

Emergence of multidrug resistant *Escherichia coli* as a common causative agent in urinary tract infection in Bangladesh

Md Fazlul Haque^{1*}, Sabina Sultana¹, Somen Palit², Moni Krishno Mohanta¹ and Istiak Mahfuz¹

¹ Department of Zoology, University of Rajshahi, Rajshahi-6205, Bangladesh

² Department of Public health, Ningxia Medical University, Yinchuan Ningxia China

Abstract: Detection of resistance pattern of pathogens to frequently prescribed antibiotics is vital and supportive in improving the quality of empirical treatment. Hence, the aim of this study was to explore the pattern of antibiotic resistance of *E. coli* isolated from patient with Urinary tract infections (UTIs). In this retrospective and observational study, 366 test reports of antibiotic sensitivity of bacterial isolates were used for data analyses which were collected from 9 districts of Bangladesh between June 2017 and August 2018 from the UTI patients. It was found that *Escherichia coli* (79.51%) was the most common causative agent in UTIs in both male and female patients. The females (>25 years old) and aged male (> 50 years) were more prone to UTIs than other groups. Among the 34 tested antibiotics viz. Meropenem, Netilmicin, Imipenem and Amikacin were highly sensitive to *E. coli*. But, 25 of tested antibiotics were resistant or intermediate to more than 50% isolates of *E. coli*. It can be concluded that the *E. coli* isolates which are resistant to the most of the antibiotics except Meropenem, Netilmicin, Imipenem and Amikacin are emerging as a common causative agent of UTIs in female and aged male in Bangladesh.

Key words: Multidrug-resistant, *Escherichia coli*, Urinary tract infection

Introduction

Urinary Tract Infections (UTIs) are one of the most common infections in human which are affecting 150 million people each year worldwide (Flores-Mireles *et al.*, 2015). UTIs are a major cause of morbidity in females of all ages as well as in infant boys and older men. Serious sequelae of UTIs are frequent recurrences, renal damage, pyelonephritis with sepsis, pre-term birth and other complications (Flores-Mireles *et al.*, 2015). UTIs are caused by microbial agents including bacterial, fungal and parasitic pathogen, but most of which are caused by bacterial agents. However, approximately 85% of community acquired UTIs and 50% of hospital acquired UTIs are caused by *E. coli* (KV and Shafiya, 2011; Barate and Ukesh, 2012).

Several beta lactams drugs especially fluoroquinolones and cephalosporins are commonly used to treat UTIs (KV and Shafiya, 2011). But, progressive increases in fluoroquinolone resistance among clinical isolates of *E. coli* have been reported since 2000 which was augmented recently by the emergence and proliferation of a dominant multidrug-resistant (MDR) subclone of sequence type 131 (ST131) (Denisuik *et al.*, 2013). Similarly, the emergence of extended-spectrum β -lactamases (ESBLs) and

β -lactamases mediated resistance acquired by UTIs pathogens to other antibiotics is a new challenge for treatment of UTIs (Bradford, 2001). β -lactamases, ESBLs and plasmid-mediated ESBL produced by *E. coli* are capable of hydrolyzing and inactivating a wide variety of β -lactams, including penicillin, cephalosporin and monobactam (Tada *et al.*, 2012). Hence, study of resistance pattern of uropathogenic *E. coli* possesses vital importance in healthcare sectors. Moreover, antibiotics resistance pattern of microorganisms vary from country to country, time to time and hospital to hospital. In Bangladesh, the problem of antibiotic resistance is alarming because of availability of low cost pharmaceuticals, preventative medication with broad spectrum antibiotics and overuse of these drugs (Sutradhar *et al.*, 2014). In addition, people are familiar to buy antibiotics from local drug stores without any prescription of qualified healthcare providers (Sutradhar *et al.*, 2014). However, there is no systematic national surveillance of antibiotic resistance as well as no adequate data to quantify the problem. Hence, detection of UTI causing pathogens and resistance of these pathogens to commonly prescribed antibiotics in clinical set ups is essential and helpful in improving the efficacy of empirical treatment (Sabir *et al.*, 2014).

The present study was designed to explore factors related to bacterial UTIs and to determine the pattern resistance of *E. coli* isolates to antibiotics.

