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PREVALENCE & ANTIBACTERIAL RESISTANCE OF ESBLs AMONG PREGNANT WOMEN WITH UTI

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ABSTRACT

Urinary tract infection (UTI) remains the common infections diagnosed in outpatients as well as in hospitalized patients. Worldwide data show that there is an increasing resistance among urinary tract pathogens to conventional drugs. Extended spectrum beta lactamases (ESBL) hydrolyse expanded spectrum cephalosporins like ceftazidime, cephotaxime which are used in the treatment of UTI. ESBL-producers are not easily detected by the routine disk diffusion susceptibility test, and this result in the failure of treatments due to inappropriate use of antibiotics. No information on ESBL producing organisms causing UTI is available from Tiruchirappalli, Tamil Nadu. Urinary isolates from symptomatic UTI cases attending or admitted to a hospital in Tiruchirappalli were identified by conventional methods. Antimicrobial susceptibility testing was done by Kirby Bauer's disc diffusion method. Isolates resistant to cephotaxime were tested for ESBL production by double disc synergy test method. Of the 936 isolates, 236 (25.2%) were found to be ESBL producers. In the present study, a large number of uropathogens were found to be ESBL producers. Most of the ESBL producing isolates were multidrug resistant. Careful detection of ESBL production and antimicrobial susceptibility testing are necessary to avoid treatment failure in patients with UTI.

INTRODUCTION: Despite the widespread availability of antibiotics, urinary tract infection (UTI) remains the most common bacterial infection in the human population [1]. To ensure appropriate therapy, current knowledge of the organisms that cause UTI and their antibiotic susceptibility is mandatory [2]. Many gram-negative bacilli produce extended-spectrum β-lactamases (ESBL), which are enzymes that mediate resistance to all β-lactams except cephamycins and carbapenems [3, 4].

ESBL-producing bacteria were first isolated in Germany in 1983 [5], but they have since been reported worldwide [6]. *Klebsiella spp.* and *Escherichia coli* are the predominant ESBL-producers. Infections due to these organisms often occur in outbreaks, and ESBL have therefore become a serious problem in hospitalized patients [7, 8].

Moreover, since ESBL-producing organisms are frequently also resistant to aminoglycosides, trimethoprim- sulfamethoxazole (cotrimoxazole), and quinolones, the therapeutic choices are limited [9, 10].

Though few reports are available on ESBL-producing isolates in hospitals in India [1, 11], yet there are no published reports concerning the prevalence and

resistance of ESBL – producing Enterobacteriaceae in Tiruchirappalli, South India.

Though ESBLs have been reported in many countries, the prevalence and phenotypic characteristics among clinical isolates may vary between geographical areas. Hence we carried out a survey of ESBL – producing clinical isolates of those bacteria in a major hospital in the heart of the city. The main objective of the survey was to determine the prevalence of ESBL – producing members of Enterobacteriaceae as causative agents of UTI in patients treated at the hospital over a 1-year period. In addition, the antibiogram pattern for these organisms was also analyzed.

MATERIALS AND METHODS: During the year 2005, a total of 1046 urine samples were received in the Department of Microbiology, CSI Mission General Hospital, Tiruchirappalli. From these urine samples of symptomatic UTI patients, 936 urinary isolates were identified by conventional techniques [12].

Antibiogram of the isolates was done by Kirby Bauer's method [13], using antibiotic disks from Hi-media, Mumbai. The following antimicrobial agents were tested: amikacin (30 mcg), amoxicillin / clavulanic acid (20/10 mcg), ampicillin (10 mcg), gentamycin (10mcg), cefuroxime (30mcg), norfloxacin (10mcg), ciprofloxacin (5 mcg), ofloxacin (5 mcg), and Imipenem (10 mcg). The results were interpreted according to the criteria recommended by the National Committee for Clinical Laboratory Standards [14].

