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Research Article

SINGLE CENTRE REVIEW OF THE CLINICAL AND MICROBIOLOGICAL PROFILE OF UROSEPSIS *E. COLI* ISOLATES

Pragya Agarwala[1], *Archa Sharma[2] and Kamal Sharma[3]
[1]Department of Microbiology, All India Institute of Medical Sciences, Raipur
[2]Department of Microbiology, All India Institute of Medical Sciences, Bhopal
[3]Department of Cardiology, U. N. Mehta Institute of Cardiology and Research Centre, Ahmedabad, Gujarat, India
**Author for Correspondence: drarchasharma@gmail.com*

ABSTRACT
In this paper we reviewed the clinical and microbiological profile of urosepsis *E. coli* isolates of the year 2014. This study was carried out from January 2014 to December 2014 in a tertiary care centre in India. The susceptibility patterns and multidrug resistance rates of the urosepsis *E. coli* isolates were studied and compared with the non-urosepsis isolates. Relevant demographic and clinical details of the urosepsis patients were obtained from the medical records, and the associated factors were studied. A total of 773 isolates of *E.coli* were isolated from blood cultures in 2014. Of them 120 were identified to be associated with urosepsis. The prevalence of Extended spectrum beta lactamase production (ESBL), as screened by disc diffusion testing using ceftazidime was almost similar in the two groups, 69% in the isolates from urosepsis, and 70% in the other group (p value=0.90). Our data indicated high prevalence of ESBL production in blood stream *E. coli* isolates. High susceptibility towards aminoglycosides and carbapenems was seen in *E. coli* isolates associated with urosepsis. Thus these two groups can serve as empiric antibiotics of choice in a female patient with known predisposing factors for developing a UTI, and presenting with signs and symptoms of urosepsis.

INTRODUCTION
Urosepsis refers to the presence of systemic inflammatory response syndrome secondary to a severe infection of the urinary tract, with the risk of multi-organ dysfunction and shock (Kalra and Raizada, 2009). Urosepsis accounts for approximately 25% of all sepsis cases and may develop from a community or nosocomial acquired urinary tract infection (UTI). The underlying UTI is almost exclusively a complicated one with involvement of parenchymatous urogenital organs (e.g. kidneys, prostate) (Wagenlehner *et al*,, 2011).
The majority of the cases of urosepsis are attributable to gram-negative bacilli. *Escherichia coli* (*E.coli*) is the predominant organism responsible for a large number of cases of community as well as hospital acquired UTI, across all age groups. *E.coli* has been reported to cause 50% to 75% of cases of urinary tract infection (UTI) with bacteremia, from ((Kalra and Raizada, 2009; Al-Hasan *et al.*, 2010). The other organisms implicated in causing urosepsis include *Proteus* spp., *Enterobacter* spp, *Klebsiella* spp. and *Pseudomonas spp*. Less frequently involved are Gram-positive organisms like *Enterococcus* spp, Methicillin resistant *Staphylococcus aureus* and *Staphylococcus epidermidis*.
In this paper we reviewed the clinical and microbiological profile of urosepsis *E. coli* isolates of the year 2014.

Aim and objectives
1. To analyze the antimicrobial susceptibility profile of *E.coli* isolates causing urosepsis and to compare it with the susceptibility profile of other isolates of *E. coli* from blood stream infection.
2. To study the various factors associated with *E. coli* urosepsis cases seen in 2014.

MATERIALS AND METHODS
This study was carried out from January 2014 to December 2014 in a tertiary care centre in south India. All non-duplicated consecutive isolates of *E.coli* causing blood stream infection in the year 2014 were included in the study. Blood culture was performed on the samples with the BacTAlert automated

system (bioMe´rieux). The growth positive specimens were Gram stained and subcultured onto Blood agar and MacConkey agar. The gram negative bacilli were identified based on the cultural characteristics and biochemical reactions using preliminary screening media- mannitol motility medium, triple sugar iron agar, indole production and citrate utilization. Antimicrobial susceptibility by Kirby Bauer disk diffusion was performed, as per Clinical and Laboratory Standards Institute (CLSI 2014) guidelines. The *E coli* isolates were classified into two groups, first group comprising of isolates causing urosepsis and the other including isolates from sepsis without a concomitant or preceding UTI. An isolate was considered as an urosepsis isolate only if the same organism grew in blood culture along with or subsequent to a growth in urine culture, with the two showing the same antimicrobial susceptibility pattern. The susceptibility patterns and multidrug resistance rates of the urosepsis *E. coli* isolates were studied and compared with the non-urosepsis isolates. Relevant demographic and clinical details of the urosepsis patients were obtained from the medical records, and the associated factors were studied.

RESULTS

A total of 773 isolates of *E.coli* were isolated from blood cultures in 2014. Of them 120 were identified to be associated with urosepsis. The mean age of the urosepsis patients was 48.78 years (SD 19.25) and 74 (61.7%) were females. The various demographic and associated factors for the urosepsis cases are mentioned in the table below.

