Original Article

Frequency, Risk Factors and Antibiotic Sensitivity Pattern of Extended-Spectrum Beta-Lactamase Producing *Escherichia coli* and *Klebsiella pneumoniae* Causing Urinary Tract Infection: Experience from a Tertiary Care Hospital of Bangladesh

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Abstract

Background: *Urinary tract infection (UTI) due to extended-spectrum beta-lactamase (ESBL) producing organisms are increasing. This study was designed to evaluate the frequency of ESBL-positive Escherichia coli and Klebsiella pneumoniae causing UTI, their antibiotic sensitivity pattern and possible risk factors.*

Methods: *This case-control study was done in BIRDEM General Hospital, Dhaka, Bangladesh from January to March 2016. Patients with UTI due to ESBL-positive E. coli and K. pneumoniae were cases and non-ESBL organisms were controls.*

Results: *Total 98 patients with UTI due to E. coli (84) and K. pneumoniae (14) were eligible for analysis. Two-thirds of E. coli (56/84, 66.7%) and two-fifths of K. pneumoniae (6/14, 42.9%) were ESBL-positive (cases, 62) and rest 36 patients were controls (UTI due to non-ESBL E. coli or K. pneumoniae). There was no significant difference in relation to age (p=0.757), sex (p=0.548), presence (p=0.696), duration (p=0.050) or control of diabetes (p=0.448) between cases and controls. Regarding risk factors responsible for UTI due to ESBL-positive organisms, long duration (≥5 years) of diabetes was significant (OR=6.87, 95% CI=2.34-20.16, p=0.0004). On multivariate logistic regression, presence (p=0.002) and long duration of diabetes (p=0.002), past history of UTI (p=0.004) and history of hospitalization due to UTI (p=0.005) appeared as significant risk factors for UTI due to ESBL-positive E. coli or K. pneumoniae. Imipenem, amikacin, gentamycin and nitrofurantoin were among the most sensitive antibiotics.*

Conclusion: *Almost two-thirds of the UTI cases were due to ESBL-positive organisms in this study. Imipenem, aminoglycosides and nitrofurantoin were among the most sensitive antibiotics. Long duration of diabetes, past history of UTI and hospitalization due to UTI were significant risk factors for ESBL-positivity.*

Key words: *antibiotic sensitivity, extended-spectrum beta-lactamase, frequency, prevalence, risk factor, urinary tract infection.*

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Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections in adults. Antibiotics remain the cornerstone for management of UTI. Empiric and non-judicious use of antibiotics lead to resistant strains of bacteria. Extended-spectrum beta-lactamase (ESBL) producing strains are an ever increasing problem throughout the world.[1-4] In Bangladesh, only a few studies were reported on ESBL-positive organisms, mostly describing their prevalence and antibiotic sensitivity patterns.[5-9] Diabetes mellitus (DM), past history of UTI and prior antibiotic use are reported risk factors for UTI due to ESBL-positive organisms.[10,11] In this study, we have tried to evaluate the frequency of UTI due to ESBL-positive *Escherichia coli* and *Klebsiella pneumoniae*, their antibiotic sensitivity patterns and risk factors.

Methods

This case-control study was done in the Department of Internal Medicine of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital from January to March 2016. BIRDEM General Hospital is a 700-bed tertiary care hospital in Dhaka, the capital city of Bangladesh. This hospital was initially established and dedicated for serving diabetic patients, later converted into a general hospital and now serving as teaching hospital for BIRDEM Academy and Ibrahim Medical College.

