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Prevalence of extended spectrum beta-lactamase (ESBL) and AmpC beta-lactamase producing bacteria in urinary tract infection patients in Bangladesh

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ABSTRACT

Aims: This study aimed to determine the prevalence of pathogens in urinary tract and their antimicrobial susceptibilities, based on extended-spectrum beta-lactamase (ESBL) and AmpC beta-lactamase production in Bangladesh.
Methodology and results: The prevalence of pathogenic microorganisms in urinary tract and their antimicrobial resistance patterns were identified in 200 isolates from patients with urinary tract infections. Combined disc diffusion was performed to identify the presence of ESBL-producing strains. Moreover, disc approximation assay, disc potentiation test and double disc synergy test were performed to determine the presence of AmpC beta-lactamase producing bacterial strains. This study demonstrated a higher prevalence of UTIs in females (83.5%) than in males (16.5%). The most common pathogen was found *Escherichia coli* (44.5%), followed by *Enterococcus fecalis* (24%), *Klebsiella pneumoniae* (7.5%), *Staphylococcus aureus* (6%), *Pseudomonas aeruginosa* (5.5%) and *Staphylococcus saprophyticus* (4.5%). ESBL and AmpC beta-lactamase production occurred more frequently in *E. coli* (25.84%) and *P. aeruginosa* (100%) respectively.
Conclusion, significance and impact of study: The result of this study would provide physicians with important information which help them to make a judicious choice of antibiotics for therapeutic purposes. However, it is emphasized that continuous surveillance of antibiogram of medically important organisms causing UTI is necessary for adopting a rational antibiotic policy in the country.

Keywords: Urinary tract infection, ESBL, bacteria, antibiotic resistance

INTRODUCTION

Urinary tract infection (UTI) is one of the most prevailing infectious diseases of the community along with the hospital settings (Rashedmarandi *et al.*, 2008). It is an important cause of morbidity and mortality not only in developing but also in developed countries of the world, affecting diverse age and sex groups (Akram *et al.*, 2007; Alipourfard and Nili, 2010; Dogra *et al.*, 2012). UTIs are frequently brought about by *Enterobacteriaceae* (Gales *et al.*, 2000; Akram *et al.*, 2007). Gram negative bacteria are the most prevalent and accounts for 80-85% while (Forbes *et al.*, 2007) Gram positive for 15-20% for UTI (Gul *et al.*, 2004). More than half of UTIs in patients are accounted for *Escherichia coli* (Blomgran *et al.*, 2004). *Klebsiella*, *Staphylococci*, coagulase negative *Staphylococci*, *Proteus*, *Enterococci*, *Enterobacter*, *Pseudomonas* and others are also able to cause UTIs (Forbes *et al.*, 2007).

Gram negative microorganisms, especially *Entero-bacteriaceae* produces beta-lactamases. During the last few decades, several new beta-lactam antibiotics have been selectively designed to be resistant to the hydrolytic action of beta-lactamases (Medeiros, 1997; Normark and Normark, 2002). The leading cause of resistance to beta-lactam antibiotics such as penicillin, cephamycin, monobactum and cephalosporins was the presence of extended spectrum beta lactamases (ESBL) produced by Gram negative bacteria. In 1983, the first ESBL producing bacteria was detected in Germany (Kliebe *et al.*, 1985). Detection of ESBL producing organisms from urine samples will be useful as this notice an epidemiologic marker of population migration (Ahmed *et al.*, 2014).

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Furthermore, AmpC beta-lactamases are clinically important cephalosporinases encoded on the chromosomes of many of the *Enterobacteriaceae*, where they mediate resistance to cephalothin, cefazolin, cefoxitin, most penicillins, and beta-lactamase inhibitors (Coudron *et al.*, 2000; Jacoby, 2009). In many *Enterobacteriaceae*, AmpC expression is low but inducible in response to beta-lactam exposure (Jacoby, 2009).

In this study, we have conducted a retrospective study to compare the frequency of numerous urinary pathogens isolated from urine cultures received from both male and female volunteer patients with community acquired UTIs at BUHS hospital, Dhaka, Bangladesh as well as identification of ESBL and AmpC production among the uropathogens.

MATERIALS AND METHODS

Ethical statement

Ethical clearance from the Ethical Review committee of Bangladesh University of Health Sciences (BUHS) Hospital, Dhaka, Bangladesh and patients were admitted after written informed agreement was obtained (Memo no: BUHS/BIO/EA/13/054).

