



Prevalence of Multidrug-Resistant, Extensively Drug-Resistant and Pandrug-Resistant Uropathogens Isolated From Urinary Tract Infection Cases in Dhaka, Bangladesh

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Abstract

Background: The resistance pattern of uropathogens is increasing very rapidly because of the unsorted, insufficient, and incoherent usage of antibiotics. The aim of this study was to evaluate the prevalence of multidrug-resistant (MDR), extensively drug-resistant (XDR), and pandrug-resistant (PDR) uropathogens which were isolated from the urinary tract infection (UTI) cases in Dhaka, Bangladesh.

Methods: In this cross-sectional study, a total of 21167 urine samples were collected from January 2016 to December 2018, followed by using conventional methods, as well as Kirby-Bauer disc diffusion method for urine culture and susceptibility, respectively. Finally, SPSS software was utilized to analyze the obtained data.

Results: From among 21167 urine samples, 2469 (11.66%) cases were bacteriologically positive. In UTI cases, males proportion were higher compared to females (in ≤ 10 and > 60 to ≤ 90 years age groups) and females in the age groups between 10 and 60 and >90 years suffered more than males ($P < 0.05$). In addition, 172 (7.0%), 1337 (54.2%), and 845 (34.2%) cases were identified as XDR, single drug-resistance (SDR), and non-drug-resistance (NDR), respectively. Although the number of female XDR cases was higher than males, the percentages of male cases were higher compared to female cases in this study. The most predominant drug-resistance cases (18.7%) were found in the age group between 21 and 30 years ($P < 0.05$). Eventually, the isolates of *Escherichia coli* were the most prevalent cases that carried XDR (5.4%) and MDR (39.7%).

Conclusions: In general, it is extremely alarming to increase XDR and MDR uropathogens. This bacterial resistance can be prevented through control measures that limit the spread of resistant bacteria and the regular monitoring of this resistance phenotype of uropathogens, along with the rational use of antimicrobial therapy.

Keywords: UTI, MDR, XDR, PDR, Uropathogens



Background

The resistance of antimicrobial agents in pathogenic bacteria has become a significant public health problem. According to Magiorakos et al, (1) this pattern occasionally extends to multidrug-resistant (MDR) or extensively drug-resistant (XDR) or even pandrug drug-resistant (PDR). Urinary tract infection (UTI) is considered as a different type of infection which is caused by the above-mentioned resistant bacteria. It is known that UTI is the most common infection in the world, especially

Bangladesh. This infection is due to the main colonization of normal and opportunistic microflora (2). In the third world country like Bangladesh, the rate of UTI patients is high due to poor hygiene, long time catheterization, uncontrolled sexual intercourse, pregnancy, spermicidal contraception, and the like (3-6).

Many of antibiotics and their super generations are used to prevent the UTIs. Unfortunately, several studies indicate that many uropathogens have become resistant to a wide range of antibiotics due to abuse, overuse,

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and uncompleted dosages (7-9). Some are also getting resistant to efficacious antibiotics by adopting genetic transformations and different mechanism of mutations (10-13). In addition, this resistant bacterium provides daily challenges for individuals to infectious diseases throughout the world (14), leading to fatalities from simple microbial infections to treatment-mediated complications (15).

Furthermore, worldwide increases in SDR, MDR, and XDR bacteria are certainly well-known. The incidence of the following bacteria has also received special attention, especially in developing countries:

- Methicillin-resistant *Staphylococcus aureus*
- Vancomycin-resistant *S. aureus*
- Coagulase-negative staphylococci
- Glycopeptides intermediate-sensitive *S. aureus*
- Vancomycin-resistant *Enterococcus* species
- Penicillin-resistant *Streptococcus pneumoniae*
- Extended-spectrum β -lactamase-producing bacteria
- Carbapenem-resistant bacteria (16).

Accordingly, the present study sought to investigate the prevalence of MDR, XDR, and PDR uropathogens in Dhaka which caused UTIs as per standardized international terminology created by the European Centre for Disease Control, along with the Centre for Disease Control and Prevention, Atlanta (1).

Materials and Methods

Study Design and Setting

The study was designed to collect urine samples from 21167 cases with (>70%) or without the symptoms of UTIs. After getting permission from IBN SINA trust Ethical Committee, verbal informed consent was obtained from the subjects, and they completed a written standardized questionnaire which was kept confidential during the research. The whole study was conducted in the Microbiology Laboratory (IBN SINA D. Lab, Badda, Hosen Market, Dhaka-1212, Bangladesh) which was approved by the International Standards Organization and Gulf Accreditation Center.

