Int J Pharm Bio Sci 2016 April; 7(2): (P) 18 – 23

Original Research Article **Pharmacology**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

ANTIBIOTIC RESISTANCE PATTERN AMONG IN-PATIENTS OF URINARY TRACT INFECTION AT TERTIARY CARE HOSPITAL OF COASTAL KARNATAKA- A RETROSPECTIVE STUDY

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ABSTRACT

The main determinant of empiric treatment of urinary tract infections (UTI) is antibiotic sensitivity patterns of uropathogens in a population. The patterns of resistance among uropathogensin tertiary care hospital in South India can help establish local guidelines on treatment of UTI. A retrospective observational study was conducted at Kasturba Hospital, Manipal, from 1st Jan 2012 to 31st Dec 2012. The case records of 500 patients of either sex who were admitted to Kasturba Hospital, Manipal with diagnosis of UTI were studied. Sensitivity testing was done in each isolate. *E.coli* comprised 64%; *Klebsiella* 16%; *Proteus* 3.7%; *Pseudomonas* 6.15%; *Staphylococcus* 2.8%; and *Enterococcus* 4.92% of the isolates. Extended-spectrum beta-lactamase (ESBL) producers among *E coli*, *Klebsiella* and *Proteus* were 63.41%, 53.84% and 33.33% respectively.*E.coli* was highly resistant to amoxicillin-clavulanate (67.8%), and ciprofloxacin (67%) whereas it was least resistant to imipenem (1%), cefoperazone-sulbactam (3.9%) and amikacin (9.8%). *Klebsiella*was highly resistant to ciprofloxacin (69.2%) whereas it was least resistant to imipenem (0%) and cefoperazone-sulbactam (3.2%). *Proteus* was highly resistant to amoxicillin-clavulanate (67.3%) and ceftriaxone (66.7%), whereas it was least resistant to cefoperazone-sulbactam (0%), imipenem (12.5%), amikacin (16.7%) and netilmicin (16.7%). High prevalence of extended spectrum beta lactamase (ESBL) producers among uropathogens were seen in our study. Moreover, alarming rate of resistance to ampicillin, amoxicillin-clavulanate and ciprofloxacin should prevent the use of these commonly used antibiotics for empiric treatment of UTI.

KEYWORDS: **UTI, antibiotic resistance, E. Coli, ESBL**

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INTRODUCTION

Urinary tract infection (UTI) is associated not only with high healthcare but also social cost. According to one study, In USA, it accounts for 7 million annual clinic visits with a huge cost of alomost$1.6 billion. In developing countries, it is considered as the most common type of body infection which clinicians encounter with an approximate incidence of 18/1000 persons per year[1] .Usually *Escherichia coli* (*E. coli*) is the most common organism, responsible for 75% to 90% of uncomplicated UTI isolates, among both outpatients and inpatients. Other less commonly isolated organisms in patients with UTI include *Staphylococcus saprophyticus*, *Klebsiella spp.*, *Proteus spp*., *Enterococcus spp*. and *Enterobacter spp*[2]. Today, antibiotic resistance pathogens have become more prevalent and UTI is not an exception. This in turn leads to an increased number of UTIs in outpatient as well as in inpatient settings. However, the prevalence of reported antimicrobial resistance varies regionally and nationally depending on prior antibiotic use, the patient population and other factors[3]. It has been seen that urinary pathogens especially from community patients are resistant to majority of the commonly used antimicrobial agents which requires periodic monitoring of susceptibility pattern especially in a rural setting[4]. Monitoring antibiotic susceptibility patterns of uropathogens at a local level is essentialas it will help to know the current trends of antibiotic resistance and will also provide assistance in selecting appropriate empirical therapy.[1]Moreover, routine study to know the resistance pattern of community acquired uropathogens has not been done extensively[5]. This study was conducted to determine the trends of the antimicrobial resistance pattern of the uropathogens, which can enable the clinicians to endorse a potent and rationale anti-microbial policy for treatment of UTI.

