

Original Article**Prevalence of Fluroquinolone and Third-Generation Cephalosporin Resistance among the Patients With Urinary Tract Infection Due to Escherichia Coli**

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Abstract

Background: Urinary tract infection (UTI) has become the most frequent bacterial infections worldwide. It is well established that Escherichia coli is the predominant cause of UTI. The aim of our study was to evaluate the rates of resistance to fluroquinolone and third generation cephalosporin among the patients with UTI due to E.Coli and to assess the potential correlation between both trends.

Methods: The study was a cross sectional observational study conducted at the Department of Pharmacology and Therapeutics in collaboration with Department of Microbiology of Sylhet Women's Medical College and Hospital from 1st July 2019 to 30th June 2020.

Results: A total of 246 urine samples were collected from patients with UTI followed by isolation and identification of E.coli strains. Antibiotic sensitivity and resistance analysis was performed by the disc diffusion method employing multiple antibiotic discs. The sensitivity was monitored by zone of inhibition around the disc. Overall rates of resistance to fluroquinolone and third generation cephalosporin were 70.31% and 65.10% respectively. The rates of co-resistance to both fluroquinolone and third generation cephalosporin was 53.13%.

Conclusion: Our study suggests that fluroquinolone should be reserved and third generation cephalosporin should be used with caution among patients with E.coli.

Key words: Antibiotic resistance, UTI, E.coli, Fluroquinolone, Third-generation Cephalosporin.

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Introduction

Urinary tract infection is extremely common in the worldwide.

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It is estimated that UTI contributes to seven million hospital visits, one million emergency consultations and more than ten million hospitalizations annually in the USA alone¹. In the global scenario due to rise of antibiotic resistance worldwide, it presents a substantial public health challenge². Primary care settings often diagnose and manage patients with UTI³. They often empirically manage a broad spectrum of pathologies from acute cystitis to pyelonephritis⁴. In addition, they care for a broad range of patients, ranging from low risk groups such as young adults to vulnerable populations such as elderly patients, pregnant women, spinal cord injury patients and patients requiring permanent or intermittent bladder catheterization⁵. It is well established that

Escherichia coli (*E.coli*) is the most frequently found bacteria in both community and hospital-acquired UTI^{6,7}. Fluroquinolone and third generation cephalosporin are commonly prescribed to provide empirical coverage against this pathogen among patients with UTI⁸. However, the effectiveness of these first line drugs has been accomplished by the uprising of antibiotic resistance⁸. As a result of their extensive use, a continuous decline of the therapeutic effectiveness of these antimicrobial agents has been observed⁵. The Infectious Disease Society of America (IDSA) discourages empirical use of antimicrobials for UTI when resistance rates exceed 10 to 20%⁶. The aim of our study was to assess the rates of resistance to fluroquinolone and third generation cephalosporin in patients with UTI due to *E.coli* and also to assess a potential co-resistance between both agent.

Materials And Methods

This cross sectional observational study was carried out during the period from 1st July, 2019 to 30th June, 2020 in the Department of Pharmacology and Therapeutics, in collaboration with the Department of Microbiology of Sylhet Women's Medical College and Hospital. A total of 246 patients with UTI (clinically diagnosed) were enrolled during the study period. Patients with subsequent UTI episodes within 30 days after the first episode were excluded from the study. Then their urine samples were cultured to identify the causative organism. Patients with positive urine culture report for *E.coli* were included in this study. After fulfilling the inclusion and exclusion criteria, 192 patients were selected for this study and their urine samples were further tested for sensitivity against fluroquinolone (ciprofloxacin) and third generation cephalosporin (cefixime and ceftriaxone). Non susceptibility was determined according to individual guidelines for

susceptibility testing. Fluroquinolone resistance was stated as non susceptibility to ciprofloxacin. Third-generation cephalosporin resistance was categorized as non susceptibility to cefixime and ceftriaxone. History and clinical examination were recorded in a prescribed data collection form. Data from each patient were recorded in previously designed data collection sheet. Data were processed manually and analyzed with the help of SPSS (Statistical Package for Social Sciences) version 16.0. Both descriptive and inferential statistics were used. Mean values were calculated and compared by ANOVA using SPSS. Ethical approval was taken from the institutional ethical committee. A probability value (p) of less than 0.05 was considered statistically significant.