Materials and Methods:

This retrospective and observational study was carried out in 9 districts of Bangladesh. After approval of the patients or their legal guardian and the responsible authority of hospital and clinics, 366 test reports of antibiotic sensitivity were collected in the period of June 2017 to August 2018 from outdoor and indoor patients whose urine sample were positive for growth of uropathogenic bacteria. The total 366 test reports (50 from Rajshahi medical college and hospital, Rajshahi; 50 from Khulna medical college and hospital, Khulna; 30 from Rangpur medical college and hospital, Rangpur; 36 from Queen hospital and Ibn Sina diagnostic and consultation centre, Jessore; 45 from Sylhet mag osmani medical college and hospital, Sylhet; 45 from Shaheed ziaur rahaman medical college and hospital, bogura; 44 from Sadar hospital, Sirajganj, 30 from Sadar hospital, Naogaon, 36 from Chittagong medical college and hospital, Chittagong) were collected from different hospital and clinics located in 9 districts of Bangladesh. Antibiotic sensitivity pattern of *E. coli* isolates was determined by the respective hospital and clinics on Muller Hinton agar plates by standard protocol of Kirby-Bauer disc diffusion method (Bauer *et al.*, 1966; Biemer, 1973; Saha *et al.*, 2009). Total 34 types of antibiotics (Penicillin, Cefradine, Vancomycin, Amoxiclav, Cotrimoxazole, Clarithromycin, Amoxicillin, T-Sulfamethoxazole, Mecillinam, Erythromycin, Cefixime, Cloxacillin, Cefuroxime, Clindamycin, Cefoxitin, Cefaclor, Doxycycline, Cephalexin, Ceftriaxone, Ceftazidime, Ciprofloxacin, Azithromycin, Fusidic acid, Levofloxacin, Tetracycline, Cefotaxime, Cefepime, Chloramphenicol, Nitrofurantoin, Gentamicin, Imipenem, Netilmicin, Amikacin, and Meropenem) were used for sensitivity test in the respective hospital and clinics. Isolates were declared as sensitive or intermediate or resistant on the basis of zone of inhibition following the criteria of Clinical Laboratory Standards Institute. The data (age and sex of patient, specimen used for growth of microorganism and species of microorganism) entry was made from the test reports into the Statistical Package for the Social Sciences (IBM Corp., Armonk, NY, USA) and Prism software (GraphPad, La Jolla, CA, USA) for statistical analysis and graph preparation.

Results

Causative agents of urinary tract infection and age and sex of infected patients:

In this study, it was observed that the most of urinary tract infections were caused by *Escherichia coli* (79.51%) followed by *Citrobacter* (8.20%) and *Pseudomonas* (5.74%) in both male and female patients (Fig. 1). However, female (61.72%) were more prone to UTIs than male (38.28%) (Fig. 2).

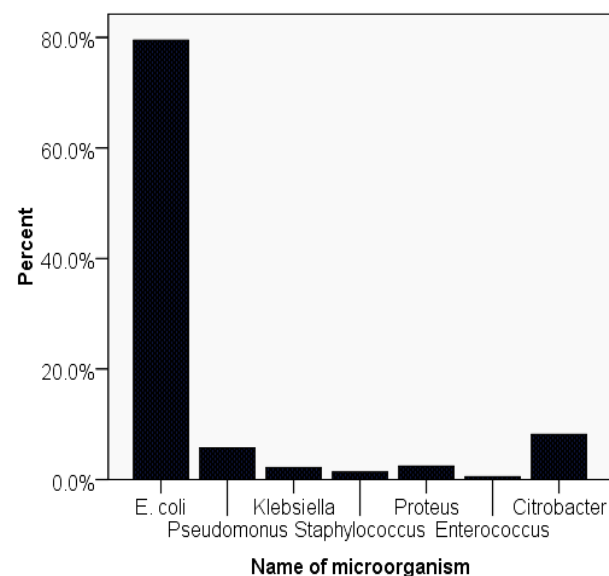


Figure 1 Major pathogens for Urinary tract infection.

The prevalence of UTIs also varied with age of the patients. The elderly as well as the adult females who were more than 25 years old were more susceptible to UTIs as compared with the susceptibility to UTIs of younger female who were less than 25 years old (Fig. 2). Contrary, only old male of >50 years age group were more vulnerable to UTIs as compared with that of other age groups (Fig.2).

