

Original Articles

Frequency of Extended-Spectrum Beta-Lactamase Producing Organisms Causing Urinary Tract Infection and Their Antibiotic Sensitivity Pattern

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Abstract

Background: The spectrum of bacteria causing urinary tract infection (UTI) and their antibiotic sensitivity pattern is not uniform. *Escherichia coli* and *Klebsiella sp.* are two common organisms responsible for UTI through-out the world. The incidence of UTI due to infection with extended-spectrum beta-lactamase (ESBL) producing organisms are increasing. This study was aimed to describe the frequency of ESBL positive organisms causing UTI and their antibiotic sensitivity pattern.

Methods: This cross-sectional study was done in the Department of Internal Medicine, BIRDEM General Hospital from January to April, 2016.

Results: Total number of patients was 137 with females predominance (M:F ratio 1 : 3.7). Mean age was 60.3 ± 11.7 years. Most patients (131, 95.6%) of the study population were diabetic and glycaemic control was poor (mean HbA1c 9.3 ± 2.3) in these subjects. Common symptoms were fever, vomiting, increased urinary frequency, dysuria, suprapubic pain, and loin pain. Neutrophilic leukocytosis was common (94.9%). *E. coli* (73.7%) was the commonest aetiological agent followed by *Klebsiella* (8.8%), *Enterococcus* (4.4%), *Citrobacter* (3.6%), *Staphylococcus aureus* (3.6%), *Acinetobacter* (2.9%), *Enterobacter* (1.5%), and *Pseudomonas* (1.5%). Over half of *E. coli* and of *Klebsiella sp.* and 100% of *Enterobacter* organisms were ESBL positive. Imipenem (100%), amikacin, netilmycin, and nitrofurantoin were among the most sensitive antibiotics.

Conclusion: More than half (71, 51.82%) of UTI cases were due to ESBL positive organisms. Imipenem, amikacin, netilmycin, and nitrofurantoin remain the drug of choice.

Key words: antibiotic; extended-spectrum beta-lactamase; sensitivity; urinary tract infection.

Introduction

Urinary tract infection (UTI) is common and globally up to 90% of UTI cases are due to *Escherichia coli* and *Klebsiella pneumoniae* infection.¹⁻³ Antibiotics are the cornerstone for treating UTI. Extended-spectrum beta-lactamase (ESBL) producing organisms are increasingly being isolated in cultures from urine samples in Bangladesh.⁴⁻⁶ These

organisms are inherently resistant to penicillins and cephalosporins; thus treatment with these drugs are of no use. Increasing age, diabetes mellitus (DM), catheterisation, history of hospitalization and antibiotic intake are risk factors for ESBL positivity.^{7,8} Statistics regarding ESBL positive organisms are limited in Bangladesh. This study was designed to describe the frequency of ESBL positive organisms causing UTI and their antibiotic sensitivity pattern in a tertiary care setting from a developing country.

Methods

This cross-sectional study was done in the Department of Internal Medicine, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Shahbag, Dhaka, Bangladesh from January to April, 2016. Hospitalized adult patients with clinical diagnosis of UTI were primarily enrolled for study. Those with significant growth of micro-organisms (>10⁵cfu/ml) from midstream urine sample cultures were finally

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included for analysis. Patients with no/insignificant growth of pathogens or growth of candida, catheterized patients and pregnant patients were excluded from the study. Standard clean-catch technique was applied for collection of midstream urine. Urine samples were sent to microbiology laboratory in one hour, where it was inoculated in McConkey's and blood agar media within two hours. Those with growth of micro-organisms were further tested for antibiotic sensitivity using double disc-diffusion methods. Data were collected in semi-structured case record forms. Data were analyzed by using SPSS version 20.0. Results were presented in tables.

Results

Total patients were 137, male were 29 and female 108. Mean age was 60.3±11.7 (range 18-94) years. Base-line characteristics are presented in table I. Common co-morbidities were DM (131, 95.6%), hypertension (83, 60.6%), chronic kidney disease (58, 42.3%) dyslipidaemia (47, 34.3%), ischaemic heart disease (24, 17.5%) and fatty liver disease (27, 19.7%).

Fever (128, 93.4%), vomiting (82, 59.9%), increased urinary frequency (65, 47.4%), dysuria (55, 40.1%), supra-pubic pain (45, 32.8%) and loin pain (40, 29.2%) were common symptoms. Cystitis was common (64.1%), followed by pyelonephritis (33.5%). Bilateral pyelonephritis was present in 5 (3.6%) cases.