Results

A total of 246 patients with UTI (clinically diagnosed) were enlisted. Out of the 246 patients, 192 (78.05%) patients with *E. coli* positive urine culture medias were included in this study after fulfilling the inclusion and exclusion criteria. These samples were then further tested for sensitivity against fluroquinolone (ciprofloxacin) and third generation cephalosporin (cefixime and ceftriaxone) and then data was analyzed. Demographic characteristics of the recruited patients showed in Table-1. Female 139(72.4%) was found to be predominant over male 53(27.6%) patient in this study. Mean age was 29.13±21.58 years, ranging from 6 years to 79 years. Maximum number of patients were from old (>55 years) followed by adult (36 – 55 years), young (18 – 35 years), and children (<18 years) age groups; 97(50.52%), 51(26.56%), 33(17.19%) and 11(5.73%) respectively. Sources of urine samples were 108(56.25%) from out-patient department and 84(43.75%) from in-door of the hospital. Resistance pattern of *E. coli* to fluroquinolone and third-generation cephalosporin also showed in Table-1. Overall

rates of resistance to fluoroquinolone and third-generation cephalosporin were 135(70.31%) and 125 (65.10%) respectively; 102(53.13%) patients had combined drug resistance. Older groups were found to be mostly affected; 61(45.19%) in fluoroquinolone, 57(45.6%) in third generation cephalosporin and 39(38.24%) in combined drug groups. Second affected group was adult patient group 47(34.81%), 40(32.0%) and 38(37.25%) respectively followed by young patient group 22(16.29%), 20(16.0%) and 18(17.65%) respectively. The children group was the least

affected group 5(3.71%), 8(6.4%) and 7(6.86%) respectively.

Resistance pattern according to the gender showed that the female was more prevalent compared to the male patients in both drug groups and also in combined drug groups. Data showed in Table-I. Resistance pattern of fluoroquinolone and third generation cephalosporin separately and in combined drug groups were 47(34.81%), 41(32.80%) and 31(30.39%) respectively in case of male and were 88(65.19%), 84(67.20%) and 71(69.61%) respectively in case of female.

Table-I: Patients demographics, stratified by fluoroquinolone resistance, third-generation cephalosporin resistance and co-resistance, for patients with UTI due to E.coli

Characteristic	Overall no. of episodes (%)	No. of resistant episodes/ No of episodes per category (%)		
		Fluroquinolone	Third- generation Cephalosporin	Fluroquinolone and Third- generation Cephalosporin
All	192 (100 %)	135(70.31%)	125(65.10 %)	102(53.13%)
Age group				
Children(<18 years)	11 (5.73%)	5(3.71%)	8(6.4%)	7(6.86%)
Young(18-35 years)	33 (17.19%)	22(16.29%)	20(16.0%)	18(17.65%)
Adult(36-55 years)	51 (26.56%)	47(34.81%)	40(32.0%)	38(37.25%)
Old(>55 years)	97 (50.52%)	61(45.19%)	57(45.6%)	39(38.24%)
Sex				
Female	139 (72.40%)	88 (65.19%)	84 (67.20%)	71 (69.61%)
Male	53(27.60%)	47 (34.81%)	41 (32.80%)	31 (30.39%)
Source of sample				
Out-door	84(43.75%)	31(36.9%)	29(34.5%)	24(28.6%)
In-door	108(56.25%)	88(81.5%)	12(11.1%)	8(7.4%)

Table-II: Distribution of resistance and sensitivity pattern against fluoroquinolone and third-generation cephalosporin in different age groups

Drug	Status	Age				p-value *
		Children (n = 11)	Young (n = 33)	Adult (n = 51)	Old (n = 97)	
Fluroquinolone	Resistant	5	22	47	61	0.001
	Sensitive	6	11	4	36	
Cephalosporine	Resistant	8	20	40	57	0.029
	Sensitive	3	13	11	40	
Both drugs	Resistant	7	18	38	39	0.001
	Sensitive	4	15	13	58	

* p value reached from chi-square test.

The distributions of drug resistance and sensitivity between the different age groups (Table II) found to be significant in case of fluoroquinolone group ($p = 0.001$), third generation cephalosporin group ($p = 0.029$), and also in combined drug group ($p = 0.001$). However, distributions of drug resistance were

not statistically significant between fluoroquinolone and third generation cephalosporin ($p = 0.795$), fluoroquinolone and combined drug group ($p = 0.579$), and third generation cephalosporine and combined drug group ($p = 0.729$).

Table-III: Distribution of resistance and sensitivity pattern against fluoroquinolone and third-generation cephalosporin in genders

Drug	Female	Male	p-value*
Fluroquinolone	88	47	0.001
Cephalosporine	84	41	0.02
Both drugs	71	31	0.358

* p value reached from chi-square test.

Distributions of drug resistance and sensitivity between the genders (Table III) found to be significant in fluoroquinolone ($p = 0.001$), and third generation cephalosporin ($p = 0.02$) groups. Combined drug group did not show significant difference ($p=0.358$). However, distributions of drug resistance between fluoroquinolone and third generation cephalosporin ($p= 0.73$), fluoroquinolone and

both drugs ($p = 0.47$), and third generation cephalosporin and both drugs ($p = 0.69$) were not significantly differ.