Study subjects

In total, 200 age and sex matched UTI patients were included in the present study. The study was carried out in the Department of Microbiology, Bangladesh Institute of Health Sciences (BUHS) Hospital, Dhaka, Bangladesh from January 2014 to June 2014. Two hundred clinical specimens (only urine) were collected from both sexes reported with UTI only, the UTI with other diseases were exempted from this study.

Collection of urine sample

The patients were given a sterile, dry wide mouthed, leak-proof container and explained the importance of collecting a specimen with a little contamination as possible. Patients were voluntary agreed to give their sample (Gradwohl *et al.*, 1980). Female patients were instructed to clean the area around the urethral opening with clean water, dried the area and collected the urine with the labia held apart. About 20 mL of urine was collected in each container from every patient (Gradwohl *et al.*, 1980). During collection of samples, basic PPE such as gloves and mask, were worn and other precautionary practices were taken for personal safety. After collection, the specimen containers were carefully capped, labeled with the date, the identification number and the time of collection. The specimens were transported to the microbiology laboratory as soon as possible for further analysis.

Sample preparation

About 5 mL of urine sample was taken in a clean sterile centrifuge tube and centrifuged at 3000 rpm for 10 min. After the centrifugation, the supernatant was discarded. The sediment was then examined by wet mount preparation. Microscopic examination of urinary sediments by wet mount included the detection of WBC (pus cells) and RBC. Number of WBC and RBC were estimated as number per HPF i.e., number of objects seen in 40× objective of microscope.

Isolation and identification of uropathogens

The pathogens in urine sample were identified through microscopy, culture, and biochemical tests. After conducting microscopic examination (Vandepitte, 2003) several culture tests were performed to isolate different types of uropathogens. MacConkey Agar (MA) was used for gram-negative enteric bacteria isolation at 37 °C for 24h-48 h interval. Bacterial identification was done by phenotypic examination of the culture, looking for typical characteristics, and by Gram staining. In addition, suspected Gram-negative organisms were identified on the basis of some facts such as colony characteristics, oxidase reaction, motility, urease production, citrate utilization, gas and indole production and sugar fermentation reactions. Cysteine Lactose Electrolyte Deficient (CLED) medium was used for isolating Gram-positive bacteria. Moreover, suspected Gram-positive organisms were identified by colony characteristics, catalase test, coagulase test, grow on to mannitol media and sensitivity pattern of Novobiocin (differentiation disk, not antibiotic) (Forbes *et al.*, 2007).

Antibiotic susceptibility testing

Antimicrobial susceptibility pattern of isolated bacterial pathogens was performed by Kirby Bauer disc diffusion method according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI). Following antimicrobial agents were used for determining antibiogram of isolated organisms: Amikacin 30 µg, Clavulanic acid/amoxicillin 30 µg, Ampicillin 10 µg, Cefotaxime 30 µg, Cefoxitine 30 µg, Cephradine 30 µg, Colistine 10 µg, Ciprofloxacin 5 µg, Gentamycin 120 µg, Imipenem 10 µg, Doxycycline 30 µg, Tetracycline 15 µg, Pipercillin/ Tazobactam 110 µg, Tigeycline 15 µg, Nalidixic Acid 30 µg, Nitrofurantoin 300 µg, Netilmycin 30 µg, Chloramphenicol 5 µg, Ceftazimide 30 µg and Vancomycin 30 µg. Most of the antibiotic discs and culture media used in this study were purchased from Oxoid, UK. The diameters of the zones of inhibition for individual antimicrobial agents were translated into susceptible and resistant categories according to National Committee for Clinical Laboratory Standards criteria (Wayne, 2009).

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Detection of ESBL by the combined disc method

Cultured strains along with positive (*K. pneumoniae* ATCC700603) and negative (*E. coli* ATCC 25922) control strains were inoculated onto Muller-Hinton agar (Sisco Research Laboratories Pvt. Ltd., Maharashtra, India). Commercialized discs containing ceftazidime (Ca) 30 µg and ceftazidime plus clavulanate (Cac) 30 µg plus 10 µg respectively were used in this method. After 24 h of incubation at 37 °C, an increase in diameter of ≥5mm with ceftazidime plus clavulanate (Cac) disc as compared to ceftazidime (Ca) disc alone was considered positive for ESBL detection (Kumar *et al.*, 2006; Wayne, 2009).

