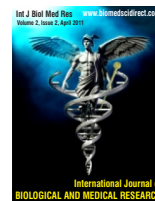




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Original article

Changing trends in the spectrum of antimicrobial drug resistance pattern of uropathogens isolated from hospitals and community patients with urinary tract infections in Tumkur and Bangalore.

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ABSTRACT

Antimicrobial drug resistance is one of the major threats due to widespread use of antimicrobial drugs in general population. Also, it is known that the common infecting organism and pattern of resistance changes over time. The present study highlights the trend of organisms and their susceptibility patterns in the current scenario. A total number of 6350 samples were analysed in various hospitals at Tumkur and Bangalore during the study period. The study analysed resistance pattern of most common uropathogens in 30 antimicrobials of different classes. Culture positive cases of urinary tract infections (UTI) were included for the analysis. About 12 different species of uropathogens were identified from 6350 cases {in the present study}. Among them *E.coli* was the most common uropathogen which constituted 59.2% of the total samples followed by *Klebsiella* spp (12.1%), *Enterococcus* spp (10.1%) and *Pseudomonas* spp (9.3%). Also female patients (58.5%) were more vulnerable to UTI than male patients (41.5%). Out of 30 antimicrobials tested, Ampicillin has shown the highest resistance by different uropathogens i.e. 80.4% followed by ciprofloxacin (73%), amoxicillin (70.4%), norfloxacin (53.3%) while Penicillin, Furazolidone, Azithromycin, Doxycycline, Linezolid and Novobiocin offered least resistance. The present study identifies the changing etiologic trends of UTI and also a steady increase in development of antimicrobial resistance especially against drugs which were highly effective

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1. Introduction

Urinary Tract Infection [UTI] remains one of the most common bacterial infections and second most common infectious disease in the community practice. Approximately about 150 million people were diagnosed with UTI each year. In present scenario, the essence of antimicrobial drug resistance of major uropathogens has posed a global threat [1]. Of the various uropathogens, the most common organisms are *E.Coli*, *Enterococcus fecalis*, *Staphylococcus aureus*, *Enterococci* spp and *Klebsiella* spp [1-3]. But most of these organisms have developed resistance to antimicrobial agents like (cotrimoxazole, ampicillin, amoxicillin,

nitrofurantoin)[2-5], (piperacillin, nalidixic acid)[2,6], (erythromycin, chloramphenicol)[3] Fluoroquinolones[7,8], (tetracyclines, carbenicillin)[9] and 3rd generation cephalosporins [10].

Inappropriate and empirical usage of wide spectrum antibiotics, insufficient hygiene, immunosuppression and prolonged hospitalization are some of the major aetiological factors that elevate the chances of infection [2,3]. The use of low standard antimicrobials further adds to the emerging drug resistance, which could turn to be one of the biggest factor for mortality in developing and underdeveloped countries [1].

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There were many studies conducted in the past in different geographical regions of the world, to assess the antimicrobial resistance in uropathogens. Most of the studies disclosed the augment of antimicrobial resistance to a panicking situation. Many studies also exposed the common uropathogens that caused UTI and also the gender that was more vulnerable. The commonest infecting organism and pattern of resistance keep changing over time. Hence, the present study was performed to identify the changing etiologic trends of UTI and the antimicrobial resistance.

2. Materials and Method

This was a retrospective study which used laboratory report sheets of urine culture results and antibiograms carried out at various hospitals in Tumkur and Bangalore.

Table. 2.1. Classification of Antimicrobial Agents used in the Study.