MATERIALS AND METHODS

A retrospective observational study was carried out at Kasturba Hospital, Manipal, a tertiary care teaching hospital from 1st Jan 2012 to 31st Dec 2012. The case record files of patients with a diagnosis of UTI were retrieved from the medical records section after obtaining approval from Institutional Ethics Committee (letter no. IEC/324/2011). All the patients with a diagnosis of UTI based on clinical, laboratory and culture sensitivity report during the above period were included in the study. Patients diagnosed with UTI associated with other systemic infection and malignancies were excluded. We reviewed the culture sensitivity report of above patients. To evaluate the culture sensitivity report, a specially designed proforma containing relevant details such as demographics (age, gender), clinical data (symptoms, laboratory findings), and drug data was used. In our hospital, antibiotic susceptibility was confirmed by disk diffusion technique on Muller- Hinton medium (Becton Dickinson Microbiological Systems, Cockysville, MD), and was performed according to the Clinical Laboratory Standard Institute (CLSI) guidelines[6] . Statistical analysis was primarily descriptive.

RESULTS

The case records of 500 patients who were admitted to Kasturba Hospital, Manipal with a diagnosis of UTI from 01st Jan 2011 to 31st Dec 2011 were studied. Out of 500 patients with UTI, 294 (58.80%) were male and 206 (41.20%) were female. The study revealed peak incidence of UTI in the age group of 61-70 years in males and 41-50 years in females. The age distribution of study sample is shown in figure 1.Out of 500 patients, 325 (65%) reported positive growth on culture during data collection. The gram negative bacteria isolated were *E.coli, Klebsiellaspp*, *Proteus spp*, *Pseudomonas spp*. and *Acinetobacterspp*, whereas gram positive bacteria isolated were *Enterococcus spp*, *Streptococcus spp* and *Staphylococcus spp*. Overall, *E.coli* was most commonly isolated organism (63.07%) followed by *Klebsiellaspp*(16%), *Pseudomonas spp* (6.15%), *Enterococcus spp* (4.92%) and *Proteus spp* (3.69%) as shown in figure 2.Comparision of antibiotic resistance pattern of E. coli and Klebsiella spp. is shown in figure 3. Out of the total isolates, there were 205 isolates of E.coli, 52 isolates of Klebsiella spp. and 12 isolates of Proteus spp. ESBL producers among E. coli isolates, Klebsiella spp., Proteus spp. were 63.41%, 53.84% and 33.33% respectively (Figure 4).Antibiotic resistance pattern of other gram negative bacterial isolates was shown in Table 1.

Table 1

Antibiotic resistance pattern of other gram negative bacterial isolates (percentage)

Organism	amx	Ct	ctx	ctz	gen	cip	amk	ntl	Cfpm/cpr	Ipm/mem	tzp	scf	caz	tobi
***Acinetobacter spp.*(n=8)**	75	25	25	25	0	0	0	0	0	0	0	0	-	-
***Proteus spp.*(n=12)**	67.3	66.7	66.7	25	33.3	50	16.7	16.7	50	12.5	25	0	-	-
***Pseudomonas spp.* (n=20)**					80	80	60	60	70	6	20	20	60	40

**** amx - Amoxicillin- clavulanic acid; ctx- Ceftriaxone; cxm- Cefuroxime; ctz- Cotrimoxazole; gen-Gentamicin; cip- Ciprofloxacin; amk-Amikacin; ntl- Netilmicin; cfpm/cpr- Cefipime/cefpirome; tc- Ticarcilllin-clavulanic acid, ipm/mem- Imipenem/meropenem; tzp- Piperacillin-tazobactam; scf- Cefoperazone-sulbactam; caz- Ceftazidime; Tm- Tobramycin***