Emergence of multidrug resistance UTI causing *E. coli*:

The results of this study reveal that among the 366 UTIs patients, 291 patients were infected with *E. coli* while rest of them was infected with other type of uropathogenic bacteria. Total 34 types of antibiotics were used to test sensitivity of *E. coli* which were isolated from urine sample of 366 patients. But, all of those antibiotics were not used together to test the sensitivity of each isolate of *E. coli*. Therefore, observation number for tested antibiotics was different as follows: 140 for Amoxiclav, 189 for Cefixime, 146 for Cefuroxime, 300 for Ciprofloxacin, 150 for Cefradine,

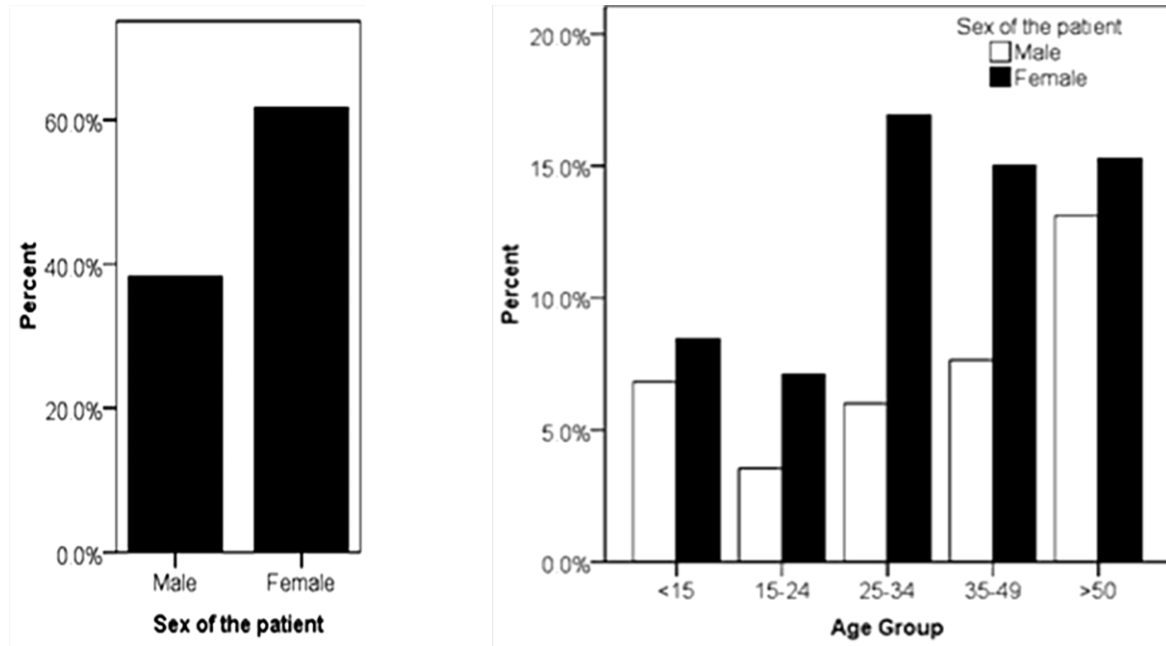


Figure 2 Female and aged male (>50 years age) were more prone to urinary tract infection.

