Original article

Antibiotic resistance pattern of bacteria causing urinary tract infection in a private medical college hospital, Dhaka

Siddiqua M[1], Alam AN[2], Akter S[3], Ferdousi RS[4]

Abstract:

Background and objective: Urinary tract infection (UTI) is one of the frequently seen infections both in the world and in our country as well. *Escherichia coli (E. coli)* aremost frequently isolated in complicated or uncomplicated, nosocomial or community acquired urinary tract infections. To guide the empirical therapy, the resistance pattern of *E. coli* responsible was evaluated throughout the period in this study. ***Material and Method:*** Urine samples from outpatient / inpatient department of Ibn Sina Medical College Hospital between 1st January, 2015 and 31st December, 2015 were retrospectively analyzed. Presence of $\geq 10^5$ colony forming units/ml in urine culture was considered as significant for UTI. Isolated bacteria were identified by standard laboratory techniques and antibiotic susceptibility testing was performed by Kirby-Bauer disk diffusion method using Clinical Laboratory Standard Institute (CLSI) criteria. ***Result:*** A total of 271(13.4%) uropathogens were isolated. Overall *E. coli* accounted for 180 (66.42%) of all isolates. Resistance rates of *E. coli* to antimicrobial agents was demonstrated to be as follows: cefuroxime 82%, nalidaxic acid 74%, azithromycin 56%, cefotaxime52%, ceftazidime50%, cefixime 47%, cotrimoxazole 43%, ceftriaxone 41%, ciprofloxacin38%, amoxicillin-clavulanic acid 31%, cefepime30%, and low resistance which ranges from 9 to 1% included gentamycin 9%, meropenem 3%, imipenem2%, nitrofurantoin2% and amikacin 1%. ***Conclusion:*** As resistance rates show regional differences, it is necessary to regularly monitor regional resistance pattern to determine the appropriate empiric antibiotic treatment. The national antibiotic usage policies must be reorganized according to data obtained from these studies.

Keywords: Urinary tract infection (UTI); Antibiotic resistance pattern; *Escherichia coli (E. coli)*

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Introduction:

Urinary tract infections (UTIs) are a major cause of morbidity world wide and second most common infectious disease in community. Approximately 150 million cases are diagnosed each year[1]. It is estimated that about 35 % of healthy women suffer from symptoms of urinary tract infection at some point in their life. The incidence of UTI is greater in women as compared to men, which may be either due to anatomical predisposition or other host factors[2]. Vaginal colonization with uropathogens precedes most UTIs and also sexual activity, pregnancy, obstruction are among the other factors contributing to increasing frequency of UTI in female[3].

UTI is commonly caused by *Escherichia coli, Proteus, Klebsiella, Enterococcus, and Enterobacter* spp[4]. Most frequently *Escherichia coli* are isolated in complicated or uncomplicated, nosocomial or community acquired urinary tract infections[5,6,7]. Antimicrobial resistance among

1. Dr. Mahmuda Siddiqua, Associate Professor, Department of Microbiology, Ibn Sina Medical College, Dhaka.
2. Dr. Ahmed Nawsher Alam, Principal Scientific Officer, Institute of Epidemiology Disease Control and Research, Dhaka.
3. Dr. Sonia Akter, Assistant Professor, Department of Microbiology, Ibn Sina Medical College, Dhaka.
4. Professor Reena Saad Ferdousi, Head, Department of Microbiology, Ibn Sina Medical College, Dhaka.

Correspondence to: Dr. Mahmuda Siddiqua, Associate Professor, Department of Microbiology, Ibn Sina Medical College, Dhaka. **E-mail:** mahmuda99@yahoo.com

uropathogenic *E. coli* may be increased with temporal and geographic fluctuations which may introduce multidrug resistant *E. coli* into the community[8]. It has been recommended that guiding data adjusted to epidemiological data should be used in the selection of routine treatment[5,9]. Therefore region-specific microorganisms and their antimicrobial susceptibilities should be determined.

Indiscriminate use of antimicrobial agents is a common practice in underdeveloped and many developing countries that often leads to emergence of resistant microorganisms. So, the scope for effective antibiotic to combat bacterial infections including UTI sgradually decreased[10].As a common practice, empirical antimicrobial treatment is initiated before the laboratory results of urine culture are available which may lead to emergence and spread of antimicrobial resistant strains. Factually, antimicrobial resistance is one of the principal causes of treatment failure in infectious diseases and a great concern for UTIs[11]. The prevalence and pattern of antimicrobial resistance of uropathogens are dependent on many factors. Continuous monitoring of resistance pattern is of paramount importance for not only selecting appropriate drugs but also for rational choice of empirical therapy[12].

The present investigation was carried out to determine the recent status of prevalence of bacterial pathogens and their antimicrobial resistance in UTI patients. The aim of this study is to guide physicians to provide information about choice of proper antibiotic for empirical treatment.