Detection of AmpC beta-lactamases

As per CLSI guidelines for detection of AmpC class of beta-lactamases, no valid technique has been established yet. Initiation of AmpC beta-lactamase synthesis was AmpC based on the disc approximation assay using several inducer substrate combinations such as Imipenem/Ceftazidime, Cefoxitin/Piperacillin, Imipenem/ Cefoxitin, Imipenem/Cefotaxime, Imipenem/Piperacillin – tazobactam (Dunne and Hardin, 2005). Disc potentiation (DP) test and double disc synergy test (DDST) using 3-aminophenylboronic acid (APB) (100 mg/mL dissolved in DMSO) were performed as confirmatory test (Yagi *et al.*, 2005). An increase in zone size of ≥5mm around the Ceftazidime- APB disk compared to ceftazidime only disc was recorded as a positive result for disc potentiation test. In DDST, the presence of change in the shape of growth inhibitory zone around ceftazidime or cefotaxime disc through the interaction with the 3- Aminophenyl boronic acid containing disc was interpreted as positive for AmpC production.

RESULTS

Age and sex distribution of patients

During the 6 months study period, a total of 200 patients of different age and sex who showed culture positive urine were included in this study. Of 200 cases, 33 (16.5%) were males and 167 (83.5%) with a male female ratio of 1:5. Most of the patients (28%) were between 61-70 years of age and only 2% were under 20 years of age. In each age group, the percentage of female patients were high but there were no female patients in ≤ 20 age group (Table 1).

Table 1: Age and sex distribution of study population.

Age group	No. of patient	%	Female	%	Male	%
≤ 20	4	2	0	0	4	2
21-30	16	8	16	8	0	0
31-40	25	12.5	24	12	1	0.5
41-50	29	14.5	27	13.5	2	1
51-60	42	21	38	19	4	2
61-70	56	28	44	22	12	6
>70	28	14	18	9	10	5
Total	200	100	167	83.5	33	16.5

Identification of uropathogens

Culture of 200 urine samples yielded a total of 130 (65%) gram negative bacterial growth including 89 (44.5%) of *E. coli*, 15 (7.5%) of *K. pneumoniae,* and 11 (5.5%) of *P. aeruginosa*, whereas remaining 70 (35%) were proved as gram positive bacterial growth including 48 (24%) of *E. fecalis*, 12 (6%) of *S. aureus* and 9 (4.5%) of *S. saprophyticus* (Tables 2 and 3).

Prevalence of ESBL-producing organisms

Identified isolates were further tested for the production of ESBL (Figure 1). Twenty-three (25.84%) of the total 89 *E. coli* were identified as positive for ESBL. All 11 *P. aeruginosa* isolates were negative for ESBL (100%); fourteen (93.34%) of 15 *K. pneumoniae* samples were negative and one (100%) of the 1 sample of *Citrobacter spp*. and *Edwardsiella* were positive. Seven (100%) of the 7 *Enterobacter* spp. and four (100%) of the 4 *Acinetobacter* spp. samples were ESBL negative respectively. In this current study, ESBL positive isolates were mainly detected with *E. coli* (25.84%) (Table 4).

Table 2: Gram Negative bacteria isolated from UTI patients (n=200).

Name of organism	No of patient	(%)	Female	(%)	Male	(%)
Escherichia coli	89	44.5	78	87.64	11	12.35
Klebsiella pneumoniae	15	7.5	14	93.33	1	6.66
Pseudomonas aeruginosa	11	5.5	11	100	0	0
Enterobacter spp	7	3.5	6	85.7	1	14.3
Acinetobacter spp	4	2	4	100	0	0
Proteus mirabilis	2	1	0	0	2	100
Edwardsiella	1	0.5	1	100	0	0
Citrobacter spp	1	0.5	1	100	0	0
Total	130	65	113	56.5	17	8.5

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Table 3: Gram positive bacteria isolated from UTI patients (n=200).

Name of Organism	No of patient	(%)	Female	(%)	Male	(%)
Enterococcus fecalis	48	24	36	75	12	25
Staphylococcus aureus	12	6	9	75	3	25
Staphylococcus saprophyticus	9	4.5	9	100	0	0
Staphylococcus epidermidis	1	0.5	0	0	1	100
Total	70	35	54	27	16	8

Table 4: The number and percentages of ESBL and AmpC beta-Lactamases producing organisms (n= 200).

