

Original Article

Extended-Spectrum Beta-Lactamase Producing *Escherichia coli* and *Klebsiella pneumoniae* are Emerging as Major Pathogens Responsible for Urinary Tract Infection

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Abstract :

Background: *Escherichia coli* and *Klebsiella pneumoniae* are two common organisms responsible for urinary tract infection (UTI) world-wide. Extended-spectrum beta-lactamase (ESBL) producing *E. coli* and *K. pneumoniae* are increasingly being reported as urinary isolates.

Objectives: This study was aimed to describe the frequency of ESBL positive *E. coli* and *K. pneumoniae* causing UTI, associated risk factors and antibiotic sensitivity pattern of these organisms.

Methods: This prospective cross-sectional study was conducted in BIRDEM General Hospital from January 2014 to March 2014. One hundred consecutive culture positive UTI cases due to *E. coli* or *K. pneumoniae* infection, irrespective of ESBL positivity were purposively included in this study. UTI due to organisms other than *E. coli* and *K. pneumoniae* and culture negative cases were excluded from the study.

Results: Total patients were 100, male were 21 and female 79. Mean age was 59.1 (range 19-81) years. Out of 100 patients, 96 were diabetic. Fever, vomiting, dysuria and increased urinary frequency were common symptoms. Among the 100 culture positive samples, *E. coli* were 84 and *K. pneumoniae* were 16. Forty eight (48/84, 57.1%) of *E. coli* and 10 (10/16, 62.5%) of *K. pneumoniae* were ESBL positive. Female patients, presence of diabetes mellitus (DM), long duration and poor control of DM, chronic kidney disease (CKD), renal stone and past history of UTI were significant risk factors for ESBL positivity. Amikacin, netilmycin and imipenem were among the most sensitive antibiotics.

Conclusion: Two-thirds of the *E. coli* and *K. pneumoniae* in this study were ESBL positive. Female gender with poor control of DM, CKD and past history of UTI were significant risk factors for ESBL positivity. Aminoglycosides and carbapenems remain the drug of choice.

Key Words: *Escherichia coli*; extended-spectrum beta-lactamase; *Klebsiella pneumoniae*; urinary tract infection.

Introduction :

Urinary tract infection (UTI) is common and reported as being the second most common infection through-out the world¹.

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Escherichia coli and *Klebsiella pneumoniae* are responsible for UTI in 80-90% cases²⁻⁴. Extended-spectrum beta-lactamase (ESBL) producing *E. coli* and *K. pneumoniae* are increasingly being isolated in cultures from urine samples in Bangladesh⁵⁻⁸. Advanced age, diabetes mellitus (DM), use of urinary catheters, previous hospital admission and antibiotic intake are reported as risk factors for ESBL positivity^{9,10}. Data regarding ESBL positive organisms are limited in our country. This study was designed to describe the frequency of ESBL positive *E. coli* and *K. pneumoniae* causing UTI, their associated risk factors and antibiotic sensitivity pattern in a tertiary care setting of Bangladesh.

Methods :

This prospective cross-sectional study was done in the Department of Nephrology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from January 2014 to March 2014. Adult patients who got admitted with a clinical diagnosis of UTI were initially enrolled for the study. Those with a growth of micro-organism from their urine samples were then selected for the study and finally one hundred consecutive culture positive UTI cases due to *E. coli* or *K. pneumoniae* infection, irrespective of their ESBL positivity were purposively included in this study.

Culture negative UTI cases and UTI due to organisms other than *E. coli* and *K. pneumoniae* were excluded from the study. Data were collected in pre-designed case record forms from the study subjects including demographic characteristics, co-morbidities, clinical presentation and investigations. Data were analyzed by statistical package for social sciences (SPSS) version 15.

Results :

Total patients were 100 (out of 124 culture positive UTI cases during the study period), male were 21 and female 79. Mean age was 59.1 ± 11.7 (range 19-81) years. Base-line characteristics are presented in table I. Common co-morbidities were DM, hypertension, chronic kidney

disease (CKD) and dyslipidemia. Other co-morbidities are presented in table II.

Fever, vomiting, dysuria and increased urinary frequency were common symptoms (table III). Among the 100 culture positive samples, *E. coli* were 84 and *K. pneumoniae* were 16. Forty eight (48/84, 57.1%) of *E. coli* and 10 (10/16, 62.5%) of *K. pneumoniae* were ESBL positive. Female patients, long duration and uncontrolled DM, past history of UTI, CKD and renal stone were significant risk factors for ESBL positivity (table IV). Amikacin, netilmycin, imipenem and nitrofurantoin were among the most sensitive antibiotics (table V).