Name of the group	Name of antimicrobials
Fluoroquinolones	Ciprofloxacin, Norfloxacin, Ofloxacin
Macrolides	Erythromycin, Azithromycin
Tetracyclines	Doxycycline
Nitrofurans	Nitrofurantoin
Penicillins	Ampicillin, Amoxycillin, Piperacillin, Carbenicillin
Cephalosporins	Cephalexin, Cefuroxime, Cefixime, Cefuroxime, Ceftriaxone, Ceftazidime, Cefepime
Monobactams	Aztreonam
Carbapenems	Imipenem
Aminoglycosides	Gentamicin, Netilmicin, Tobramycin, Amikacin
Nitro benzene derivatives	Chloramphenicol
Oxazolidinone	Linezolid
Others	Clindamycin, Cotrimoxazole, Novobiocin

A total number of 6350 samples were reviewed in this study, from August 2005 to July 2010. This study assessed resistance in a total number of 30 antimicrobials (Table 2.1). All Culture positive samples report from community acquired as well as nosocomial UTI was considered. Infection reports belonging to all the age group and both the sex were reviewed during the study. In the study, patients were divided into four different age groups i.e. NB (New Born)-19 years, 20-49 years, 50-79 years and patients who aged more than 80 years old. The study assessed the following variables from the record sheets which were analysed and recorded for study purpose: age and sex of patients, microbial species (as recorded in urine culture reports), and drug resistance as recorded in antibiograms forms.

3. Results

The study analysed 6350 samples of positive urinary tract infection record sheets in a period of one year. The recorded data sheets included reports from those of new born up to geriatrics more than 90 years old.

Table 4.1. Common Uropathogens

Organisms isolated	Number (%)
E.coli	3761 (59.2%)
Klebsiella spp	773 (12.1%)
Enterococcus spp	645 (10.1%)
Pseudomonas spp	592 (9.3%)
Citrobacter spp	231 (3.6%)
Acinetobacter spp	152 (2.3%)
Enterobacter spp	55 (0.87%)
Candida spp	48 (0.75%)
Proteus spp	47 (0.74%)
Staphylococcus spp	27 (0.42%)
Providencia spp	12 (0.18%)
Salmonella spp	07 (0.11%)

About 12 species of microorganisms were identified that offered resistance to different antimicrobials in different pattern. E.coli (59.2%) topped the charts among the most commonly identified uropathogens, followed by Klebsiella spp (12.1%), Enterococcus spp (10.1%) and Pseudomonas spp (9.3%). (Table 4.1)

Table 4.2 : Antimicrobial Resistance Pattern

Antimicrobials	Resistance
Ampicillin	80.4 %
Ciprofloxacin	73%
Amoxicillin	70.4%
Norfloxacin	53.3%
Cephalexin	49.4%
Cotrimoxazole	47.9%
Cefuroxime	47.4%
Ceftazidime	46.5%
Ceftriaxone	43.2%
Gentamicin	40.2%
Cefepime	14.4%
Ofloxacin	7.7%
Imipenem	7.5%
Carbenicillin	7.5%
Netilmicin	7.2%
Amikacin	6.9%
Aztreonam	5.8%
Tobramycin	5.6%
Nitrofurantoin	5.3%
Piperacillin	4.4%
Cefixime	2.2%
Chloramphenicol	0.4%
Novobiocin	0.1%
Linezolid	0.1%
Doxycycline	0.1%
Azithromycin	0.1%
Furomycin	0.1%

The specific antimicrobial resistance pattern was assessed in the most common uropathogens, in top ten antimicrobials that showed highest resistance.

The antimicrobial resistance spectrum assessment revealed that 80.4% of the identified organisms were resistant towards ampicillin, 73% against ciprofloxacin and 70.4% towards amoxycillin. The study showed 40%-53% of the identified organisms were resistant against norfloxacin, cephalexin, cotrimoxazole, cefuroxime, ceftazidime, Ceftriaxone and gentamicin. A detailed insight of antimicrobial resistance pattern is been illustrated in table (4.2).

Table 4.3. Antimicrobial drug resistance in the commonly isolated organisms

Name of the antimicrobial	Name of the organisms			
	<i>E.coli</i>	<i>Klebsiella spp</i>	<i>Enterococcus spp</i>	<i>Pseudomonas spp</i>
Ampicillin	91%	98%	57.5%	99%
Amoxycillin	84%	90%	26.2%	98%
Ciprofloxacin	76%	37%	70%	85%
Norfloxacin	74.5%	34%	61.5%	90%
Cotrimoxazole	63%	42%	10.8%	100%
Cephalexin	62%	42.9%	13.8%	28%
Cefuroxime	62%	43.6%	10%	42%
Ceftazidime	58%	46.5%	12%	35%
Ceftriaxone	56.4%	42.9%	6.7%	42%
Gentamicin	42.5%	21.4%	17.6%	55.6%

