

Gender and Antibiotic Resistance Pattern of Uropathogen in a Tertiary Care Level

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ABSTRACT

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Background: Antibiotic therapy for UTI has become more difficult in the recent years, due to the widespread emergence of drug resistance (especially multi-drug resistance) among urinary pathogens. This study was designed to analyse the impact of the sex of the patient on antibiotic resistance.

Materials and Methods: A retrospective study, based on laboratory data on the bacterial isolates from urine samples submitted for culture and antibiotic susceptibility to the department of microbiology during the period of 2008 to 2011.

Result: Out of 1239 bacterial isolates included in this study, 745 (60.1%) were obtained from in-patients, while 494 (39.9%) were obtained from out-patients. 494 (39.87%) of the total isolates were from males, while 745 (60.13%) were from females. Higher susceptibility rates to all antibiotics tested, except for ciprofloxacin, were seen in females. This was found to be statistically significant, except with cotrimoxazole. The difference in susceptibility rates among in-patients and out-patients (higher susceptibility rates for all antibiotics, except ciprofloxacin) were statistically significant for all antibiotics, except with ampicillin, cotrimoxazole and ciprofloxacin.

Conclusion: Antibiotic resistance is more likely in urinary isolates from male patients and from in-patients. Greater caution is warranted in selecting antibiotics to treat these patients and should ideally be guided by urine culture and antibiotic susceptibility results.

Keywords: UTI, Antibiotic Resistance, Sensitivity, Uropathogens, Urinary Infection

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BACKGROUND

Urinary tract infections (UTI) are one of the commonest type infections, necessitating antibiotic use, encountered in clinical practice.¹ Antibiotic therapy for UTI has become more difficult in the recent years, due to the widespread emergence of drug resistance (especially multi-drug resistance) among urinary pathogens.^{2,3} Some of the common antibiotics used in the therapy of UTI are ampicillin, cephalosporins, gentamicin, quinolones, cotrimoxazole and nitrofurantoin.^{3,5} However, bacterial uropathogens show significant levels of resistance to almost all these antibiotics.^{2,3}

It had been observed in our laboratory that bacterial isolates from males with UTI were more likely to exhibit drug resistance than similar isolates from female patients. This study was, thus, designed to analyse the

impact of the sex of the patient on antibiotic resistance.

MATERIALS AND METHODS

This was a retrospective study, based on laboratory data on the bacterial isolates from urine samples submitted for culture and antibiotic susceptibility to the department of microbiology. The study was conducted in Sree Gokulam Medical College, a tertiary-care teaching hospital in Trivandrum, Kerala, India, and was cleared by the Institution Ethics Committee.

Among all the patients who were subjected to urine culture in our laboratory from 01.01.2008 to 31.08.2011, all those with significant bacteriuria (more than 1,00,000 colony forming units per ml of urine) were included in this study. Among these, the following were excluded from the study: Isolates of Enterobacteriaceae family lacking data on susceptibility to ampicillin,

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cefazolin, cefuroxime, cefotaxime, gentamicin, ciprofloxacin, cotrimoxazole or nitrofurantoin, Isolates of *Pseudomonas aeruginosa* lacking data on susceptibility to ceftazidime, gentamicin or ciprofloxacin and Isolates of Gram positive cocci lacking data on susceptibility to ampicillin, cefazolin, gentamicin, cotrimoxazole or nitrofurantoin. Isolates of *Pseudomonas aeruginosa* are known to be intrinsically resistant to ampicillin, cefazolin, cefuroxime, cefotaxime cotrimoxazole and nitrofurantoin.^{6,7} Hence these isolates were counted as resistant to these drugs.

Second and third generation cephalosporins are not usually tested in Gram positive urinary isolates.⁸ Our laboratory normally did not test Gram positive urinary isolates for quinolone susceptibility. Hence, for Gram positive urinary isolates, no data were available for the susceptibility of Gram positive urinary isolates to cefuroxime, cefotaxime, ceftazidime and ciprofloxacin.

As per the above criteria, 1239 urinary isolates were included in this study. These organisms had been isolated in culture and identified as per standard microbiological techniques. Antibiotic susceptibility testing had been performed using disc-diffusion method, as per the CLSI guidelines which were recommended at that time.^{8,11} Some of the susceptibility results (such as cephalexin for *Staphylococcus aureus* and cotrimoxazole for *Enterococcus faecalis*) were interpreted using the CLSI guidelines, rather than being directly tested. This data was extracted from the laboratory database and fed into Libre Office Calc (version 3.5.7.2). After organising the data in Calc, it was analysed using the statistical software R (version 2.14.1).