Discussion

Unjustifiable and widespread use of antibiotics leads to the development of antibiotic resistant bacterial strains. In Bangladesh, presences of these two factors are in alarming situation.

Extensive use of quinolone antibiotics in poultry industry causes further increasing emergence of quinolone-resistance strains. Here, we investigate the current resistance pattern of fluoroquinolone and third generation cephalosporin in patients with UTI due to *E.coli*. *E. coli* is the commonest cause of UTI in Bangladesh. *E. coli* was the major isolates from urine sample in several previous studies done in Bangladesh, like 85.15%⁹, 79.51%¹⁰ and 79%¹¹. Similar higher prevalence rate also reported in neighboring countries; such as 80% UTI cases in Pakistan¹² and 61% cases in India¹³. Our result showed similar higher prevalence rate (78.05%) of positive *E. coli* culture in patients with UTI. Female predominance (72.40%) observed in this study. Similar predominance also observed in previous studies; among all age groups^{9, 14}, even when studied on children only¹¹.

Several studies from Dhaka City reported a variation in resistance pattern against fluoroquinolone and cephalosporins at different times. In 2015, Yasmeen et al. reported about 40% resistance against both ciprofloxacin and levofloxacin each, 68% against cefixime and about 30% against ceftriaxone⁹. Higher resistance of ciprofloxacin and ceftriaxone (about 80% in each drug) against *E. coli* reported by Moue et al¹⁴ in the same year from the same city of Bangladesh. However, another study from the same region reported lower rate of resistance of ceftriaxone (28%) and cefixime (26%), but the rate of ciprofloxacin is still high (52%)¹¹.

A study in northern portion of Bangladesh showed prevalence of ciprofloxacin resistance to *E. coli* from urinary source was about 20% in 2017¹⁵. Another research in subsequent year, where data was collected from nine northern districts, found that the resistance developed against fluoroquinolone groups (ciprofloxacin and levofloxacin individually) raised more than 60% and against cephalosporin groups (cephradine,

cefuroxime and cefepime separately) more than 70%¹⁰.

Kibert and Abera studied resistance pattern of *E. coli* from different sources (such as urine, ear discharge, eye discharge and wound swab) and observed that resistance against ceftriaxone (37.4%) was almost double than ciprofloxacin (19.9%) in Ethiopia¹⁶.

Similar higher prevalence of fluoroquinolone and cephalosporins resistance to *E. coli* also observed in Pakistan (54.2% against ciprofloxacin and 43.3% against ceftriaxone)¹². In this research, we observed that resistance to fluoroquinolone, third generation cephalosporins and co-resistance to both, for *E.coli* were 70.31%, 65.10% and 53.13% respectively. This findings was supported by Monique et.al. 2019 (34.5%, 28.6% and 11.3% respectively).

In this study the mean \pm SD age of total patients was 29.13 \pm 21.58 years. Both genders were affected but the females (72.4%) were predominant which is consistent with the findings of Monique et.al (2019)¹⁷. They have analyzed 9944 patients with UTI. The average age of the study population was found to be 27.5 years and the majority of UTI patients were female (65.7%). In our study the rate of drug resistance increases along with the age of the patients. The highest frequencies found in old age groups (45.19% in fluoroquinolone, 45.6% in third generation cephalosporin, and 38.24% in combined drug groups) followed by adult (45.19% in fluoroquinolone, 45.6% in third generation cephalosporin, and 38.24% in combined drug groups), young (16.29%, 16.0% and 17.65% respectively) and children age groups (3.71%, 6.4% and 6.86% respectively). These findings were supported by Monique et.al. (2019), Asensio et.al (2011) where they observed highest frequency in old age group (>65 years) and the rate is 52.4%¹⁷ and 30.1%¹⁸ respectively.

Study Limitation

The study was conducted in a tertiary care hospital which does not represent the general population of the whole country.

The study was conducted in a single centre.

This study assess only the resistance rates of *E.coli*, didn't assess resistance rates among other uropathogens.

Conclusion

For empirical treatment of UTI the most frequently selected drugs are fluoroquinolone and third-generation cephalosporin. As fluoroquinolone resistant *E.coli* found in our large number of patients, we propose that fluoroquinolone should not be used empirically in patients with UTI. Moreover, our results indicate that caution should be taken while using third-generation cephalosporin, such as cefixime and ceftriaxone, as empirical treatment for patients with UTI. Due to risk of co-drug resistance among these patients, alternative to both fluoroquinolone and third-generation cephalosporin should be used empirically. Despite some limitations and draw back we tried to do our work sincerely. We think that characterization of these resistance trends still provides valuable actionable information for clinicians.