Detection of ESBL Production: ESBL production was detected using the double-disk synergy test (DSST) (15). ESBL presence was assayed using the following antibiotic disks: Cefotaxime (30 mcg), Ceftazidime (30 mcg), amoxyclavulanic acid (20/10 mcg). *Klebsiella pneumoniae* ATTC 700603 and *Escherichia coli* ATCC 25922 strains served as positive and negative controls respectively. For all ESBL – producing isolates, the susceptibility test was reported as resistant to all penicillins, cephalosporins and aztreonam, irrespective of the individual invitro test result, as recommended by the NCCLS [15].

RESULTS AND DISCUSSION: During the 1-year study period, 936 urinary isolates were isolated (**Table 1**) various organisms have been reported to be isolated from patients with UTI. *E.coli* and *K.pneumoniae* have been reported as the most common organisms causing UTI [16].

TABLE 1: SCREENING OF URINARY ISOLATES OF PREGNANT WOMEN FOR ESBL - PRODUCTION

Urinary isolates	No. of isolates	No. of non ESBL-producers	No. of ESBL producers
Escherichia coli	412	312	100
Klebsiella pneumoniae	136	100	36
Acinetobacter baumannii	52	34	18
Pseudomonas aeruginosa	58	48	10
Aeromonas hydrophila	78	58	20
Citrobacter freundii	36	28	08
Enterobacter aerogenes	28	14	14
Proteus mirabilis	06	02	04
Providencia stuarti	04	04	--
Morganella morganii	54	44	10
Other non fermenter gram negative bacilli	66	50	16
Total	936	700	236

Of the 1046 clinical samples, 927 samples showed the growth of bacteria and no growth was observed in 119 cultures.

Among the 936 Gram negative bacteria, the ESBL producing phenotype was found most frequently among *E. coli* (412, 44%), *Klebsiella pneumoniae* (136, 14.53%), *Acinetobacter baumannii* (52, 5.56%), *Pseudomonas aeruginosa* (58, 6.2%), *Aeromonas species* [*A.hydrophila* (68, 7.26%), *A. sobria* (10, 1.07%)] followed by *Citrobacter freundii* (36, 3.85%), *Enterobacter aerogenes* (28, 2.99%), *Morganella morganii* (54, 5.77%), *Proteus mirabilis* (6, 0.64%), *Providencia stuarti* (4, 0.42%) and the remaining (66, 7.05%) were other non-fermentor Gram negative bacilli.

All the isolates were tested by using the combination discs, and 236 (25.2%) isolates were confirmed as being ESBL producers.

The ESBL phenotype was least prevalent among *Morganella, Proteus* and *Citrobacter* species, while no ESBL production was observed in *Providencia* species. It was found that Gram negative organisms predominated in the etiology of the UTI infection.

Of the 236 ESBL – producers studied, antibiogram revealed that 177 (75.0%) and 219 (92.8%) isolates to be resistant to co-trimoxazole and ampicillin respectively, indicating maximum resistance to these drugs. Piperacillin (100 mcg) Gatifloxacin (5 mcg) and Imipenem (10 mcg) constitute the reasonable option for treatment of UTI as 135 (57.2%), 127 (53.8%) and 97 (41.1%) isolates were sensitive to these antibiotics respectively.

The prevalence of ESBL – producing Enterobacteriaceae has been studied in many countries[1, 2,3,11]. To our knowledge, the present study is the first survey in Tiruchirappalli focusing on the ESBL – producing urinary isolates. Although, *E.coli* was more frequently isolated than *K.pneumoniae*, ESBL production was more prevalent in *K.pneunoniae*, which is in accordance with findings reported in previous studies [17].

During the entire period, all ESBL – positive isolates were susceptible to carbapenems, indicating that they are the drugs of choice for treating serious infections caused by ESBL – producing bacteria [17].

In conclusion, the results of this study also suggest the importance of ESBL – producing Enterobacteriaceae as a cause of infections. The high prevalence of multidrug-resistant organisms should be taken into account when choosing therapeutic agents. Further studies aimed at unraveling the molecular mechanisms of resistance will provide a better understanding of the epidemiology associated with ESBL-producing species of Enterobacteriaceae.

Hence an effort was undertaken to examine (i) the prevalence of ESBL producers among the members of Enterobacteriaceae in urinary tract infections and (ii) to determine the antibiotic susceptibility pattern of ESBL producers.

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