RESULTS

As mentioned earlier, 1239 bacterial isolates were included in this study, among which, 745 (60.1%) were obtained from in-patients, while 494 (39.9%) were obtained from out-patients. 494 (39.87%) of the total isolates were from males, while 745 (60.13%) were from females.

The commonest organisms encountered were *Escherichia coli* (761 isolates: 61.42%), *Klebsiella pneumonia* (174 isolates: 14.04%), *Pseudomonas aeruginosa* (87 isolates: 7.02%) and *Enterococcus faecalis* (40 isolates: 3.23%). **Table 1** gives the details of all the other isolates.

Among the total isolates, susceptibility rates were lowest for ampicillin (14.12%) and highest for nitrofurantoin (76.43%). **Table 2** gives the susceptibility rates of all the other antibiotics-tested.

Table 1. Bacterial isolates in UTI

Organism	IP	OP	Total
<i>Acinetobacter baumannii</i>	16	14	30
<i>Citrobacter freundii</i>	27	9	36
Coagulase negative Staphylococci	13	16	29
<i>Enterobacter aerogenes</i>	8	5	13
<i>Enterococcus faecalis</i>	33	7	40
<i>Escherichia coli</i>	438	323	761
<i>Klebsiella oxytoca</i>	3	3	6
<i>Klebsiella pneumoniae</i>	102	72	174
<i>Proteus mirabilis</i>	6	4	10
<i>Proteus vulgaris</i>	5	4	9
<i>Pseudomonas aeruginosa</i>	71	16	87
<i>Serratia marcescens</i>	2	0	2
<i>Staphylococcus aureus</i>	4	4	8
<i>Streptococcus spp.</i>	17	17	34
Total	745	494	1239

A comparison between the susceptibility rates of urinary isolates from men and those from women revealed that the isolates from men showed a much lower susceptibility rate with all the antibiotics tested, except for ciprofloxacin and cotrimoxazole (**Table 3**). Ciprofloxacin was found to have a higher susceptibility rate among urinary isolates from males, whereas the susceptibility rates of urinary isolates from both males and females were almost the same. Estimation of the p-value using Pearson's chi square test showed that these differences in susceptibility rates among males and females were statistically significant ($p < 0.05$) for all antibiotics, except with cotrimoxazole ($p = 0.688$).

Similar comparisons between the susceptibility rates of isolates from out-patients and in-patients showed that the susceptibility rates of these organisms were higher in out-patients than in in-patient with all antibiotics tested, except for ciprofloxacin and cotrimoxazole (**Table 4**). Isolates showed similar susceptibility to cot-

Table 2. Susceptibility of bacterial isolates in UTI

Antibiotic	Resistant	Susceptible	Not Tested	Susceptibility Rate (%)
Ampicillin	1064	175	0	14.12
Cefazolin	804	435	0	35.11
Cotrimoxazole	715	524	0	42.29
Cefuroxime	681	447	111	36.08
Cefotaxime	654	474	111	38.26
Ciprofloxacin	641	487	111	39.31
Ceftazidime	613	515	111	41.57
Gentamicin	539	700	0	56.50
Nitrofurantoin	292	947	0	76.43

Table 3. Comparison between susceptibility rates of bacterial isolates from males and females with UTI			
Antibiotic	Susceptibility rate (%)		P-value
	Male	Female	
Ampicillin	10.12	16.78	0.001
Cefazolin	21.66	44.03	<0.001
Cefuroxime	22.06	45.37	<0.001
Cefotaxime	24.29	47.52	<0.001
Ceftazidime	30.57	48.86	<0.001
Gentamicin	46.15	63.36	<0.001
Ciprofloxacin	46.36	34.63	<0.001
Cotrimoxazole	41.50	42.82	0.688
Nitrofurantoin	70.45	80.40	<0.001

rimoxazole, while with ciprofloxacin, susceptibility rate of isolates from in-patients were higher than that of isolates from out-patients.