Table I

Base-line characteristics of the study population (N=137)

Total number of patients	137
Mean age (years)	60.3 ±11.7 (range 18-98)
Male : female	1 : 3.7
DM : non-DM	21.8 : 1
Mean duration of DM (years)	9.6 ±4.9
Mean HbA1c (%)	9.3 ±2.3
Mean RBS at admission (m.mol/L)	13.9 ± 6.6

RBS = Random blood sugar

Among the 137 culture positive samples, *E. coli* (101, 73.7%) was the commonest aetiological agent followed by *Klebsiella* (12, 8.8 %), *Enterococcus* (6, 4.4%), *Citrobacter* (5, 3.6%), *Staphylococcus* (5, 3.6 %), *Acinetobacter* (4, 2.9 %), *Enterobacter* (2, 1.5%), and *Pseudomonas* (2, 1.5%). Over half (61/101, 60.4 %) of *E. coli*, *Klebsiella* (7/12, 58.3%) , *Citrobacter* (1/2, 50%) and all *Enterobacter*(2/2, 100%) were found positive for ESBL enzyme. Among them 16 (22.5%) cases were complicated with acute kidney injury (AKI). Imipenem, amikacin, netilmycin, and nitrofurantoin were among the most sensitive antibiotics (table II).

Table II

Antibiotic sensitivity and resistance patterns of ESBL positive E. coli, Klebsiella Enterobacter and Citrobacter:

Bacterial organism	E. coli n= 61 (%)		Klebsiella sp. n=7 (%)		Enterobacter n=2 (%)		Citrobacter n=1 (%)	
	sen	res	sen	res	res	Sen	res	sen
Amikacin	59(96.7)	2(3.3)	7(100)	0(0)	0(0)	2(100)	1(100)	0(0)
Augmantin	0 (0)	61(100)	0 (0)	7(100)	0(0)	2(100)	0(0)	1(100)
Cefixime	0 (0)	58(100)	0 (0)	7(100)	0(0)	2(100)	0(0)	1(100)
Ceftazidime	0 (0)	60(100)	0 (0)	7(100)	0(0)	2(100)	0(0)	1(100)
Ceftriaxone	0 (0)	61(100)	0 (0)	7(100)	0(0)	2(100)	0(0)	1(100)
Cefuroxime	0 (0)	61(100)	0 (0)	7(100)	0(0)	2(100)	0(0)	1(100)
Ciprofloxacin	2(3.3)	59(96.7)	1(14.3)	6(85.7)	0(0)	2(100)	0(0)	1(100)
Colistin	-	-	-	-	2(100)	0(0)	-	-
Co-trimox	28 (45.9)	33(54.1)	1(14.3)	6(85.7)	0(0)	2(100)	0(0)	1(100)
Gentamicin	29(47.5)	32(52.5)	1(14.3)	6(85.7)	0(0)	2(100)	1(100)	0(0)
Imipenem	61(100)	0(0)	0 (0)	7(100)	2(100)	0(0)	1(100)	0(0)
Mecillinam	26(42.6)	35(57.4)	7(100)	0(0)	2(100)	0(0)	1(100)	0(0)
Netilmicin	56(91.8)	5(8.2)	7(100)	0(0)	0(0)	2(100)	1(100)	0(0)
Nitrofurantoin	54(88.5)	7(11.5)	0 (0)	7(100)	0(0)	2(100)	1(100)	0(0)
Vancomycin	-	-	-	-	-	-	-	-
Piperacilin	-	-	-	-	-	-	-	-
PPC+Tazobac	-	-	-	-	2(100)	0(0)	-	-

*Not all specimens were tested against all antibiotics listed; sen=sensitive; res=resistant; PPC=piperacilin.

Discussion

In this cross-sectional study, we have evaluated the frequency of ESBL positive organisms causing UTI and their antibiotic sensitivity patterns in a tertiary care setting of Bangladesh.

Mean age of the study population was 60.3 ± 11.7 years. In two different reports from Dhaka, Bangladesh, patients suffering from UTI were of much lower age^{6,9} but patients having infections due to ESBL positive organisms had a mean age of 71 years in Spain.⁷

In current study, it was seen that, 60.4% of *E. coli* and 58.3% of *Klebsiella sp.* were positive for ESBL. This frequency is much higher than previous four reports from Bangladesh.^{5,6,9,10}

ESBL positive organisms are increasing in Korea and USA. In Korea¹¹ it was 3.6% in 2006 and 14.3% in 2011. In USA¹² it was 4% in 2006 and 14% in 2012. In one report from Nepal ESBL positive *E. coli* and *Klebsiella sp.* were responsible for UTI in 13.41% and 16.55% cases respectively. One North Indian report showed these figures 5% and 13% respectively.⁸

Regarding antibiotic sensitivity patterns, most organisms were sensitive to imipenem, aminoglycosides and nitrofurantoin. Carbapenems were the most sensitive antibiotic in India⁸, Nepal¹³, Korea¹¹, Spain⁷ and other reports from Bangladesh.^{5,6,9,10}

Limitations of the study

The study duration was short and sample size was small. It was a hospital based study and most of the patients were diabetic. Patterns of ESBL positive micro-organisms and their antibiotic sensitivity in non-diabetic population and in community are not clear.