E.coli was the most common aetiological agent of UTI in our study. *E.coli* was highly resistant towards ampicillin (91%) followed by amoxycillin (84%). The most commonly identified uropathogens chiefly belonged to the family of Enterobacteriaceae (*E.coli*, *Klebsiella spp* and *Enterococcus spp*) and Pseudomonaceae (*Pseudomonas spp*) (Table 4.3). The resistance pattern of these organisms from different families differed from one class of drugs to another, i.e. the organisms that belonged to Enterobacteriaceae family showed predominant resistance against Penicillins (amoxycillin, ampicillin), Fluoroquinolones (ciprofloxacin, norfloxacin), Aminoglycosides (gentamicin) and Cephalosporins (cephalexin, cefuroxime, Ceftriaxone and ceftazidime). The resistance of the organisms from Enterobacteriaceae family varied from 42%-98%, except *Enterococcus spp* which had offered relatively less resistance to all other class of drugs except Fluoroquinolones (ciprofloxacin 90%) (Table 4.3). As mentioned before, ten antimicrobials were identified in this study that tendered resistance from 12 different species of uropathogens. The antimicrobial resistance ranged anywhere from 42% to 98%. Some antimicrobials like Novobiocin, Azithromycin, Doxycycline, Linezolid and Furomycin showed least or considerably negligible resistance of 0.1% to different uropathogens. (Table 4.2)

Resistance Pattern of Pseudomonas spp (Table 4.4)

Name of the antimicrobial	Resistance in percentage
Ofloxacin	81.4%
Netilmicin	75.6%
Imipenem	72%
Carbenicillin	69.3%
Amikacin	65.6%
Aztreonam	55%
Tobramycin	53.4%
Piperacillin	37.5%

Pseudomonas spp, which were one of the top 4 most regularly, recognized organism in this study depicted a completely different resistance pattern when compared with the organisms from Enterobacteriaceae family. *Pseudomonas spp* were more resistant to Fluoroquinolones (Ofloxacin), Aminoglycosides (Netilmicin, Amikacin and Tobramycin), carbapenems (imipenem) and Monobactams (Aztreonam) (Table 4.4).

Sex distribution of UTI (Table 4.5)

Gender	Number of organisms isolated (%)
Male	2635 (41.5%)
Female	3715 (58.5%)

As cited before 6350 samples were assessed, with Male: Female ratio being 1.4:1 (Table 4.5), showing high vulnerability of females towards UTI.

Age distribution of UTI (Table 4.6)

Age group	Most Common Isolated Uropathogens From Different Age Groups					Total (%)
	<i>E.coli</i>	<i>Klebsiella spp</i>	<i>Enterococcus spp</i>	<i>Pseudo-monas spp</i>	Others	
NB-19	735	162	84	71	28	1080 (17%)
20-49	1145	245	240	218	248	2088 (32.9%)
50-79	1631	288	278	269	265	2731 (43%)
80>	250	78	43	34	46	451 (7.1%)

Total number of cases reviewed: 6350

In this study UTI was more prevalent in the age group of 50-79 years. And *E.coli* was the most commonly isolated uropathogen irrespective of age groups. (Table 4.6)

4. Discussion

Constant survey of antimicrobial resistance plays a very important role in the empiric treatment of UTI. In a health care setting, a very little extra venture on antimicrobial resistance survey can facilitate to accrue extremely practical information of the resistance pattern. The present study reveals the resistance pattern of uropathogens isolated from both community acquired as well nosocomial UTI. Ampicillin, amoxycillin, ciprofloxacin, norfloxacin, cephalexin were some of the antimicrobials that bade heavy resistance from organisms that belonged to Enterobacteriaceae family. While *Pseudomonas spp* offered heavy resistance against Ofloxacin, imipenem, netilmicin etc. Among the 12 species of uropathogens that were identified in the study, *E.coli* (59.3%) emerged as the most predominant organism followed by *Klebsiella spp* (12.3%), which is in par with similar studies [3,4,10,13,16,18-20,23,25,27]. The study also revealed that females (60.5%) were more susceptible to UTI than males, which is also similar to other studies [1,10,11].