Table I: Base-line characteristics of the study population (N=100)

Total number of patients	100 (80.6% of all culture positive UTI cases)
Mean age (years)	59.1 ± 11.7 (range 19-81)
Male: Female	1:3.8
DM: non-DM	24:1
Mean duration of DM (years)	9.7 ± 4.9
Mean HbA1c (%)	9.5 ± 2.3
Mean RBS at admission (m.mol/L)	15.7 ± 6.6RBS = random blood sugar

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Table II: Co-morbidities among the study subjects (N=100)

Comorbidity	Frequency	Percentage
DM	96	96
Hypertension	58	58
IHD	19	19
CKD	39	39
Stroke	4	4
Dyslipidaemia	42	42
Fatty liver	19	19

IHD = ischaemic heart disease

Table III: Presenting features of the study subjects (N=100)

Presenting features	Frequency	Percentage
Fever	94	94
Increased urinary frequency	42	42
Dysuria	41	41
Loin pain	31	31
Supra-pubic pain	37	37
Incontinence	11	11
Vomiting	72	72

All patients had more than one symptom, so multiple response table has been used

Table IV. Risk factors for infection with ESBL producing organisms

Risk factors	ESBL positive organisms (n=58)	Non-ESBL positive organisms (n=42)	Odds Ratio	p value
Sex				
Female	41	26	1.48	0.002
Male	17	16		
DM				
Present	56	40	1.40	0.001
Absent	2	2		
Duration of DM				
5 years or more	55	37	2.48	0.001
<5 years	3	5		
HbA1c				
7% or more	57	36	9.50	0.001
<7%	1	6		
Catheterized				
Yes	19	5	3.61	0.322
No	39	37		
CKD				
Yes	49	17	8.01	0.003
No	9	25		
Renal stone				
Yes	2	1	1.46	0.002
No	56	41		
Past history of UTI				
Yes	19	4	4.63	0.002
No	39	38		
History of antibiotic intake in last one year (any duration)				
Yes	15	3	4.53	0.561
No	43	39		
History of hospitalization in last year (for any reason)				
Yes	11	2	4.68	0.342
No	47	40		

Table V: Antibiotic sensitivity and resistance patterns of ESBL positive *E. coli* (n=48) and ESBL positive *K. pneumoniae* (n=10)

Antibiotic	<i>E. coli</i> (ESBL positive) n (%)		<i>K. pneumoniae</i> (ESBL positive) n (%)	
	Sensitive	Resistant	Sensitive	Resistant
Augmentin	0 (0)	48 (100)	0 (0)	10 (100)
Cefixime	0 (0)	48 (100)	0 (0)	10 (100)
Ceftazidime	0 (0)	48 (100)	0 (0)	10 (100)
Ceftriaxone	0 (0)	48 (100)	0 (0)	10 (100)
Cefuroxime	0 (0)	48 (100)	0 (0)	10 (100)
Amikacin	47 (97.9)	1 (2.1)	10 (100)	0 (0)
Gentamicin	20 (41.7)	28 (58.3)	10 (100)	0 (0)
Netilmicin	44 (91.7)	4 (8.3)	10 (100)	0 (0)
Ciprofloxacin	0 (0)	48 (100)	0 (0)	10 (100)
Co-trimoxazole	22 (45.8)	26 (54.2)	0 (0)	10 (100)
Imipenem	48 (100)	0 (0)	10 (100)	0 (0)
Mecillinam	18 (37.5)	30 (62.5)	10 (100)	0 (0)
Nitrofurantoin	43 (89.6)	5 (10.4)	0 (0)	10 (100)

Discussion :

ESBL positive organisms are now a global health threat¹¹. These organisms have implications on physicians and patients; they are associated with treatment failure, increased morbidity and mortality, prolonged hospital stay, poor outcome and increased health care costs¹². In this study, we have evaluated the frequency of ESBL positive *E. coli* and *K. pneumoniae* causing UTI, their associated risk factors and antibiotic sensitivity patterns.

Mean age of our study population was just below 60 years. In two different reports from Dhaka, Bangladesh, patients suffering from UTI were of much lower age, but patients having infections due to ESBL positive organisms had a mean age of 71 years in Spain^{6,9,13}.

In current study, it was seen that, 57% of *E. coli* and 62.5% of *K. pneumoniae* were positive for ESBL. This frequency is much higher than previous four reports from Bangladesh^{5,6,13,14}. ESBL positive organisms are also increasingly being identified in Korea¹⁵ and USA¹⁶. In Korea, it was 3.6% in 2006 and 14.3% in 2011 and in USA it was 4% in 2006 and 14% in 2012. In one report from Nepal, ESBL positivity for *E. coli* and *K. pneumoniae* from urine samples were 13.41% and 16.55% respectively¹⁷. One North Indian report showed these figures as 5% and 13% respectively¹⁰.

Female patients, presence of DM, long duration and poor control of DM, CKD, renal stone and past history of UTI were risk factors for ESBL positivity in our study. Long hospital stay (>3 days), past history of UTI and prior antibiotic use were risk factors in a study from Spain⁹. DM and increasing age were noted as risk factors for ESBL positivity in one report from India¹⁰.

Regarding antibiotic sensitivity patterns, most organisms were sensitive to imipenem and amikacin in our study. As CKD was a common co-morbid condition in our study population, we preferred carbapenems. Carbapenems were the most sensitive antibiotic as reported from India¹⁰, Nepal¹⁷, Korea¹⁵, Spain⁹ and other reports from Bangladesh^{7,8,14}.

The study duration was short and sample size was small. It was a hospital-based study and most of the patients were diabetic. It is not clear whether pattern of micro-organisms causing UTI and their ESBL positivity and antibiotic sensitivity differ from non-diabetic population and in community.

In conclusion, it can be said that two-thirds of the *E. coli* and *K. pneumoniae* causing UTI were ESBL positive. Female patients, presence of DM, long duration and poor control of DM, past history of UTI, CKD and renal stone were important risk factors for ESBL positivity. Carbapenems remain the drug of choice. It might be recommended that urine samples should be sent for culture and antibiotic sensitivity test before starting antibiotic in suspected UTI cases and every laboratory should routinely screen for ESBL positivity.

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