Hospitalized patients with a clinical diagnosis of UTI were initially enrolled for the study purpose. UTI cases were clinically diagnosed depending upon clinical features later confirmed by positive urine cultures. A clean catch technique was applied for urine (preferably early morning midstream specimen) collection. Collected samples were then sent to the microbiology laboratory of the institute within half an hour where these samples were inoculated in MacConkey agar and blood agar media within two hours. Significant culture positive cases (semi-quantitative colony count $>1X10^5$ colony forming units/ml) were then included for the study purpose. Catheterized patients, pregnant ladies, patients with inadequate/no growth or growth of candida on urine culture were excluded from the study. Growth of organisms was further evaluated by their colony characters and biochemical tests including triple sugar iron (TSI), motility indole urea (MIU) and Simon citrate. Then the selected samples were sub-cultured for antibiotic sensitivity in Muellar-Hilton (MH) agar by Kibry-Bauer disc susceptibility test.[12] ESBL-positivity

was determined phenotypically by Double Disc Synergy Test.[13] Finally patients with UTI due to ESBL-positive *E. coli* and *K. pneumoniae* were selected as cases and those with non-ESBL organisms were taken as controls.

Selected study participants were then further evaluated by history regarding risk factors including presence of and if yes, then duration of diabetes, history of UTI within last one year, history of antibiotic intake within last one year and history of hospitalization due to UTI within last one year and their laboratory reports like glycated haemoglobin (HbA1c) were recorded. Data were collected in semi-structured case record forms. Data were analyzed by statistical package for social sciences (SPSS) version 20.0. Comparison of qualitative and quantitative variables between cases and controls were made by appropriate tests and a *p* value of <0.05 was considered as significant.

Results

During the study period, a total of 136 culture proven UTI cases were recorded. *E.coli* (84, 61.8%) was the most common organism followed by *Klebsiella* (14, 10.3%). Total 98 cases of UTI due to *E. coli* and *Klebsiella* were included in this study. Other less common organisms were *Enterobacter spp.* (2, 1.5%), *Citrobacter* (6, 4.4%), *Pseudomonas* (3, 2.2%), *Burkholderia pseudomallei* (1, 0.7%), *Enterococcus* (10, 7.4%), *Acinetobacter* (6, 4.4%), *Staphylococcus aureus* (7, 5.1%), meticillin resistant *S. aureus* (1, 0.7%) and *Streptococcus* (2, 1.5%). Two-thirds (56/84, 66.7%) of *E. coli* and two-fifths (6/14, 42.9%) of *Klebsiella* were ESBL-positive. Base-line characteristics of the cases (62) [ESBL-positive *E. coli* (56) and *Klebsiella* (6)] and controls (36) [Non-ESBL *E. coli* (28) and *Klebsiella* (8)] are presented in Table I.

Table I. Base-line characteristics of the study participants (N=98)

Characteristics	Cases (ESBL-positive)	Controls (Non-ESBL)	*p* value
Number	62	36	0.510
Mean age (years)	56.42±14.84	55.50±12.91	0.757
Sex (F:M)	2.3:1	3:1	0.548
DM:non-DM	61:1	35:1	0.696
Mean DM duration (years)	9.36±5.25	7.14±5.51	0.050
Mean HbA1c (%)	9.06±1.63	9.38±2.53	0.448
Past history of UTI	31	16	0.596
History of prior antibiotic use	34	17	0.465
Past history of hospitalization due to UTI	29	10	0.064
Neutrophil leukocytosis	57	34	0.645

Fever, dysuria and increased urinary frequency were among the most common presentations. Other features are presemted in Table II.

Long (≥5 years) duration of diabetes was significant risk factor for UTI with ESBL-postive organisms among the study subjects (Table III). On multivariate logistic regression analysis, presence of DM (p=0.002), long duration of DM (p=0.002), past history of UTI (p=0.004) and history of prior hospitalizaton due to UTI within one year (p=0.005) were significant risk factors for ESBL-postivity. Antibiotic sensitivity pattern of the study subjects are shown in Table IV.