Name of the organism	No of patient	ESBL producing		AmpC producing	
		Freq	%	Freq	%
Escherichia coli	89	23	25.84	11	12.35
Klebsiella pneumoniae	15	1	6.66	3	20
Pseudomonas aeruginosa	11	0	0	11	100
Acinetobacter spp	4	0	0	2	50
Citrobacter spp	1	1	100	0	0
Proteus mirabilis	2	0	0	0	0
Edwardsiella	1	1	100	0	0
Enterobacter spp	7	0	0	6	85.71
Total	130	26	20	33	25.38

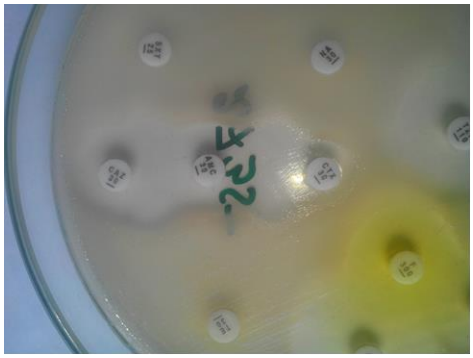

Figure 1: ESBL producing microorganisms. In the figure, the presence of key shape zone of inhibition of Ceftazidime (CAZ), Amoxyclav (AMC) and Cefotaxime (CTX) indicate the ESBL production.

Antibiotic Susceptibility pattern of ESBL and AmpC beta-lactamase producing uropathogens

ESBL positive isolates were further tested for the production of AmpC (Figure 2). Table 5 has illustrated the prevalence of the ESBL producing organisms in our isolates, particularly *E. coli* and *Klebsiella* of the *Enterobacteriaceae* family. Double disc diffusion method was used for the detection of ESBL. In addition, table 6 showed the prevalence of the AmpC beta-lactamase producing organisms in our isolates, particularly *E. coli*, *P.aeruginosa* and *Enterobacter* sp. Prevalence of ESBL and AmpC beta-lactamase in the urinary isolates was found to be 13% and 16.5% respectively.

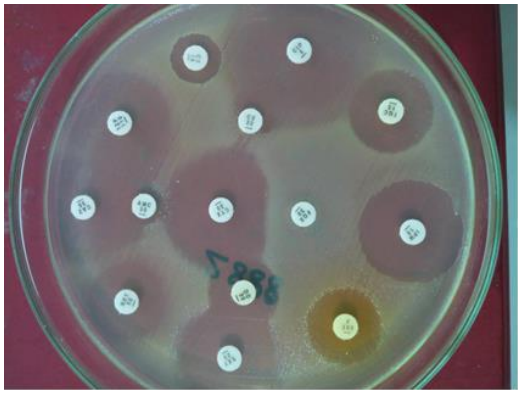

Figure 2: AmpC beta-lactamases producing microorganisms. Here, resistance to Cefoxitin (FOX) indicates the AmpC production.

DISCUSSION

UTIs have already been very common around the world with diverse pattern. The findings of this study have disclosed the relationships between sex, age, isolated bacterial strains and antibiotic resistance of UTIs. Our study demonstrated a high prevalence of UTIs in females (83.5%) than in males (16.5%) which correlates with other findings which declared that the frequency of UTIs is higher in females as compared to males (Rajalakshmi and Amsaveni, 2011). The reason behind this higher frequency of UTI in females may be due to close proximity of the external urethral orifice to the anus, smaller urethra, incontinence, sexual intercourse, and bad toilet (Aiyegoro *et al.*, 2007, Orrett and Davis, 2006).

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Table 5: Antibiotic susceptibility pattern of ESBL (N=26).

Organisms / Susceptibility pattern	*E. coli* (n=23)				*Klebsiella* (n=1)				*Citrobacter* (n=1)				*Edwardsiella* (n=1)			
	S		R		S		R		S		R		S		R	
	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%
AK	21	91.3	2	8.7	0	0	1	100	1	100	0	0	1	100	0	0
CIP	2	8.7	21	91.3	1	100	0	0	0	0	1	100	0	0	1	100
CT	19	82.6	4	17.4	1	100	0	0	1	100	0	0	1	100	0	0
FOX	23	100	0	0	1	100	0	0	1	100	0	0	1	100	0	0
IPM	22	95.6	1	4.4	1	100	0	0	1	100	0	0	1	100	0	0
DO	16	69.6	7	30.4	0	0	1	100	0	0	1	100	1	100	0	0
TZP	23	100	0	0	1	100	0	0	1	100	0	0	1	100	0	0
TGC	23	100	0	0	1	100	0	0	1	100	0	0	1	100	0	0
NA	0	0	23	100	0	0	1	100	0	0	1	100	0	0	1	100
F	21	91.3	2	8.7	1	100	0	0	1	100	0	0	1	100	0	0
SXT	8	34.8	15	65.2	0	0	1	100	0	0	1	100	1	100	0	0
NT	21	91.3	2	8.7	1	100	0	0	0	0	1	100	1	100	0	0
LEV	12	52.2	11	47.8	1	100	0	0	0	0	1	100	1	100	0	0

AK:, Amikacin; CIP, Ciprofloxacin; CT, Colistine; FOX, Cefoxitine; IPM, Imipenem; DO, Doxycycline; TZP, Pipercillin/Tazobactam; TGC, Tigecycline; NA, Nalidixic Acid; F, Nitrofurantoin; SXT, Cotrimazole; NT, Netilmycin; LEV, Levofloxacin.