Estimation of the p-value using Pearson’s chi square test showed that these differences in susceptibility rates among in-patients and out-patients were statistically significant ($p < 0.05$) for all antibiotics, except with ampicillin ($p = 0.074$), cotrimoxazole ($p = 0.591$) and ciprofloxacin ($p = 0.061$). The proportion of in-patients was much higher in males (65.79%) than in-females (56.38%). This was found to be statistically significant ($p = 0.001$) using the Pearson’s chi square test.

Analysis of the age and sex distribution of the patients included in the study revealed that both sexes have a higher likelihood of contracting UTI in the extremes of age (**Figure 1**).

However, females show an additional peak in likelihood of UTI in the reproductive age-group (18 – 45 years). Furthermore, among females, the majority (60.28%) out of a total of 287 cases in this age-group were out-patients.

Table 4. Comparison between susceptibility rates of bacterial isolates from out-patients and in-patients with UTI			
Antibiotic	Susceptibility rate (%)		P-value
	Out-patients	In-patients	
Ampicillin	16.40	12.62	0.074
Cefazolin	43.93	29.26	<0.001
Cefuroxime	43.32	31.28	<0.001
Cefotaxime	45.34	33.56	<0.001
Ceftazidime	47.37	37.72	0.002
Gentamicin	64.98	50.87	<0.001
Ciprofloxacin	35.43	41.88	0.061
Cotrimoxazole	43.32	41.61	0.591
Nitrofurantoin	80.97	73.42	0.003

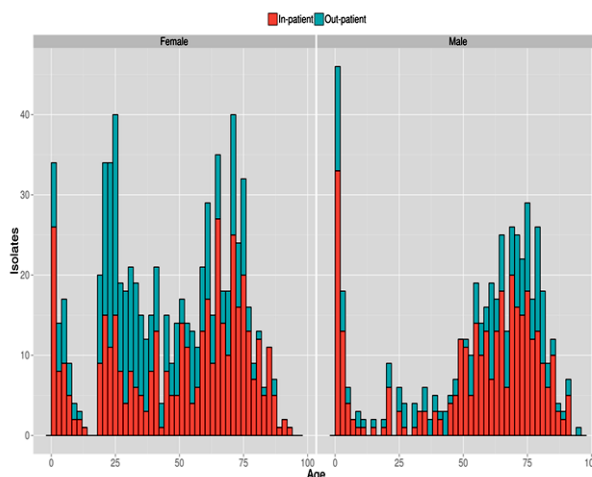


Figure 1. Age and sex distribution in cases of UTI

DISCUSSION

The commonest organisms encountered in this study were *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Enterococcus faecalis*. This is similar to the results of numerous studies from all over the world.

Studies from around the world show wide differences in the susceptibility rates of urinary isolates to the different antibiotics tested. For example, the susceptibility rate of cefotaxime/ceftriaxone was as high 85% in a study from Taiwan and as low as 58.7% in a study from Nagpur, India.^{4,12} Quinolone susceptibility levels also varies from study to study: a study from Bangladesh showed a susceptibility rate of 74%, while the study from Nagpur reported a susceptibility rate of 44.9%.^{4,13}

Our study showed that the male sex is a significant risk factor in acquiring UTI with antibiotic resistant strains: this was consistent with similar observations made in a study from the United States of America as well as a study from the United Kingdom^{14,15} Nitrofurantoin was found to be the most useful antibiotic tested, with an overall susceptibility rate of 76.43%. This is consistent with several other studies as well.^{16,18} Nitrofurantoin, thus, appears to be a very useful first-line drug in the therapy of uncomplicated lower UTI, especially in women.

Analysis of our data revealed that males with UTI were more likely to be in-patients than females with similar illnesses. Separately exploring the age-wise distribution of male and female patients revealed the possible reason for this phenomenon: **Figure 1** clearly shows that a significant proportion of female patients (38.52%) were from the reproductive age-group (18-45

years). Of these, the majority were out-patients. On the other hand, male patients were primarily from the 0-5 year age group and from the 50-70 year age group, and were thus, more likely to be in-patients.

UTI being one of the commonest hospital acquired infections, it stands to reason that the population with higher proportion of in-patients would be more likely to contract UTI with multi-drug resistant hospital flora.

CONCLUSION

Antibiotic resistance is more likely in urinary isolates from male patients and from in-patients. Greater caution is warranted in selecting antibiotics to treat these patients and should ideally be guided by urine culture and antibiotic susceptibility results.

Nitrofurantoin appears to be a very useful first-line antibiotic in the therapy of uncomplicated lower UTI, especially in females.

END NOTE

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