Figure 1
Age distribution of study sample

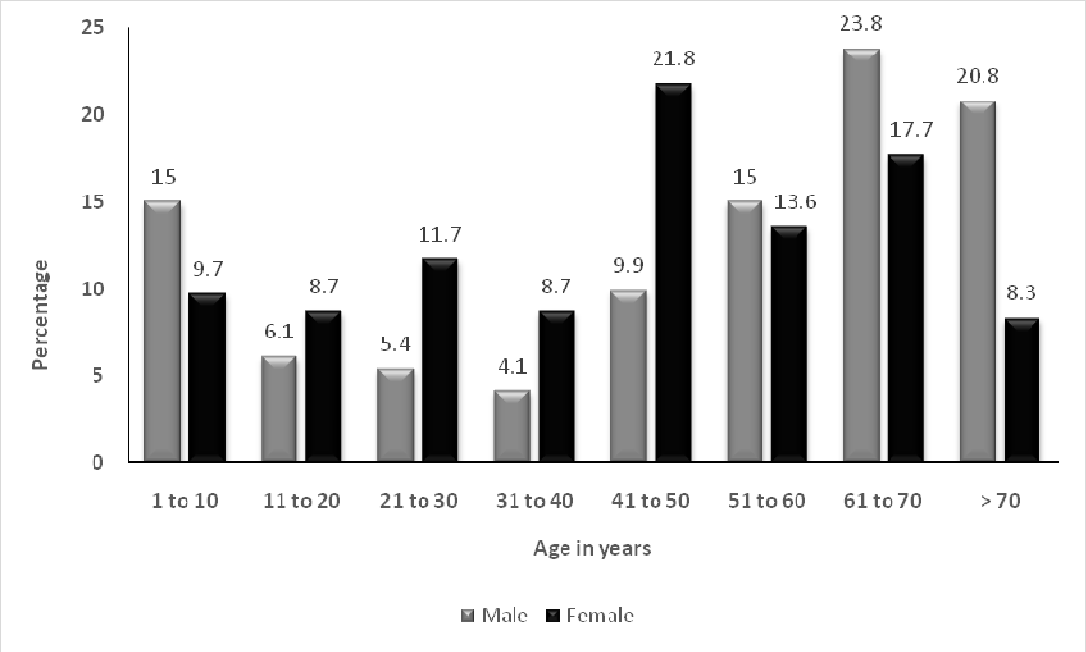


Figure 2
Pathogens causing UTI among positive urine culture (n=325)

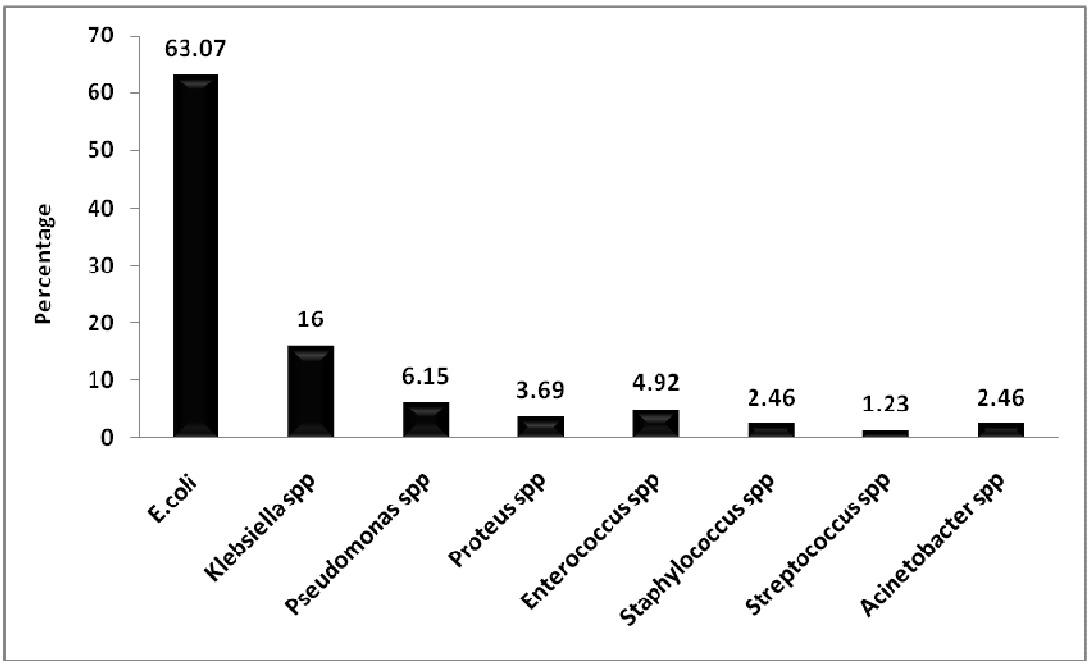


Figure 3
Antibiotic resistance pattern of E. coli and Klebsiella spp.