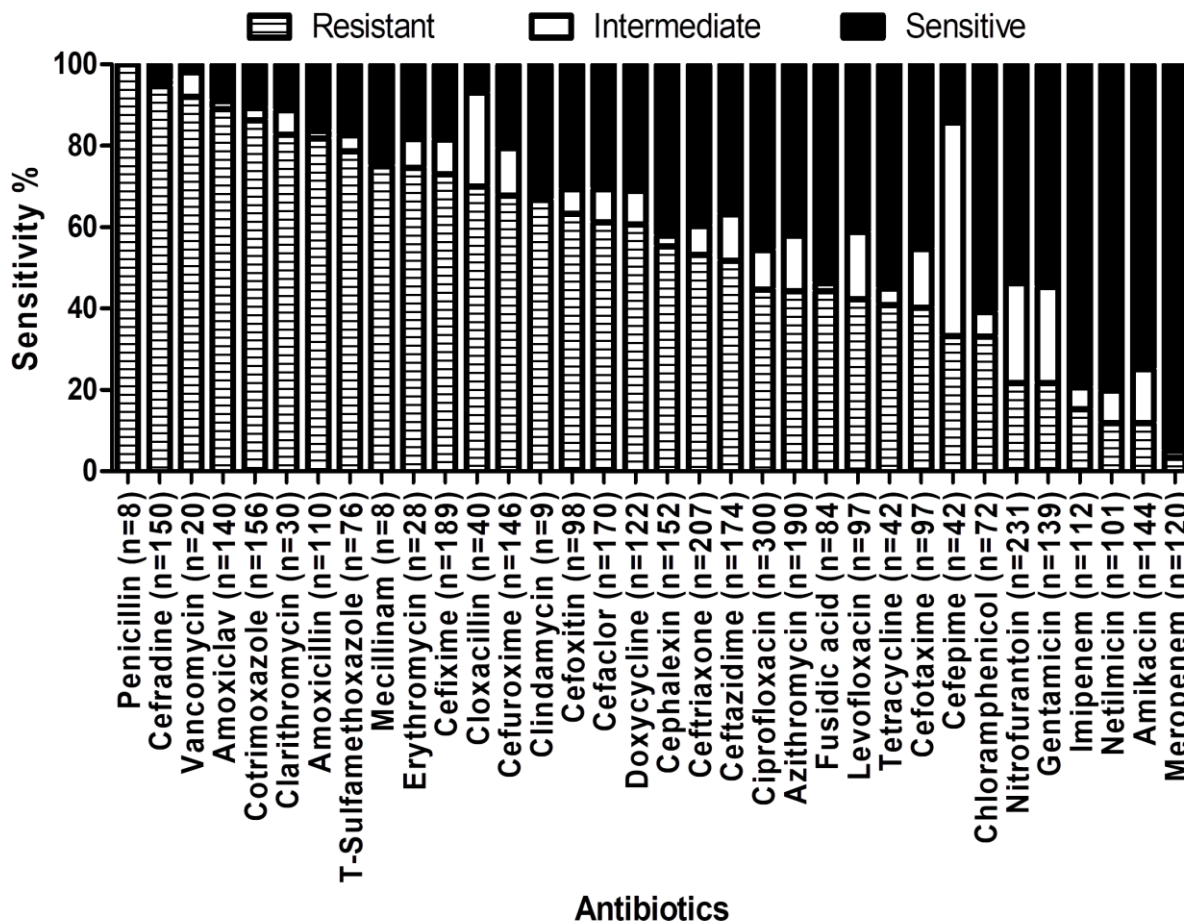


Figure 3 *E. coli* isolates were resistant to the most of the antibiotics. Here, “n” is the number of observation for that particular antibiotic.

207 for Ceftriaxone, 156 for Cotrimoxazole, 174 Ceftazidime, 76 for Trimethoprim Sulfamethoxazole, 97 for Levofloxacin, 20 for Vancomycin, 30 for Clarithromycin, 190 for Azithromycin, 170 for Cefaclor, 97 for Cefotaxime, 152 for Cephalexin, 122 for Doxycycline, 28 for Erythromycin, 110 for Amoxicillin, 40 for Cloxacillin, 8 for Mecillinam, 8 for Penicillin, 9 for Clindamycin, 42 for Cefepime, 98 for Cefoxitin, 84 for Fusidic acid, 231 for Nitrofurantoin, 139 for Gentamicin, 42 for Tetracycline, 72 for Chloramphenicol, 112 for Imipenem, 101 for Netilmicin, 144 for Amikacin and 120 for Meropenem (Fig. 3). Among the 34 tested antibiotics, 12 antibiotics viz. Penicillin, Cefradine, Vancomycin, Amoxiclav, Cotrimoxazole, Clarithromycin, Amoxicillin, T-Sulfamethoxazole, Mecillinam, Erythromycin, Cefixime and Cloxacillin were resistant to the more than 70% isolates of *E. coli* (Fig.3). Only 4 antibiotics viz. Meropenem, Netilmicin, Imipenem and Amikacin were sensitive to the more than 70% isolates of *E. coli* (Fig.3) indicating that these antibiotics are still effective for treatment of UTIs. However, the most (25 of 34) tested antibiotics were resistant or intermediate to more than 50% isolates of *E. coli* (Fig.3).