Author Contributions

Dr. Miftaul Jannath Chowdhury designed the study, collected the data and drafted the article; Dr. Chowdhury Muhammad Omar Faruque designed the study and revised the article; Dr. Jilwatun Noor collected the data; Dr. Choudhury Mizanur Rouf revised the article; Dr. Md. Mokbul Hossain helped in drafting the manuscript, Dr. Hussain Ahmad critically revised the article; Dr. KM Hafizur Rahman performed the statistical analysis and helped in drafting the manuscript. All of the authors reviewed and approved the final version to be published.

Conflict of Interest

None declared.

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References

- 1 Foxman B . Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med* 2002; 113 Suppl 1A: 5S-13S.
- 2 Ussai S, Rizzo M, Liguori G, Umari P, Pavan N. Antibiotic Treatment of Urinary Tract Infections (UTIs) In Primary Care: An Italian Pilot Study. *J Pharmacovigilance* 2016; 4: 215. doi:10.4172/2329-6887.1000215.
- 3 Little P, Turner S, Rumsby K, Warner G, Moore M. Developing clinical rules to predict urinary tract infection in primary care settings: sensitivity and specificity of near patient tests (dipsticks) and clinical scores. *Br J Gen Pract* 2006; 56: 606-612.
- 4 Fair RJ, Tor Y. Antibiotics and bacterial resistance in the 21st century. *Perspect Medicin Chem* 2014;6: 25-64.
- 5 Hooton TM, Stam WE. Management of acute uncomplicated urinary tract infection in adults. *Med Clin North Am* 1991 ;75: 339-357.
- 6 Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, Moran GJ, Nicolle LE, Raz R, Schaeffer AJ, Soper DE. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011; 52:e103–e120. doi: 10.1093/cid/ciq257.
- 7 Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 international clinical practice guidelines from the Infectious Diseases Society of America. *Clin Infect Dis* 2010; 50:625–663. doi :10.1086/650482.

- 8 Pallett A, Hand K. Complicated urinary tract infections: practical solutions for the treatment of multiresistant Gram-negative bacteria. *J Antimicrob Chemother* 2010; 65(Suppl 3):iii25–iii33.
- 9 Yasmeen BHN, Islam S, Islam S, Uddin MM, Jahan R. Prevalence of urinary tract infection, its causative agents and antibiotic sensitivity pattern: A study in Northern International Medical College Hospital, Dhaka. *Northern International Medical College Journal* 2015; 7(1):105-109.
- 10 Haque MF, Sultana S, Palit S, Mohanta MK, Mahfuz I. Emergence of multidrug resistant *Escherichia coli* as a common causative agent in urinary tract infection in Bangladesh. *University Journal of Zoology Rajshahi University* 2018; 37:8-13.
- 11 Sharmin L, Akter S. Bacterial Aetiology and Antibiotic Resistance Pattern of Community-Acquired Urinary Tract Infections in Children in a Tertiary Care Hospital in Bangladesh. *Journal of Enam Medical College* 2017; 7(3):134-139.
- 12 Sabir S, Anjum AA, Ijaz T, Ali MA, Khan MR, Nawaz M. Isolation and antibiotic susceptibility of *E. coli* from urinary tract infections in a tertiary care hospital. *Pakistan Journal of Medical Science* 2014; 30(2):389-392.
- 13 Khan AU, Zaman MS. Multiple drug resistance pattern in Urinary Tract Infection patients in Aligarh. *Biomedical Research* 2006; 17(3):179-181.
- 14 Moue A, Aktaruzzaman SAQM, Ferdous N, Karim MR, Khalil MMR, Das AK. Prevalence of urinary tract infection in both outpatient department and in patient department at a medical college setting of Bangladesh. *International Journal of Biosciences* 2015; 7(5):146-152.
- 15 Hossain MJ, Siddiqi A, Rahman MM, Khan KN, Imtiaj A. Prevalence of Urinary Tract Infection of Female Patients in Northern Bangladesh. *Merit Research Journal of Medicine and Medical Sciences* 2017; 5(6):290-293.
- 16 Kibret M, Abera B. Antimicrobial susceptibility patterns of *E. coli* from clinical sources in northeast Ethiopia. *African Health Science* 2011; 11(S1):S40-S45.
- 17 Monique RB, Melissa P, John M and Thomas PL. Fluoroquinolone and Third-Generation-Cephalosporin Resistance among Hospitalized Patients with Urinary Tract Infections Due to *Escherichia coli*: Do Rates Vary by Hospital Characteristics and Geographic Region. *PubMed Central* 2016 May; 60(5): 3170–3173.
- 18 Asensio A, Alvarez T, Fernandez J, Ramos A, Vaque J, Bishopberger C et al. Trends in yearly prevalence of third-generation cephalosporin and fluoroquinolone resistant *Enterobacteriaceae* infections and antimicrobial use in Spanish hospitals, Spain, 1999 to 2010. *Eurosurveillance* 2011;16(40) 19983.