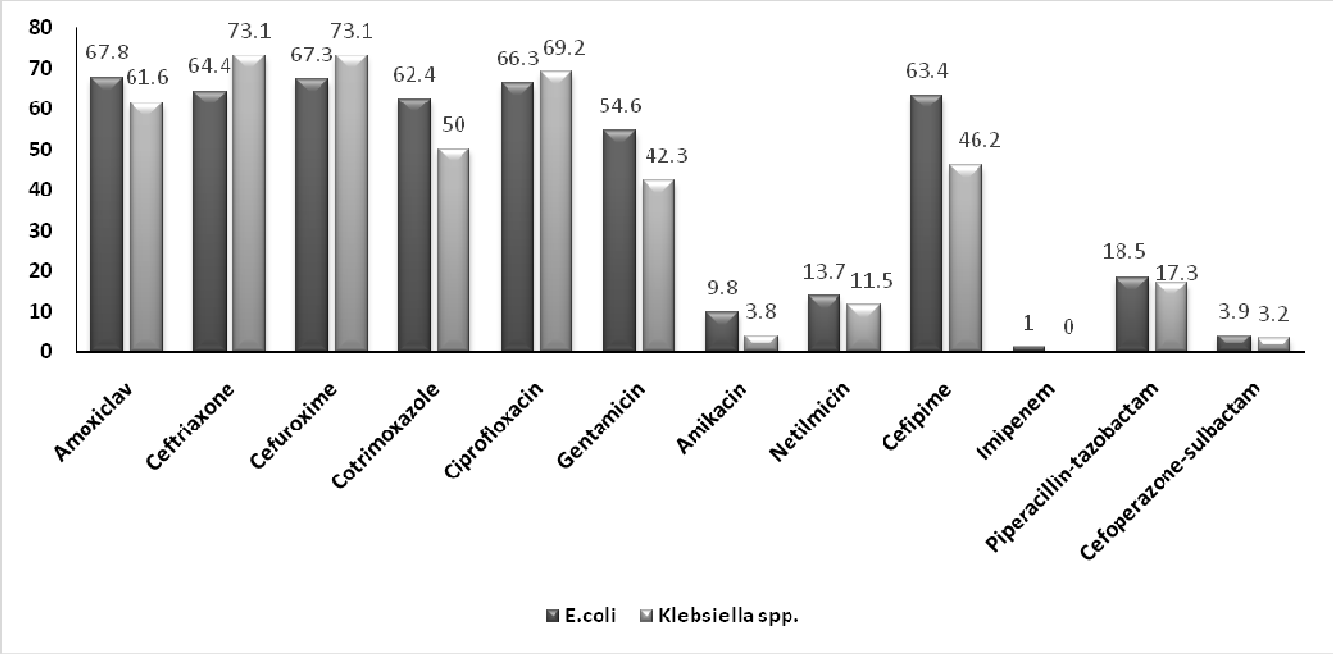
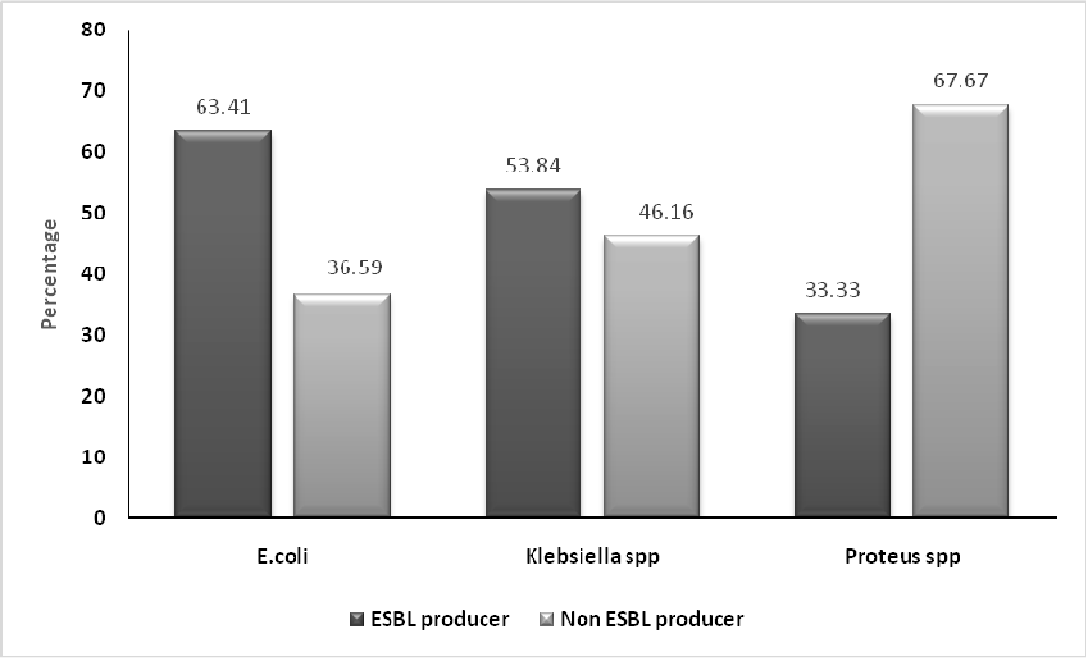