Table II. Clinical presentation of the study subjects (N=98)			
Clinical feature	Total (98)	Cases (ESBL-positive) (62)	Controls (non-ESBL) (36)
Fever	58 (59.2)	35 (56.5)	23 (63.9)
Increased frequency	32 (32.7)	17 (27.4)	15 (41.7)
Dysuria	39 (39.8)	24 (38.7)	15 (41.7)
Loin pain	32 (32.7)	19 (30.6)	13 (36.1)
Supra-pubic pain	21 (21.4)	11 (17.7)	10 (27.8)
Incontinence	15 (15.3)	9 (14.5)	6 (16.7)
Vomiting	27 (27.6)	13 (21.0)	14 (38.9)
Asymptomatic	32 (32.7)	23 (37.1)	9 (25.0)

*most patients had more than one feature

Table III. Risk factors for UTI with ESBL-positive organisms (N=98)						
Risk Factors		Cases (62) ESBL-positive	Controls (36) Non-ESBL	Odds ratio	95% CI	p value
Age (years)	<55	22	15	1.29	0.55-3.01	0.5431
	≥55	40	21			
Sex	Male	19	9	0.75	0.29-1.90	0.5515
	Female	43	27			
DM	No	1	1	1.74	0.10-28.74	0.6977
	Yes	61	35			
DM duration (years)	<5	6	15	6.87	2.34-20.16	0.0004
	≥ 5	55	20			
HbA1c (%)	<7	3	3	1.81	0.34-9.50	0.4819
	≥7	58	32			
History of UTI	No	28	19	1.35	0.59-3.09	0.4674
	Yes	34	17			
History of hospitalization due to UTI	No	33	26	2.28	0.94-5.52	0.0668
	Yes	29	10			

Table IV. Antibiotic sensitivity pattern of the ESBL-positive *E. coli* and *Klebsiella pneumoniae*

Antibiotic	ESBL-positive *E. coli* (56)	ESBL-positive *K. pneumoniae* (6)
Amikacin	52 (92.9)	6 (100.0)
Ciprofloxacin	6 (9.7)	3 (50.0)
Co-trimoxazole	20 (35.7)	2 (33.3)
Gentamicin	46 (82.1)	4 (66.7)
Imipenem	56 (100.0)	6 (100.0)
Mecillinum	34 (60.7)	3 (50.0)
Netilmicin	52 (92.9)	6 (100.0)
Nitrofurantoin	52 (92.9)	5 (83.3)

Discussion

In primary care settings, fluroquinolones and oral cephalosporins remain as the major drugs for treating UTI. High resistance against fluroquinolones in UTI is well described.[4,14] ESBL-positive organisms are inherently resistant against penicillins and cephalosporins. So, ESBL-positive UTI cases are not benefitted with such empiric treatments, rather contributes to antibiotic resistance. Not only that, ESBL positivity of micro-organisms remains an increasing problem in developed as well as in developing countries.[1-6,9,15]

In the current study, almost two-thirds of UTI cases were due to ESBL-positive organisms. In four different studies done in Bangladesh over the preceding years by Rahman MM *et al*.[5], Rahman MR *et al*.[9], Asna SMHZ *et al*.[6] and Iqbal S *et al*.[7] revealed up to 60% of all UTI cases were due to ESBL-positive organisms. In different studies in India[10], Nepal[16], Iran[17] and Turkey[18] up to 48% of UTI cases were due to ESBL-positive organisms.

Long duration of diabetes, poor glycaemic control, prior UTI and history of hospitalization due to UTI were significant risk factors for ESBL positivity in this study. Risk factors are comparable with different study reports through-out the world.[10,16-19] Antibiotic sensitivity patterns were also similar.[6-10,16-18]

Current study had some limitations. It was a single center study, comprising small number of study population over a short period of time and most of our study participants were diabetic.

In conclusion, it can be said that ESBL-positive organisms were almost two-thirds of UTI cases studied. Two-thirds of *E. coli* and two-fifths of *K. pneumoniae* were ESBL-positive. Imipenem, aminoglycosides and nitrofurantoin were among the most sensitive antibiotics. Long duration and poor control of diabetes, past history of UTI and hospitalization were significant risk factors for ESBL positivity. It might be recommended that, urine culture should be requested in suspected UTI cases specially if patient is diabetic one and if there is a past history of UTI and all centers should test for ESBL positivity routinely.

Conflict of interest: None declared.

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