Conclusion

In this study, it was found that two-thirds of the *E. coli* and *Klebsiella sp.* causing UTI were ESBL positive. Imipenem, amikacin, netilmycin, and nitrofurantoin remain the drug of choice. It might be recommended that urine samples should be sent for culture and antibiotic sensitivity testing before starting antibiotic in suspected UTI cases and every laboratory should routinely screen for ESBL positivity.

Conflict of Interest : None

References

- Ireng LM, Kabego L, Vandenberg O, Chirimwami RB, Gala J-L. Antimicrobial resistance in urinary isolates from inpatients and outpatients at a tertiary care hospital in South-Kivu Province (Democratic Republic of Congo). *BMC Res Notes* 2014;7:374.
- Majumder MI, Ahmed T, Hossain D, Begum SA. Bacteriology and sensitivity patterns of urinary tract infections in a tertiary hospital in Bangladesh. *Mymensingh Med Coll J* 2014;23(1):99-104.
- Singhal A, Sharma R, Jain M, Vyas L. Hospital and Community Isolates of Uropathogens and Their antibiotic sensitivity pattern from a tertiary care hospital in North West India. *Ann Med Health Sci* 2014;4(1):51-56.
- Lina TT, Khajanchi BK, Azmi IJ, Islam MA, Mahmood B, Akter M et al. Phenotypic and Molecular Characterization of Extended-Spectrum Beta-Lactamase-Producing *Escherichia coli* in Bangladesh. *PLoS ONE* 2014;9(10):e108735/journal.pone.0108735.
- Biswas R, Rabbani R, Ahmed HS, Sarker MAA, Zafrin N, Rahman MM. Antibiotic sensitivity pattern of urinary tract infection at a tertiary care hospital. *Bangladesh Crit Care J* 2014;2(1): 21-24.
- Asna SMZH, Akter S, Rahman MM, Mohammad N, Hafez MA. Frequency and Sensitivity of Extended Spectrum Beta-Lactamase Positive Organisms in a Secondary and Tertiary Level Hospital Network in Dhaka. *J Enam Med Col* 2015;5(2):80-87.
- Rubio-Perez I, Martin-Perez E, Garcia DD, Calvo ML-B, Barrera EL. Extended-spectrum beta-lactamase-producing bacteria in a tertiary care hospital in Madrid: epidemiology, risk factors and antimicrobial susceptibility patterns. *Emerg Health Threats J* 2012;5:11589.
- Shaikh S, Fatima J, Shakil S, Rizvi SMD, Kamal MA. Risk factors for acquisition of extended spectrum beta lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* in North-Indian hospitals. *Saudi J BiolSci* 2015;22:37-41.
- Shilpi T, Ahmed MN, Huq SMA, Baul SK, Khatun M. Isolation of bacteria causing urinary tract infections and their antibiotic susceptibility profile at Anwar Khan Modern Medical College Hospital. *AKMMC J* 2013;4(2):23-27.
- Masud MR, Afroz H, Fakruddin M. Prevalence of extended-spectrum beta-lactamase positive bacteria in radiologically positive urinary tract infection. *SpringerPlus* 2014;3:216.
- Kang C-I, Cha MK, Kim SH, Ko KS, Wi YM, Chung DR et al. Clinical and Molecular Epidemiology of Community-Onset Bacteremia Caused by Extended-Spectrum Beta-Lactamase-Producing *Escherichia coli* over a 6-Year Period. *J Korean Med Sci* 2013;28:998-1004.
- Spadafino JT, Cohen B, Liu J, Larson E. Temporal trends and risk factors for extended-spectrum-beta-lactamase producing *Escherichia coli* in adults with catheter-associated urinary tract infection. *Antimicrobial Resistance and Infection Control* 2014;3:39.
- Chander A, Shrestha D. Prevalence of extended spectrum beta lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* urinary isolates in a tertiary care hospital in Kathmandu, Nepal. *BMC Research Notes* 2013;6:487.