The age wise data was analysed in order to assess the frequency of UTI in different age groups. This study portrayed that aged people i.e. 50-79 years were more prone to UTI than any other groups. This result is in comprehension with other studies [1,12,13].

Antimicrobial resistance offered by different uropathogens is one of the barricades that might hinder a successful treatment. Antimicrobial resistance pattern varies with time which might increase or decrease [9]. This study also indicated the different pattern of antimicrobial resistance in different families of uropathogen, i.e. Enterobacteriaceae family and Pseudomonaceae family. E.coli identified in this study were highly resistant to ampicillin (<90%) and amoxicillin (<80%). E.coli offered almost equal resistance towards ciprofloxacin and norfloxacin (75% and 74%), cephalosporins (56% - 62%) while Klebsiella spp were comparatively less resistant to these antimicrobials (ciprofloxacin and norfloxacin) i.e. 37% and 34%. Studies that were conducted in India showed that, the isolates of E.coli showed high resistance towards Ampicillin and amoxicillin which was in agreement with this study [1,3,7,14] but did show that ciprofloxacin resistance is escalating [15].

The Klebsiella spp was exceedingly resistant to ampicillin (98%), followed by amoxicillin (90%) which showed highest resistance to any particular drug in this retrospective survey. This high resistance to ampicillin and amoxicillin by Klebsiella spp was seen in many other studies [1,2,10,16].

Pseudomonas spp showed a different pattern of resistance than that of Enterobacteriaceae. Pseudomonas spp were more resistant to antimicrobials like amikacin (65.6%), netilmycin, ciprofloxacin (85%), Ofloxacin (81%), Aztreonam (55%), carbenicillin (69.3%), imipenem (72%).

This study had come across a few cases of ESBL (Extended Spectrum Beta Lactamases) producing E.coli, which showed high resistance mainly against cephalosporins. These cephalosporins are extensively used in all healthcare sectors for treatment of infections. These ESBL producers mainly belonged to the Klebsiella spp when it was first discovered in the mid 1980's but now the most causal organism of UTI, E.coli has picked up the trend of synthesizing ESBL, which is increasing in number. This increasing ESBL producing E.coli have also developed resistance against penicillins as well [17]. These ESBL producing E.coli has made treatment difficult and costlier. These organisms have shown high resistance towards ciprofloxacin (76.5%) and cotrimoxazole (74.4%) and susceptible towards amikacin and fosfomycin [18].

5. Conclusion

This retrospective study furnished much needed information on the common uropathogens and their drug resistance pattern. This study is clear that E.coli is on a rampage, causing most cases of UTI. Antimicrobials like ampicillin and amoxicillin have developed resistance to such a level that, prescribing them would definitely lead to treatment failure. Development of resistance against penicillins and cotrimoxazole can be predictable, which might be due to wide spread use. But, the matter of concern is resistance has also affected the use of Fluoroquinolones (Ciprofloxacin and norfloxacin) and cephalosporins.

Aminoglycosides were in use for quite a long period in the history of infectious diseases. They have not considerably developed much resistance against all uropathogens but for Pseudomonas spp. The current study shows that Pseudomonas spp has developed considerable resistance against amikacin, Netilmycin and Tobramycin.

Females and geriatrics populations are more vulnerable to UTI when compared to males and other age groups. Females are more prone to UTI because of their characteristic anatomy and physiological changes while geriatrics populations might be because of their suppressed immunity.

The Indian scenario is something different than the scenario in the west. Uropathogens show increased resistance; hence it is necessary to diagnose clinically followed by sensitivity testing, as direct empiric treatment might lead to treatment failure. UTI guidelines can only be developed after thorough surveillance of drug resistance in the Indian sub-continent.

UTI and other infectious diseases are to be considered dangerous due to global escalation of drug resistance pattern.

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