Material and methods:

A study was carried out in the Microbiology department of Ibn Sina Medical College Hospital from January 2015 to December 2015. Urine samples were collected from outpatient and inpatient department for routine microscopic examination and culture sensitivity. Culture plates were incubated at a mean ambient temperature of 35±2°C for 18–48 hours; bacterial growths of $\geq 10^5$ CFU/ml of a single species were examined. The isolates obtained were identified using conventional methods. Antimicrobial susceptibilities of isolated organisms were determined using Kirby-Bauer disc diffusion system, with the recommendations of Clinical and Laboratory Standards Institute (CLSI)[13].

Identification of the uropathogens: Uropathogens were isolated on Blood agar and MacConkey agar media. All the plates were incubated aerobically at 35±2°C for 18–48 hours and the colonies were studied. For confirmation of specific bacterial spp., standard biochemical tests (MIU, KIA, Citrate, Catalase, Coagulase, bile aesculin test) were performed.

Antimicrobial susceptibility testing: Antimicrobial susceptibility testing of the isolated bacterial spp. was performed by disc diffusion method following the CLSI guidelines[13]. Antibiotic discs used as follows: amikacin (30µg), amoxyclave (30µg), azithromycin (15µg), cefepime (30µg), cefixime (05µg), cefotaxime(30µg), ceftazidime (30µg), cefuroxime (30µg), ceftriaxone (30µg), cotrimoxazole (25µg), cloxacillin (10µg), cephradine (30µg), nalidixicacid (30µg), ciprofloxacin (5µg), imipenem (10µg), meropenem (10µg), nitrofurantoin (300µg) and gentamicin (10µg). This study was approved by local ethics committee.

Results:

A total of 2021 urine samples from patients of different age and sex of suspected UTI were included in this study. Of 2021 cases, 600 (29.68 %) were male and 1421(70.32 %) were female. A total of 271(13.41 %) bacterial growths were isolated from 2021 urine samples. Rate of prevalence of uropathogens in male and female was 8.3% and 15.6 % respectively, with a male to female ratio of 1:4.4 (Table 1).

Table1: Gender distribution and growth of uropathogens

Sex	No of Sample	Growth	No growth
Male	600 (29.68%)	50 (8.3%)	550 (91.7%)
Female	1421 (70.32%)	221(15.6%)	1200 (84.4%)
Total	2021 (100%)	271 (13.4%)	1750

E. coli was the predominant isolates 180 (66.42 %), followed by *Proteus* spp. 31 (11.44 %), *Klebsiella* spp. 22 (8.12 %), *Staphylococcus saprophyticus*13 (4.80%), *Pseudomonas* spp.11 (4.06 %), *Enterococcus* spp. 10 (3.69%) and *Staphylococcus aureus* 04 (1.48%), as shown in Table-2.

Table 2: Pattern of Bacterial Isolate from Urine Cultures

ORGANISM	Frequency	Percent
E. coli	180	66.42%
Proteus	31	11.44%
Klebsiella	22	8.12%
Staph.saprophyticus	13	4.80%
Pseudomonas	11	4.06%
Enterococci	10	3.69%
Staph. Aureus	4	1.48%
Total	271	100.00%

The antimicrobial resistance patterns of isolates are shown in Table 3. High frequency of resistance ranging from 30 to 82% to most of the drugs which included cefepime, amoxyclav, ciprofloxacin, ceftriaxone, cotrimoxazole, cefixime, ceftazidime, cefotaxime, azithromycin, nalidexic acid, and cefuroxime and low resistance which ranges from 9 to 1% included gentamycin (9%), meropenem (3%), imipenem (2%), nitrofurantoin (2%) and amikacin (1%) were shown by *E. coli*.

Proteus showed high frequency of resistance to most of the drugs like cefixime, azithromycin, ceftazidime, cefuroxime, nalidexic acid ranges from 30% to 73%, moderate resistance 16 to 29% to ciprofloxacin, cefepime, cefotaxime, ceftriaxone, amoxyclav, cotrimoxazole and low resistance to gentamycin (3%) and amikacin (3%). Meropenem and imipenem were found 100% sensitive.

Klebsiella showed high frequency of resistance to cefuroxime, ceftazidime, amoxyclav, cotrimoxazole, azithromycin, cefixime, cefotaxime, nalidexic acid, ceftriaxone, cefepime, ciporofloxacin ranges from 36 to 82%. Nitrofurantoin, gentamycin, meropenem and amikacin showed low resistance from 9 to 24%. Only imipenem was found 100% sensitive for this organism.

Staphylococcus saprophyticus was found resistant to few drugs, highest being to ceftazidime 85%, cefepime (58%), cefixime (54%), nalidexic acid (50%) and azithromycin (40%). Cephradine, amikacin and imipenem were found 100% sensitive and rest of the drugs showed low resistance started from 8 to 25%.

No drug for *Pseudomonas* found to be 100% effective. All the used drugs showed resistance started from 9% (Imipenem) to 87% (Nitrofurantoin). Nalidexic acid, azithromycin, cotrimoxazole and cefotaxime were found 100% resistant to *Enterococci* and 83-80% for ciprofloxacin and cefepime. All other drugs were found resistant from 67 to 17%. Some drugs are seen to be 100% sensitive to *Staphylococcus aureus* like nitrofurantoin, gentamycin, amikacin and imipenem. Again 100% resistance was found for nalidexic acid.