Sample Collection and Bacteriological Assessment

The early-morning midstream urine samples were aseptically collected from 21167 subjects including 5081 males and 16086 females. The MacConkey agar (Oxoid), blood agar (Oxoid), and HiCrome UTI agar (HiMedia) media were applied for the inoculation of all the urine samples, maintaining biosafety level II. To observe the growth of bacteria, all the plates were incubated at 37°C for 48 hours. Finally, the isolates were identified by using biochemical tests like Triple Sugar Iron (TSI-Oxoid), Motility Indole Urea (MIU-Oxoid), and Simmons Citrate (Oxoid) agar, as well as colonial morphology with the naked eye and/or microscopic examination (17).

Antibiotic Susceptibility Assessment

For antibacterial susceptibility, Kirby Bauer disc diffusion method (commercially available antibiotic discs in Bangladesh) was utilized (17). The following commercially available antibiotic discs were employed for susceptibility test: Amikacin (30 μ g, Oxoid), amoxycyclav (amoxicillin + clavulanic acid, 30 μ g, Oxoid), amoxicillin (20 μ g, Oxoid), azithromycin (15 μ g, Oxoid), aztreonam (30 μ g, Oxoid), colistin (10 μ g, Oxoid), cefepime (30 μ g, Oxoid), ceftriaxone (30 μ g, Oxoid), cefixime (5 μ g, Oxoid), ceftazidime (30 μ g, Oxoid), cefotaxime (30 μ g, Oxoid), ciprofloxacin (5 μ g, Oxoid), cloxacillin (5 μ g, Oxoid), doxycycline (30 μ g, Oxoid), fusidic acid (10 μ g, Oxoid), gentamicin (10 μ g, Oxoid), imipenem (10 μ g, Oxoid), linezolid (30 μ g, Oxoid), levofloxacin (5 μ g, Oxoid), meropenem (10 μ g, Oxoid), mecillinam (25 μ g, Oxoid), nitrofurantoin (300 μ g, Oxoid), nalidixic acid (30 μ g, Oxoid), netilmicin (30 μ g, Oxoid), piperacillin-tazobactam (110 μ g, Oxoid), trimethoprim-sulfamethoxazole (25 μ g, Oxoid) and vancomycin (30 μ g, Oxoid).

Then, the results were interpreted by measuring the zone of inhibition against each of the organisms. Further, American Type Culture Collection (ATCC) strains were applied as the control strain (8,18). The isolated microorganisms were classified as MDR (non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial categories), extensively resistant (non-susceptible to ≥ 1 agent in all but ≤ 2 antimicrobial categories), and PDR (non-susceptible to all antimicrobial agents listed.) microorganism as described by Magiorakos et al (1).

Statistical Analysis

SPSS (Statistical Package for Social Science) software, version 18 was used for data analysis. Furthermore, the chi-square test was utilized to compare the groups and $P < 0.05$ was considered as statistically significant.

Results

A number of 21167 urine samples were collected in this study, among which 2469 (11.66%) and 18698 (88.34%) were found bacteriologically positive and negative, respectively.

Table 1 shows the distribution of UTI cases by age and sex. Most of the subjects were female and the highest number of subjects were within 21-30 years age group. Furthermore, a higher number of males were found in the age groups of ≤ 10 and > 60 to ≤ 90 years and a higher number of females were found within the age groups of 10 to 60 and ≥ 90 years as compared to males.

Figure 1 illustrates the distribution of non-drug-resistance (NDR), single drug-resistance (SDR), MDR, XDR, and PDR uropathogens. MDR, XDR, and NDR cases were observed in 54.2%, 7%, and 4.7%, respectively. No PDR case was found in our study.

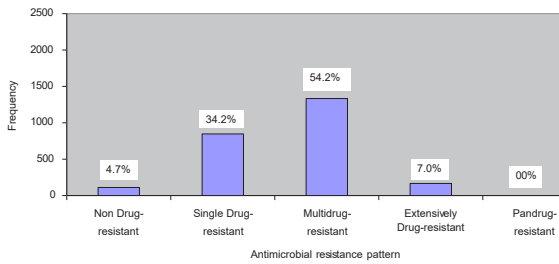


Figure 1. Distribution of antimicrobial resistance pattern. (n=2469)

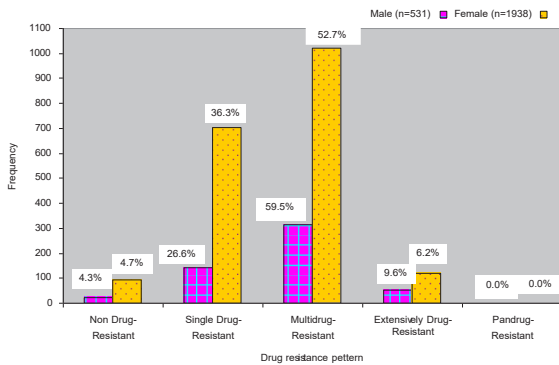


Figure 2. Distribution of drug resistance pattern by gender

Figure 2 displays the distribution of drug-resistance pattern by gender. As shown, females were predominating in all cases of SDR, MDR, and XDR.