Figure 4
Comparison between ESBL producer and non-ESBL producer (n=269)



DISCUSSION

Major factors contributing to the emergence of antimicrobial resistance include poverty, inadequate access to drugs and irrational use of drugs leading to inappropriate clinical management of UTI worldwide. In developing countries like India, important factors posing a threat for resistant uropathogens include less stringent controls on prescription practices, unaccepted antimicrobial manufacturing processes and disruption of an infection control infrastructure due to constraint of adequate resources[1]. This study was undertaken to evaluate the antibiotic susceptibility pattern in UTI among 500 patients over a period of one year in a tertiary care hospital in South India. Our study results showed higher prevalence of UTI in males as compared to females, which was consistent with studies conducted in South India by Chowta[7] and Savithaet al[8]. Another study by

Mahesh et al[9] in complicated UTI also showed higher prevalence of UTI in males as compared to females. The mean age of the patients was higher in males as compared to females. Our study showed the peak incidence of UTI in males and females was in the age group of 61-70 and 41-50 years respectively. This was consistent with similar study done in India[8]. We found that *E. coli* was the most common uropathogen responsible for UTI accounting for 63.07% of all culture-positive isolates, followed by *Klebsiella spp*. being the next most common organism which was found in 16% of isolates. Previous studies have found almost similar proportion of bacterial species isolates[10,11,12]. Our study revealed that the most common isolate *E. coli*, showed a higher resistance rate towards ampicillin, amoxicillin-clavulanic acid, cefuroxime, ceftriaxone and ciprofloxacin, which was in accordance with the findings of the studies which were done by Manjunath et al[13] and Akram et al[5]. The reason for the increased resistance rate might be the irrational treatment, prophylactic usage and the over the counter sale of the antimicrobials without a proper prescription or an appropriate dosing schedule. However, majority of the isolates showed a higher sensitivity pattern towards imipenem, cefoperazone-sulbactam and amikacin. *Klebsiella spp.* showed an increased resistance to ampicillin, cefuroxime, cefotaxime/ceftriaxone and decreased resistance to amoxicillin-clavulanic acid, cotrimoxazole and amikacin as compared to *E.coli*. *Pseudomonas spp.* showed an increased resistance towards the ciprofloxacin, gentamicin and cefepime whereas it was least resistant to imipenem and piperacillin-tazobactam. These findings were in contrast to study done by Dograet al[10] where resistance to gentamicin (51.7%) was lower but it was higher in case of imipenem (34.4%) and piperacillin-tazobactam (48.2%). *Proteus spp*. was highly resistant to amoxicillin-clavulanic acid, aztreonam, cefuroxime and ceftriaxone, whereas it was least resistant to cefoperazone-sulbactam, imipenem/meropenem, amikacin and netilmicin. In the present study, we also observed high prevalence of ESBL producing *E.coli* and *Klebsiella spp*. as compared to non ESBL*E.coli* and *Klebsiella spp.*In contrast to other studies where *Klebsiella*spp was more often reported as an ESBL producer[14,15], we observed E.coli as a major pathogen responsible for ESBL production. These differences could be due to variable patterns of prescription of antibiotics among different geographical areas. In case of *Proteus*spp, ESBL negative isolates were more as compared to ESBL positive. Since UTI is relatively common, one of the possible reason for high prevalence of ESBL producing urinary isolates could be wide spread use of broad-spectrum antibiotics in these patients. We also found that majority of the ESBL producing isolates were resistant to more than one drug. Due to increased prevalence of resistant isolates in UTI, international society like Infectious Diseases Society of America (IDSA) recommends obtaining information on local resistance rates and also emphasises to run local, regional, and national surveillance programmes. This will guide to know the suitable empirical treatment based on susceptibility of uropathogens[16]. The important limitations of our work is that it is a retrospective study. Moreover, we have included only in-patients of UTI therefore findings of our study cannot be generalised to entire population. Further prospective studies needs to be conducted to overcome the above limitations.

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