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Table 6: Antibiotic susceptibility pattern of AmpC Beta- lactamases producing organisms (N=33).

Organisms / Susceptibility pattern	*E. coli* (n=11)				*K. pneumonia* (n=3)				*Enterobacter* (n=6)				*P. aeruginosa* (n=11)				*Acinetobacter* (n=2)			
	S		R		S		R		S		R		S		R		S		R	
	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%
AK	9	81.8	2	18.2	1	33.3	2	66.6	6	100	0	0	8	72.7	3	27.2	1	50	1	50
CIP	3	27.2	8	72.7	1	33.3	2	66.6	5	83.3	1	100	7	63.6	4	36.3	1	50	1	50
CT	10	90.9	1	9.1	3	100	0	0	6	100	0	0	8	72.7	3	27.2	1	50	1	50
IPM	11	100	0	0	1	33.3	2	66.6	6	100	0	0	7	63.6	4	36.3	0	0	2	100
DO	2	18.2	9	81.8	1	33.3	2	66.6	5	83.3	1	16.6	1	9.09	10	90.9	1	50	1	50
TZP	3	27.2	8	72.7	0	0	3	100	4	66.6	2	33.3	3	27.2	8	72.7	0	0	2	100
TGC	10	90.9	1	9.1	1	33.3	2	66.6	4	66.6	0	0	5	45.5	6	54.5	1	50	1	50
NA	3	27.2	8	72.7	0	0	3	100	2	33.3	1	100	0	0	11	100	0	0	2	100
F	6	54.5	5	45.4	1	33.3	2	66.6	3	50	3	50	0	0	11	100	0	0	2	100
SXT	2	18.2	9	81.8	0	0	3	100	3	50	3	50	1	9.09	10	90.9	1	50	1	50
NT	11	100	0	0	1	33.3	2	66.6	5	83.3	1	16.6	8	72.7	3	27.2	1	50	1	50
LEV	0	0	11	47.8	1	33.3	2	66.6	6	100	0	0	6	54.5	5	45.4	1	50	1	50

AK, Amikacin; CIP, Ciprofloxacin; CT, Colistine; FOX, Cefoxitine; IPM, Imipenem; DO, Doxycycline; TZP, Pipercillin/Tazobactam; TGC, Tigecycline; NA, Nalidixic Acid; F, Nitrofurantoin; SXT, Cotrimazole; NT, Netilmycin; LEV, Levofloxacin.

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In this study, the Gram negative bacteria comprised 65% of the total bacterial isolates while Gram positive bacteria marked with 35%. This was almost similar with some previous reports which demonstrated that Gram-positive bacteria had a low contribution in causing UTIs relatively (Brad *et al.*, 2010; Gales *et al.*, 2000). The study found most frequent Gram negative bacteria isolated as *E. coli* (44.5%). This is almost similar with the results of some other studies (Jha and Bapat, 2005; Mohammadi *et al.*, 2010).

Most of the studies showed that *E. coli* is the most common uropathogen worldwide (Dimitrov *et al.*, 2004; Abubakar, 2009). Other studies showed that *Klebsiella* spp. (Aboderin *et al.*, 2009) and *Pseudomonas aeruginosa* (Ehinmidu *et al.*, 2004) are the most prevalent uropathogens. *Citrobacter* spp. was either the second most prevalent uropathogens (Baral *et al.*, 2012) or the third most prevalent urinary isolates (Shobha *et al.*, 2007). However, we have found *K. pneumoniae* 7.5%, *P. aeruginosa* 5.5% and *Citrobacter* spp. only 0.5% in our clinical samples.

Uropathogens with antibiotic resistance has become a major public health concern in Bangladesh. In the current study the antimicrobial resistance rate of Gram negative isolates was high compare to the first line antimicrobial agents such as ampicillin, cotrimoxazole, and amoxicillin/ clavulanic acid. This may due to excessive use of these drugs temporarily because they are comparatively cheap and also easy to administer orally.