Table 1: Demographic and clinical factors associated with urosepsis *E. coli* isolates

	Number	Percentage
Gender		
Male	46	38.3%
Female	74	61.7%
Age		
0-16	5	4.2%
17-40	49	40.8%
41-60	29	24.2%
>60	37	30.8%
Diabetes	49	40.8%
Urinary tract abnormalities	18	15%
Post-operative	9	7.5%
Post-labour	9	7.5%
Pregnancy	6	5%
Chemotherapy	3	2.5%

The antibiotic susceptibility rates of the urosepsis isolates were compared with the non-urosepsis isolates and are depicted in the table below.

Table 2: Percentage susceptibility of blood stream *E coli* isolates (urosepsis vs. others) to various antibiotics

Antibiotic	Urosepsis causing *E. coli* (%)	Other isolates of *E. coli* (%)	p-value
Ceftazidime	31.1	30.4	0.90
Gentamicin	55.8	49.7	0.23
Amikacin	99.1	87.8	0.0001
Netilmycin	97.5	84.7	0.0001
Ciprofloxacin	27.4	25.9	0.733
Amoxi-clav	40	Not available	-

Cotrimoxazole	37.2	Not available	-
Nitrofurantoin	83.3	Not available	-
Piperacillin/tazobactam	61	59.1	0.76
Cefoperazone/sulbactam	88.2	76.9	0.005
Meropenem	97.5	89.1	0.002
Imipenem	97.5	88.9	0.002
Tigecycline	100	97.7	0.57
Colistin	100	99.4	1

Prevalence of multidrug resistance in the two groups

The prevalence of Extended spectrum beta lactamase production (ESBL), as screened by disc diffusion testing using ceftazidime was almost similar in the two groups, 69% in the isolates from urosepsis, and 70% in the other group (p value=0.90).

Carbapenem resistance was found in 2.5% of urosepsis isolates. On the other hand, about 11% of the non urosepsis *E. coli* isolates carbapenem resistance (p value=0.002).

DISCUSSION

Infections of the urinary tract are responsible for a large number of cases of secondary healthcare-associated bacteremia. Female gender, older age, urinary catheterization, diabetes mellitus, urinary tract obstruction and pregnancy are known risk factors for developing a urinary tract infection (Platt *et al.,* 1986; Ramzan *et al.,* 2004). In this study, about 62% of the patients were females. About 41% of the infections occurred in the age group 17 to 40, followed by the elderly (31%). Diabetes mellitus was found to be the most common associated factor, seen in 49 patients (41%). Urinary tract obstruction secondary to urolithiasis, benign prostatic hyperplasia and polycystic kidney disease was seen in 15% of the patients. Pregnancy (5%), post-operative (7.5%) and post-labour states (7.5%) were the other associated factors. A very small number of patients (2.5%) were on chemotherapy.

High rates of resistance to ciprofloxacin (72.6%) and trimethoprim-sulfamethoxazole (62.8%) were noted. This is consistent with the reports of increasing resistance to these drugs seen in large population based studies (Al-Hasan *et al.,* 2009; Laupland *et al.,* 2008). High rates of prevalence of extended spectrum beta-lactamase producers was seen, which has also been reported in other studies on *E. coli* bacteremia. ESBL rates between 41% to 76% have been reported from various parts of the country(8–10). Significantly higher susceptibility to amikacin and netilmycin (99% and 97.5% respectively) was seen in urosepsis isolates, when compared to the non-urosepsis E. coli isolates (p=0.0001). On the other hand, no significant difference in susceptibility to gentamicin was seen (p value=0.23).

60% of the isolates were resistant to amoxicillin-clavulanic acid, 39% to piperacillin-tazobactam, while only 12% were resistant to cefoperazone-sulbactam. The prevalence of carbapenem resistance was found to be significantly low in urosepsis isolates (2.5%) compared to the non-urosepsis isolates (11%), p value= 0.002. These rates are comparable to the rates reported from other centres. While the multicentric SENTRY study (Castanheira *et al.,* 2011) conducted across in 14 hospitals in various Indian cities in 2006-2007 showed an overall resistance of 2.7% in Enterobacteriaceae isolates, Dutta *et al.* (2012) in their analysis of ten year resistance profile of blood stream infections found 6% carbapenem resistance in *E. coli.*

The isolates were largely susceptible to nitrofurantoin (83%). No resistance was seen to colistin and tigecycline.

Conclusion:

Our data indicated high prevalence of ESBL production in blood stream *E. coli* isolates. High susceptibility towards aminoglycosides and carbapenems was seen in *E. coli* isolates associated with urosepsis. Thus these two groups can serve as empiric antibiotics of choice in a female patient with known predisposing factors for developing a UTI, and presenting with signs and symptoms of urosepsis. On the other hand, it is imperative to look for carbapenem resistance in blood stream infections not

related to UTI. In cases of carbapenem resistance, susceptibility to colistin and tigecycline should be tested.

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