Table 3: Antibiotic resistance pattern of uropathogens

Antimicrobial agents	***E.coli* N=180**	***Proteus* N=31**	***Klebsiella* N=22**	***S.Saprophyticus* N=13**	***Pseudomonas* N=11**	***Enterococci* N=10**	***S. aureus* N=4**
	R* (%)	R (%)	R (%)	R (%)	R (%)	R (%)	R (%)
Amikacin	01	03	09	00	10	17	00
Amoxyclav	31	29	55	08	73	17	13
Cefepime	30	17	36	58	55	80	50
Cefixime	47	30	45	54	73	67	88
Cefotaxime	52	23	44	12	45	100	20
Ceftazidime	50	45	55	85	64	67	88
Cefuroxime	82	62	82	25	82	50	75
Ceftriaxone	41	26	41	08	36	50	25
Cephradine	-	-	-	00	-	50	25
Ciporofloxacin	38	16	36	08	18	83	25
Cloxacillin	-	-	-	08	-	25	50
Cotrimoxazole	43	29	48	31	50	100	25
Gentamicin	09	03	18	08	27	17	00
Imipenem	02	00	00	00	09	33	00
Meropenem	03	00	16	18	27	50	12
Nalidexic acid	74	73	43	50	82	100	100
Nitrofurantoin	02	-	24	20	87	25	00
Azthromycin	56	41	46	40	64	100	57

*R=Resistance

Discussion:

Urinary tract infection is emerging as an important community acquired and nosocomial bacterial infection. Moreover, antimicrobial resistance to various classes of antimicrobials to uropathogens continues to be a major health problem in different parts of the world.[14, 15]

Urinary tract infections (UTIs) are common in women, often associated with significant morbidity and mortality[16] and may affect women of all age groups especially sexually active ones[17].Our findings are also in agreement with this generalization and rightly coincided with a study done by Deshpande et al.[18].

We studied 2021 urine samples and found significant growth in about 13.41% cases. The frequency is close to the incidence reported by Ahmed and Avasarala (2008), and Begum et al. (2006) 12.7% and 16.4% respectively[19, 20].The findings of this study is higher than the study of Singh MM et al.(2001) [21] who reported 4.2% UTI in a community based study but lower than the study of Bashar et al. (2009), and Ahmed et al. (2016) who reported frequency of UTI is 27% and 24.85% respectively in hospital or clinic based study [22, 23].

E. coli is the most common uropathogen (66.42%) isolated from the cultured urine samples of this study population. This is similar to findings from studies done in other developing countries such as India (68%)[24]and Madagascar (67%).[25] Lower incidences from other studies observed like in India 59%[26] and 52.65%[27]. Higher incidence found by Saber et al. 77.8%[28] and by Bosch et al. 75% in South Africa.[29]

According to a guideline published by Infectious Diseases Society of America (IDSA) in the year 2011, treatment of acute uncomplicated cystitis in women with nitrofurantoin, fosfomycin, trimethoprim-sulfa-methoxazole, and pivmecillinam can be initiated, if regional resistance rates against aforesaid antibiotics does not exceed 20% and in cases of suspect acute pyelonephritis fluoroquinolones or beta-lactame antibiotics.[9]

In Bangladesh the antibiotic resistance uropathogens has now become a public health concern.[30] If the patient doesn't maintain antibiotic dose regimen properly, the organism may emerge as drug resistant variant and eventually result in both nosocomial and community acquired UTIs.[31,32] Increasing drug resistance is a great concern to common bacterial infections including UTI. For empirical use of antibiotic to treat uncomplicated UTI, many underdeveloped countries and developing countries like Bangladesh use antimicrobial agents like amoxicillin, cotrimoxazole, cephradine, nalidixic acid, ciprofloxacin, azithromycin.[33] Unfortunately, it was found that all those agents had no acceptable range of sensitivity against E coli. This finding is alarming for an effective agent to find out for treatment against UTI and very difficult situation for physicians as well. Only gentamycin, meropenem, imipenem, nitrofurantoin and amikacin were found to have good sensitivity. But in uncomplicated UTI injectable drug are not acceptable because of compliance, so gentamycin is not a drug of choice. Meropenem, imipenem and amikacin are not use routinely and are kept as reserve for critical situation. So, nitrofurantoin was found to be reasonably effective agent among all antimicrobials against *E. coli* in the current setting and similar findings were seen in other studies.[34,35,36] Nitrofurantoin has some advantages too; it is cheap, can be taken orally. This study result clearly indicated that common drugs used against uncomplicated UTI are not effective for empirical treatment.

It needs to be considered whether the antimicrobial susceptibility profile of uropathogens identified in this study can be used as representative of the general situation in Bangladesh; if not, then more study to be done and real scenarios to be found out.

Conclusion:

Globally, the increasing rate of antibacterial resistance including our country is thought to be related to erroneous strategies of antibio-therapy. So it should be closely monitored both at the regional and national levels. As antibiotic resistance increasing, compared with previous years, there should be continued monitoring of this data to evaluate trend of resistance of antimicrobials for sustained optimization of empirical therapy.

Conflict of interest: None declared.

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