Antibiotic Resistance in Extra Intestinal Pathogenic *Escherichia Coli*

**Abstract**

The increase in bacterial antibiotic resistance is a major concern in India. Infections due to multidrug resistance extra intestinal pathogenic *E. coli* unquestionably have substantial effects on morbidity and mortality. The aim of this study was to conduct a systematic review of studies reporting on the prevalence of antibiotic resistance in *E. coli* in different parts of the India.

**Introduction**

In recent years, extra intestinal *E. coli* infection and a high level of drug resistance among such ExPEC is often seen in the World. The treatment of *E. coli* infections is increasingly becoming difficult because of the multi-drug resistance exhibited by the organism. As multi-drug resistance has spread, we are already coming across infections that cannot be cured with any available antibiotics. Extended spectrum β-lactamase (ESBL) producing *E. coli* has spread as a major cause of hospital-acquired infections, as well as infections in outpatient settings [1]. Genes that encode ESBLs are often found on large plasmids that also carry genes for resistance to other antibiotics [2]. Beginning in the 1990s, the frequency of resistance to fluoroquinolone antibiotics, including ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin, and nalidixic acid in *E. coli* has increased worldwide [3]. Administration of ciprofloxacin or other fluoroquinolones is a risk factor for isolation of resistant strains of *E. coli* from patients undergoing long-term hospital care, and resistance is associated with treatment failure. In addition, multi-resistance, defined as resistance to norfloxacin in addition to two or three other antibiotics, has also increased [3,4]. Several reports have indicated that quinolone resistance in uropathogenic *E. coli* is associated with decreased prevalence or expression of virulence factors compared to quinolone-susceptible strains [5,6]. Vila suggested that a possible reason for this is that virulence genes could be lost concomitantly with a mutation at codon 83 of the gyrA gene, which affects super coiling of DNA, leading to changes in gene expression. Another reason is that with exposure to quinolones and development of resistance to these agents, there is a concomitant increase in the deletion and transposition of pathogenicity islands (PAIs) [7]. Soto et al. [6] found that uropathogenic *E. coli* strains incubated with sub inhibitory concentrations of ciprofloxacin showed partial or total loss of virulence genes encoded within PAIs [6].

In a study from India have shown high degree of resistance pattern to commonly used antibiotics such as ampicillin, piperacillin, ciprofloxacin, norfloxacin. However, around 50% isolates were resistant to cefazidime. They also observed that 25% isolates were resistant to piperacillin/tazobactam and around 35% of the isolates were resistant to ceftoperazone/subactam which is quite alarming, higher sensitivity was observed in Amikacin (84%) and Nitrofurantoin (89%). Among all the antibiotics they tested highest degree of sensitivity were observed with ertapenem (97%) and other carbapenem group of drugs [8]. A study by Banu et al. [9] in patients with *E. coli* infections found around 96% ampicillin resistance, 74% co-trimoxazole, 44% ciprofloxacin, 56% gentamicin and 35% amikacin resistance respectively [9]. Yet another study by Sharma et al in Mangalore also reported high prevalence of antibiotic resistance among the *E.coli* isolates [10].

In a study from India have reported a high rate of genotypically ESBL positive isolates (70%), which indicated a high prevalence of ESBL producers in their setup compared to western figure. They have found CTX-M as the most predominant type of plasmid among the ESBL producers (88%) and only 19% were TEM and presence of SHV type was seen in very few isolates (2%). Among the combinations of ESBL genes detected, only 6% isolates were found to carry both CTX-M and SHV among the subtypes CTX-M15 was the most predominant (92%) among the isolates [11]. Zaniani et al. [12] from Iran have also reported that 44% of their isolates to be ESBL positive among them 15% were positive with SHV and 21% were positive with TEM [12]. In India Goyal et al. [13] used specific primers for TEM, SHV and CTX-M and showed that 82 (75.2%) of 109 ESBL isolates could be typed for one or more genes which is comparable to our study. Two or more ESBL genes were present in 57.3% of typeable isolates. The bla CTX-M was the most common and was present either alone or in combination with other ESBL type(s), their finding support the hypothesis that CTX-M is emerging as the dominant ESBL type in clinical isolates [13]. CTX-M-15 is known to be an ESBL that has peculiar association with community-onset *E. coli* infections. Ensor et al. [14] have shown that in India bla CTX-M-15 are the most prevalent than any other type and it is widely distributed in both North and South India. They also reported that the Indian
population represented a significant reservoir and source of bla CTX-M-15 [14].

In a study from India reported that around 10% of the ExPEC isolates were carbapenemase producers [15]. Several other studies from India have also reported the prevalence rate of 8-10% of enterobacteriaceae isolates being carbapenemase producers [16,17]. The problem with carbapenemase producing isolates is their unrivaled broad-spectrum resistance profile. These strains are usually resistant to β-lactams, aminoglycosides and fluoroquinolones. However, they usually remain susceptible to polymyxins. No extended survey with a series of human infections with carbapenemase positive isolates has been performed to determine the optimal treatment. The only therapeutic alternative may be the therapeutic administration of polymyxins, which have recently been shown to be efficient for treating multidrug-resistant gram-negative bacilli. In any case, these molecules should not be used as monotherapy and rapid determination of MICs of aminoglycosides by MIC methods (not disk diffusions) may help to choose an aminoglycoside molecule that may have kept some activity. Hence we recommended aminoglycoside and polymyxin combination would be the ideal therapy for such infection.

Conclusion

The result of this literature review underlines the necessity to establish mechanism for periodic assessment of antimicrobial susceptibility and its determinant in different population from different part of India. Such a monitoring of the antibiotic resistance pattern will help the microbiology laboratories and hospitals to make proper antibiotic policies to limit the spread of MDR E. coli strains among the population.

References
