producing organisms among clinical isolates vary greatly geographically and rapidly changing over time. The variation in percentage of ESBL producing *E. coli* in different areas is probably due to the variation in the risk factors, extent of antibiotic use. In our country, second generation Cephalosporins like cefaclor and cefuroxime and even some third generation Cephalosporins are extensively used by general practitioners, unregistered medical practitioners and chemists and that too in inadequate doses and duration to treat not only urinary tract infections but all kinds of infections. This may be the most important reason of high prevalence of ESBL producing organisms.

In our study we have found maximum resistance among ESBL producer for Piperacillin (Table-5) which have shown resistance of 100% in our study, which is correspond to the R. Eshwar Singh *et al*. 2011 [10] and which is more than of Dinesh kumar *et al*. 2014 (80%) [11], Sasirekha *et al*. [12] 2010 (83%). Among tested antibiotics of Fluoroquinolones group, Ciprofloxacin (93%) was shown maximum resistance followed by Norfloxacin (92%) and Levofloxacin (86%). Such high level of resistance was also found by Singh *et al*. 2015 [13] where resistance rate for Ciprofloxacin was 83% and for Norfloxacin was 94%. The possible explanation for the association between ESBL production and fluoroquinolones (Ciprofloxacin, Norfloxacin) resistance is the presence of genes of the two resistance mechanisms on the same plasmid [14].

Amoxycillin-clavulanic acid showed 76% resistance to ESBL producers in this study, which is near to Dinesh kumar *et al*. 2014 (68%) [11] and Hasan Ejaz *et al*. 2011 (86%) [15], and more than that were found in Sasirekha *et al*. 2010 (39%) [12]. Hasan Ejaz *et al*. 2011 (86%) [15].

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In present study Piperacillin-tazobactam shown 24% resistance to ESBL producing uropathogenic *E. coli* which is near to the Dinesh kumar *et al*. 2014 (80%) [11] and more than that were found in Sasirekha *et al*. 2010 (9%) [12] and Hasan Ejaz *et al*. 2011 (10%) [15]. Trimethoprim-sulphmethoxazole shown 70% resistance in this study which is correspond to the Nair T Bhaskaran *et al*. 2011 (70%) [16] and less than that were found in Hasan Ejaz *et al*. 2011(78%) [16], and Singh *et al*. 2011 (78%) [17].
Nitrofurantoin that was commonly used to treat UTI was shown 6% resistance to ESBL producing *E. coli* which is near to Nair T Bhaskaran *et al*. 2011 (9%) [16] and less than that of Hasan Ejaz *et al*. 2011 (28%) [15], and Singh *et al*. 2011 (19%) [17], Dinesh kumar *et al*. 2014 (42%) [11].
Cefipime was shown 92% resistance in ESBL producing uropathogenic *E. coli* in our study which is near to R. Eshwar Singh *et al*. 2011 (94%) [9] and more than to Dinesh kumar *et al*. 2014 (42%) [11].
In this study carbapenems [Imipenem (2%), Meropenem (4%)] shown lowest resistance to ESBL producing uropathogenic *E. coli*. Such lower resistance were also found in Singh *et al*. 2015 (0%) [10], Sasirekha *et al*. 2010 (0%) [12] and Hasan Ejaz *et al*. 2011 (1.3%) [15], which were lower than that found in this study. Such increase of resistance to carbapenems probably may be due to increase use of these drugs in our geographical region.

Conclusion

Carbapenem group of antibiotics (96-98%) followed by Nitrofurantoin (94%) and Amikacin (84%) were found to be the most effective against ESBL producing uropathogenic *E coli in vitro*. Piperacillin (100%) followed by Ciprofloxacin (93%), Norfloxacin (92%) and Cefipime (92%) were found to be most resistant antimicrobials *in vitro*.

Table 1: Distribution of urine specimens

Specimens	No. of urine specimens (%)
Inpatient	856 (57)
Outpatient	644 (43)
Total	1500

Table 2: Isolation of *E. coli* from IPD and OPD

Department	Number of *E. coli* isolated (%)
Inpatient	106 (53)
Outpatient	94 (47)

Table 3: Screening for ESBL production

No. of *E. coli*	Screening positive (%)	Screening negative (%)
Inpatient, n=106	99 (93)	07 (07)
Outpatient, n=94	72 (77)	22 (23)
Total	171 (86)	29 (14)

Table 4: ESBL production among screen positive *E. coli* by CLSI combined disk method (n=171)

No. of *E. coli*	No. of positive strains (%)
IPD, n=99	46 (46)
OPD, n=72	53 (74)
TOTAL, n=171	99 (58)

Table 5: Antimicrobial resistance pattern of ESBLs producing *E. coli*

Antibiotics	Rate of resistance in ESBLs producing *E. coli (%)*		
	Total n=99	Inpatients n=46	Outpatients, n=53
Piperacillin	99 (100)	46 (100)	53 (100)
Cefipime	91 (92)	44 (96)	47 (89)
Ciprofloxacin	92 (93)	44 (96)	48 (91)
Norfloxacin	91 (92)	42 (91)	49 (92)
Levofloxacin	85 (86)	41 (89)	44 (83)
Amoxycillin-clavulanic acid	76 (77)	34 (74)	42 (79)
Piperacillin-tazobactam	24 (24)	12 (26)	12 (23)
TMP-SMX	70 (71)	38 (83)	32 (60)
Tetracycline	66 (67)	32 (70)	34 (64)
Nitrofurantoin	6 (6)	4 (8.7)	2 (3.8)
Imipenem	2 (2)	01 (2.2)	01 (1.9)
Meropenem	4 (4)	02 (4.3)	01 (1.9)
Gentamicin	35 (35)	18 (39)	17 (32)
Amikacin	16 (16)	5 (11)	11 (21)

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