Table 2 represents the drug-resistance pattern of UTI cases in different age groups. Predominant drug-resistance cases (18.7%) were found in the 21-30-year age group. The numbers of XDR cases (1.3%) were observed in the age group of 61-70 years which was higher than all the other age groups. The results of the study also revealed that the number of MDR cases were higher than that of all other drug-resistance patterns in all age groups.

The distribution of the drug-resistance pattern in the isolated pathogens of UTI cases is provided in Table 3. Based on the results, *E. coli* was the most predominant isolate (72.4%). In the present study, the highest number of XDR cases were *E. coli* (5.4%), followed by *Klebsiella* spp. (0.6%), *Pseudomonas* spp. (0.4%), and *Enterococcus* spp. (0.3%). The maximum number of MDR cases were also contributed to *E. coli* (39.7%) and *Enterococcus* spp. (4.1%).

Discussion

As previously described, the misuse and abuse of antibiotics are responsible for drug resistance and some bacteria naturally develop resistance by the consequence of their adaptation to the environment. In addition, resistance develops by the exposure of microorganisms to different antibiotics which increases the selective pressure and favors the development of resistance (12). Whether it is natural or man-made, it is a more alarming message

Table 1. Distribution of Urinary Tract Infection Cases by Age and Sex

Age Group (y)	Male (n=531)		Female (n=1938)	
	No	(%)	No	(%)
1-10	116	(21.8)	201	(10.4)
11-20	11	(2.1)	144	(7.4)
21-30	46	(8.7)	415	(21.4)
31-40	45	(8.5)	255	(13.2)
41-50	50	(9.4)	286	(14.8)
51-60	67	(12.5)	284	(14.6)
61-70	114	(21.5)	230	(11.9)
71-80	64	(12.1)	95	(4.9)
81-90	17	(3.2)	22	(1.1)
91-100	1	(0.2)	6	(0.3)
Total	531	(100)	1938	(100)

regarding increasing the drug resistance. This study aimed to evaluate the prevalence of antibiotic resistance pattern among bacteria which were isolated from patients with UTIs. For this reason, 21167 urine samples were tested, of which 2469 (11.66%) of them were bacteriologically positive. Other studies also showed that the bacteriological positivity rate in UTI cases was around 10% in Bangladesh (4, 8).

UTIs were frequently found in the age group of 21-30 years. For example, Asaduzzaman et al reported that UTIs were prevalent among the age group of 21-30 years. They further showed that people were sexually active in this age group. Furthermore, they used different types of contraceptives, foams, gels, diaphragms, and spermicides which were at higher risk of developing UTIs. The results of the study revealed that males in the age group ≤10 years further suffered from UTI compared to females because uncircumcised male infants appeared to be an increased risk of UTIs (13). A higher number of females than males were observed in the age group of 10 to 60 and >90 years (P<0.05).

Figure 1 shows the distribution of the antibiotic resistance pattern of NDR (susceptible to all listed antimicrobial agents), SDR (non-susceptible to ≥1 agent in ≥2 antimicrobial categories), MDR (non-susceptible to ≥1 agent in ≥3 antimicrobial categories), XDR (non-susceptible to ≥1 agent in all but ≤2 antimicrobial categories), and PDR (non-susceptible to all listed antimicrobial agents.) cases (1). Overall, 115 (4.7%) NDR, 845 (34.2%) SDR, 1337 (54.2%) MDR, and 172 (7.0%) XDR cases were detected in our study while not observing any PDR cases. On the other hand, Begum et al. in their study found 70.67% MDR and 14% XDR cases but no PDR cases (2). The results showed the distribution of drug-resistance pattern by gender (Figure

Table 2. Distribution of Antimicrobial Agent Resistance Pattern by the Age Group of UTI Cases

Age Group(y)	Non-drug-Resistance	Single Drug-Resistance	Multidrug-Resistance	Extensively Drug-Resistance	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
1-10	12 (0.5)	101 (4.1)	185 (7.5)	19 (0.8)	317 (12.8)
11-20	12 (0.5)	58 (2.3)	77 (3.1)	8 (0.3)	155 (6.3)
21-30	30 (1.2)	192 (7.8)	214 (8.7)	25 (1.0)	461 (18.7)
31-40	14 (0.6)	111 (4.5)	155 (6.3)	20 (0.8)	300 (12.2)
41-50	12 (0.5)	112 (4.5)	189 (7.7)	23 (0.9)	336 (13.6)
51-60	18 (0.7)	114 (4.6)	195 (7.9)	24 (1.0)	351 (14.2)
61-70	15 (0.6)	96 (3.9)	202 (8.2)	31 (1.3)	344 (13.9)
71-80	2 (0.1)	46 (1.9)	96 (3.9)	15 (0.6)	159 (6.4)
81-90	0 (0.0)	14 (0.6)	21 (0.9)	4 (0.2)	39 (1.6)
90-100	0 (0.0)	1 (0.1)	3 (0.1)	3 (0.1)	7 (0.3)
Total	115 (4.7)	845 (34.2)	1337 (54.2)	172 (7.0)	2469 (100)

Abbreviation: UTI, Urinary tract infection.