The present study demonstrated that, the *E. coli* isolates to be completely resistant to the common clinically used drugs such as penicillin and its derivatives group and also to a higher extent to broad spectrum quinolone group. The results of antibiotic susceptibility pattern in our study are consistent with the previous studies of (Kukanur *et al.*, 2015) on drug resistance in *E. coli*, where their study revealed that 92.5, 75 and 57.1% of *E. coli* isolates were sensitive to nitrofurantoin, amikacin and gentamicin respectively. However, it has been reported that, the frequency was lower in developed countries (Karlowsky *et al.*, 2002). Antibiotic abuse and practicing incomplete antibiotic dosage has considerably promoted the distribution of multidrug resistant bacteria (Hossain *et al.*, 1982; Lee and Henry, 1989). This study has reported lower resistance for less commonly used drugs such as meropenem, imipenem, nitrofurantion and amikacin and complete sensitivity to netilmycine, ceftriaxone and gentamicin among the *E. coli* isolates. This finding has been supported by the study of Sharmin *et al.* (2009) which reported a good sensitivity for imipenem, ceftazidime and amikacin against UTI-isolates of *E. coli* in Bangladesh (Sharmin *et al.*, 2009).

The most significant outcome of our study is to find out the beta-lactam group resistance bacteria compare to other previous selected studies. ESBL-producing strains demonstrated a significantly higher rate of resistance to non beta-lactam antibiotics. These findings are similar to those reported by others (Ndugulile *et al.*, 2005; Mehrgan *et al.*, 2009). Worldwide ESBL prevalence in community and hospital widely varies (Kader and Angamuthu, 2005). A total of 20% isolates were found to produce ESBL detected by the double disc diffusion test. The prevalence of ESBL was reported 22% and 64% respectively in India. (Agrawal *et al.*, 2008; Singhal *et al.*, 2005). Among the five most frequent UTI pathogens, *E. coli* (25.84 %) and *Klebsiella pneumoniae* (6.6 %) were most prevalent ESBL producers. In Bangladesh, the prevalence of ESBLs has been reported from beginning of 2000. More studies are required to know the exact magnitude of the problem in Bangladesh.

Other emerging resistance mechanisms such as AmpC enzymes are also being increasingly found in members of family *Enterobacteriaceae.* AmpC beta-lactamase is one type of cephalosporinase which is either not inhibited, or weakly inhibited by clavulanic acid. It can hydrolyze not only cephamycins also extended spectrum cephalosporins. In our study, AmpC beta-lactamase producing strains are more susceptible to Tazobactam as compared to clavulanic acid which is similar with a previous study (Philippon *et al.*, 2002). High level resistance to cefepime had been showed by both ESBL producers and non-producers while AmpC producers are very susceptible to fourth generation cephalosporins including cefepime (Livermore, 1995). In our study out of 130 Gram negative organisms, 33 samples were AmpC beta-lactamases producing organisms. Of them 12.35% *E. coli* and 20% *K. pneumoniae* are AmpC beta-lactamases positive. There is alarming news that, 100% *P. aeruginosa* and 50% *Acinetobacter* spp. are AmpC beta Lactamases positive. In this study overall AmpC prevalence was 17.2% compared to two studies in India reporting 27% (Subha *et al.*, 2003) and 47.3% (Hemalatha *et al.*, 2007). The total number of AmpC beta-lactamases producing organisms is 25.38% which is greater than ESBL producing organisms. Current study has demonstrated the drug resistance among uropathogens. On the basis of our findings, it is very urgent to analyze and follow-up the antibiotic resistance pattern continuously. In addition, development of regional surveillance programs is also necessary to provide information which would then enable the development of UTI guidelines.

CONCLUSION

In conclusion, our study showed that among the urine isolates, AmpC and ESBLs production were prevalent in Gram negative bacteria. Majority of these organisms were resistant to common antibiotics used for treatment of UTI. Further drug resistance surveillance in the hospitals and molecular characteristics of ESBLs and AmpC isolates in Bangladesh is necessary. This study is important for strict antibiotic policy implementation in hospitals to estimate the impact of higher drug resistance in bacteria and to take steps for reducing this resistance. The findings of the present study recommend that the UTI should be treated by selective antibiotics obtained from culture and sensitivity tests to minimize increasing trend of drug resistance. To eradicate multi drug resistant strains, new

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guidelines of antibiotic therapy for UTI may be necessary through more evaluation.

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