Discussion

Bacterial invasion and succeeding multiplication in urinary tract is the major cause of UTIs (Sabir *et al.*, 2014). In this study, 79.51% of the patients with bacterial UTIs had infected with *E. coli*. Similarly, it has been reported by another report that 80% of bacterial UTIs caused by *E. coli* in tertiary care hospital in Pakistan (Sabir *et al.*, 2014). However, a study in 2013 showed that 57% of UTIs causing bacteria was *E. coli* in Bangladesh (Khan *et al.*, 2013) which was comparatively lower than that showed in the present study. In this study, the UTI rate was higher in female (61.72%) patients as compared to male (38.28%). Similar findings were reported by others researcher (Shah *et al.*, 2005; Sabir *et al.*, 2014). We found that the elderly as well as the adult females (age >25 years) were more susceptible to UTIs as compared with the susceptibility of younger female (age <25 years) to UTIs. But, only old male were more susceptible to UTIs as compared with that of other age groups. Likewise, age-related variation in susceptibility to UTIs was reported in many other studies (Gupta *et al.*, 2001).

Discovery of antibiotics played the most vital role in health care sectors by killing or inhibiting the growth of microorganisms in the

twentieth century, but this success is threatened by emergence of antibiotic resistant pathogens in twenty-first century. Like many other pathogens, *E. coli* isolated from UTIs is becoming resistant to more and more antibiotics day by day, making it a main public health threat. Hence, it is very essential to evaluate the antibiotic resistance patterns in *E. coli* isolates for selecting effective antibiotic for proper and accurate treatment of patients. In the present study, 12 of 34 tested antibiotics were resistant to the more than 70% isolates of *E. coli* while only 4 antibiotics were sensitive to the more than 70% isolates of *E. coli*. However, the most (25 of 34) tested antibiotics were resistant or intermediate to more than 50% isolates of *E. coli*. It has been supported by other studies showed that UTIs with multi-drug resistant bacteria have been increased in recent times worldwide (Sabir *et al.*, 2014; Harris *et al.*, 2015; Merli *et al.*, 2015; Kulkarni *et al.*, 2017). Difficulties in treatment of UTIs have been augmented by the prevalence of extended spectrum beta-lactamases (ESBL) producing *E. coli*. However, few decades ago, *Klebsiella spp.* were notorious as ESBLs producer, most of which were nosocomial (Lautenbach *et al.*, 2001; Sabir *et al.*, 2014; Johnson *et al.*, 2017). In the present study, we found that *E. coli* isolates were resistant to most of the beta lactams and non-beta lactams antibiotics. Likewise, other studies revealed that most of the ESBL producing *E. coli* were resistant to a wide range of beta lactams antibiotics including penicillin, cephalosporin and piperacillin or tazobactam, and non-beta lactams including gentamycin, trimethoprim and fluoroquinolones (Lautenbach *et al.*, 2001; Overdevest *et al.*, 2011; Sabir *et al.*, 2014). Contrary, few recent studies in European countries reported that a higher number of *E. coli* was found sensitive to cephalosporin or penicillin (Nijssen *et al.*, 2004). Quinolone and fluoroquinolones showed moderate level of resistance to *E. coli* which is consistent with the finding of other studies (Mavroidi *et al.*, 2012; Sabir *et al.*, 2014). *E. coli* were less resistant to Amikacin, Netilmicin and Gentamicin indicating that aminoglycosides are effective for treatment UTIs caused by *E. coli*. However, this result was supported by other studies for Amikacin and Netilmicin, but there were debate on sensitivity of Gentamicin to *E. coli* (Tadesse *et al.*, 2012; Sabir *et al.*, 2014). Similarly, Meropenem and Imipenem were highly sensitive to *E. coli* indicating that Carbapenem antibiotics could be a drug of choice for treatment of UTIs.

Conclusion

It can be concluded from the results of this study that the multidrug resistant *E. coli* is emerging as a common causative agent of UTIs in Bangladesh which are more prevalent in female and elderly male. Most of the *E. coli* isolates are resistant to commonly used antibiotics except Meropenem, Netilmicin, Imipenem and Amikacin indicating that there are only few options to choose for effective treatment of UTIs in Bangladesh.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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