Table 3. Distribution of Drug-Resistance Pattern Among the Isolated Pathogens

Isolated Uropathogens	Non-drug-Resistance	Single Drug-Resistance	Multidrug-Resistance	Extensively Drug-Resistance	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
<i>E. coli</i>	82 (3.3)	593 (24)	980 (39.7)	133 (5.4)	1788 (72.4)
<i>Klebsiella</i> spp.	6 (0.2)	44 (1.8)	66 (2.7)	15 (0.6)	131 (5.3)
<i>Enterobacter</i> spp.	18 (0.7)	83 (3.4)	36 (1.5)	0 (0.0)	137 (5.5)
<i>Pseudomonas</i> spp.	1 (0.0)	9 (0.4)	33 (1.3)	11 (0.4)	54 (2.2)
<i>Proteus</i> spp.	1 (0.0)	9 (0.4)	20 (0.8)	2 (0.1)	32 (1.3)
<i>Acinetobacter</i> spp.	0 (0.0)	3 (0.1)	5 (0.2)	1 (0.0)	9 (0.4)
<i>Citrobacter</i> spp.	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)
<i>Serratia</i> spp.	0 (0.0)	2 (0.1)	0 (0.0)	0 (0.0)	2 (0.1)
<i>Staph. aureus</i>	1 (0.0)	34 (1.4)	42 (1.7)	2 (0.1)	79 (3.2)
<i>Staph. saprophyticus</i>	2 (0.1)	26 (1.1)	41 (1.7)	0 (0.0)	69 (2.8)
<i>Enterococcus</i> spp.	1 (0.0)	25 (1.0)	100 (4.1)	8 (0.3)	134 (5.4)
<i>Streptococcus</i> group B	2 (0.1)	17 (0.7)	14 (0.6)	0 (0.0)	33 (1.3)
Total	115 (4.7)	845 (34.2)	1337 (54.2)	172 (7.0)	2469 (100)

2). The percentages of male cases were higher than those of females regarding MDR (59.5%) and XDR (9.6%) cases. However, no PDR cases were detected in both males and females ($P < 0.05$).

The predominant drug resistance was found in the age group between 21 to 30 years (18.7%), followed by 14.2%, 13.9%, 13.6%, and 12.8% in the respective age group of 51-60, 61-70, 41-50, and 1-10 years, respectively (Table 2). The XDR cases in the age group of 61 to 70 were higher (1.3%) than the other age groups. The results also revealed that the percentage of all MDR cases were higher than the other drug-resistance patterns in all age groups. The age groups of 21-30 years were the most predominant subjects for NDR, SDR, and MDR cases but the most predominant age group was 61-70 years in XDR cases ($P < 0.05$).

Table 3 presented the distribution of the isolated

uropathogens by the drug-resistance pattern in UTI cases. Based on the data, *E. coli* was the most predominant isolate (72.4%) in the present study. Several studies also indicated that *E. coli* was the most predominant uropathogen (4,8). In our study, the highest number of XDR uropathogens belonged to *E. coli* (5.4%), followed by *Klebsiella* spp. (0.6%), *Pseudomonas* spp. (0.4%), and *Enterococcus* spp. (0.3%). The prevalence of MDR cases was also predominated by *E. coli* (39.7%) and then *Enterococcus* spp. (4.1%). Contrarily, XDR cases were not found in *Enterobacter* spp., *Citrobacter* spp., *Serratia* spp., *Staphylococcus saprophyticus*, and *Streptococcus* group B ($P < 0.05$).

Conclusions

The results of the study revealed that the MDR and XDR cases but not PDR cases are increasing steadily. Based on

the results, different awareness programs are needed for both the population and health professionals about the adverse effect of resistance and the importance of the correct use of antibiotics. By adopting this initiative, it is expected to control the spread of resistant bacteria which cause UTIs, and finally, reduce morbidity and mortality.

Ethical Approval

The ethical permission was obtained from the Ethical Committee of IBN SINA trust.

Patients' Consent

The verbally informed consent and filled-up written standardized questionnaire were used before study initiation.

Conflict of Interest Disclosures

The authors declare no conflict of interest.

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