

URINARY TRACT INFECTION DUE TO EXTENDED-SPECTRUM BETA-LACTAMASE PRODUCING ORGANISMS IS A RISK FACTOR FOR BACTERAEMIA AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract

Introduction: Urinary tract infection (UTI) is common among patients with diabetes mellitus and the aetiological agents are often extended-spectrum beta-lactamase (ESBL) producing bacteria. Diabetic patients with UTI are sometimes complicated by bacteraemia. This study was designed to evaluate whether UTI due to ESBL-positive organisms is a risk factor for bacteraemia among patients with type 2 diabetes mellitus.

Methods: This was a cross-sectional analytical study, done in BIRDEM General Hospital, Dhaka, Bangladesh from January to April 2016. Adult (≥18 years) type 2 diabetic subjects of either sex with culture proven UTI were included in this study. All study participants were subjected to undergo blood cultures as well. ESBL-positivity of the infective organisms for UTI was evaluated as possible risk factor for bacteraemia.

Results: Total patients were 145 including 119 (82%) females. *Eshcherichia coli* (112, 77.2%) was the most common aetiological agents followed by *Klebsiella pneumoniae* (28, 19.3%). In 54 (37.2%) patients UTI was due to ESBL-positive organisms. Ten (6.9%) patients were complicated by bacteraemia [7 (7/54, 13%) among patients with UTI due to ESBL-positive organisms and 3 (3/91, 3.3%) among patients with UTI due to non-ESBL organisms]. UTI due to ESBL-positive organisms appeared as a significant risk factor for bacteraemia (OR 4.37, 95% CI 1.08-17.38, p 0.03).

Conclusion: Nearly two-fifths of UTI cases were due to ESBL-positive organisms in this study. ESBL-positivity of the causative organisms was a significant risk factor for bacteraemia among type 2 diabetic subjects.

Key words: Bacteraemia, extended-spectrum beta-lactamase, pyelonephritis, risk factor, type 2 diabetes mellitus, urinary tract infection.

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Introduction

Urinary tract infection (UTI) is the most common bacterial infection in adults and elderly population and patients with diabetes mellitus are at increased risk for UTI.¹⁻³ UTI, specially pyelonephritis may be complicated by bacteraemia and sepsis.^{4,5} Antimicrobials remain the cornerstone for treatment of UTI and increasing antimicrobial resistance,

specially extended-spectrum beta-lactamase (ESBL) producing organisms is an ever increasing problem.⁶⁻⁹ ESBL-positive organisms are inherently resistant to penicillin and cephalosporin; thus UTI caused by ESBL-positive organism require injectable agents like carbapenems and aminoglycosides or nitrofurantoin, pivmecillinam and fluoroquinolones; many organisms causing UTI are also resistant to these oral agents.^{2,8}

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Moreover, UTI complicated by bacteraemia indicates complicated infection and merits intravenous antimicrobials in hospital settings; thus increasing treatment cost by many folds. So, this study was designed to evaluate whether UTI due to ESBL-positive organisms is a risk factor for bacteraemia among patients with type 2 diabetes mellitus.

Methods

This cross-sectional analytical 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 to April 2016. Hospitalized adult (≥18 years) type 2 diabetic subjects of either sex, who got admitted with features of pyelonephritis, were primarily enrolled for the study purpose. A clean catch technique was applied for collection of urine in a sterile container and sent to the microbiology laboratory of the institute within half an hour for culture and a blood sample of the patient was also sent for culture before starting any antibiotic. Urine and blood cultures and antibiotic sensitivity tests were performed following standard microbiological procedures. Other investigations were done as per hospital protocol and as indicated. Patients with culture proven UTI were finally included in this study. ESBL-positivity of the infective organisms was tested by double disc diffusion method described elsewhere.¹⁰ Pregnant patients, patients with kidney and ureteric stones, enlarged prostate, indwelling urinary catheter and recurrent UTI were excluded from the study. ESBL-positivity of the infective organisms was evaluated as possible risk factor for bacteraemia. Data were analyzed by statistical package for social scientists (SPSS) version 16.0 and the results

Results

Total patients were 145 including 119 (82%) females. Mean age of the study participants was 59.2 years. Base-line characteristics are shown in Table I.

Table-I

Base-line characteristics of the study participants (N=145)

Characteristics	Parameters
Mean (range) age	59.2 (21-72) years
Male: Female	1: 4.6
Mean (range) duration of diabetes	6.3 (1-13) years
Random blood glucose at admission	13.1 (7.2-21.3) mmol/L
Mean (range) HbA1c	9.7 (8.1-11.5) %
Hypertension	68 (46.9%)
Chronic kidney disease	41 (28.3%)

Eshcherichia coli (112, 77.2%) was the most common aetiological agents followed by *Klebsiella pneumoniae* (28, 19.3%). Other organisms are presented in Table II. In 54 (37.2%) patients UTI was due to ESBL-positive organisms and in 91 (62.8%) patients UTI was due to non-ESBL organisms. Ten (6.9%) patients were complicated by bacteremia; 7 (7/54, 13%) among patients with UTI due to ESBL-positive organisms and 3 (3/91, 3.3%) among patients with UTI due to non-ESBL organisms. UTI due to ESBL-positive organisms appeared as a significant risk factor for bacteraemia (p 0.03) (Table III).

Table II

Patterns of infective organisms for UTI (N=145)

Organism	ESBL-positive	Non-ESBL	Total
<i>E. coli</i>	38 (33.9)	74 (66.1)	112
<i>K. pneumoniae</i>	11 (39.3)	17 (60.7)	28
<i>Enterobacter</i>	4 (100)	0 (0)	4
<i>Citrobacter</i>	1 (100)	0 (0)	1

Table III

ESBL-positivity as a risk factor for sepsis among patients with UTI (N=145)

ESBL positivity	Sepsis (10)	No sepsis (135)	OR, 95% CI, p value
Yes (54)	7	47	4.37, 1.08-17.38, 0.03
No (91)	3	88	

Discussion

Bacteraemia is not uncommon in UTI, both in community and hospital settings and in all age groups—adults, elderly and neonates; but the burden varied widely in different studies.¹¹⁻¹³ Generally, outcome of UTI complicated by bacteraemia is worse than those without.¹⁴ In the present study, we found nearly 7% of our type 2 diabetic subjects diagnosed with UTI had concomitant bacteraemia. In different studies percentage of patients of UTI complicated by bacteraemia was much higher^{11,12}; elderly patients are likely to have urinary obstruction that might explain such high rates in western studies.¹¹

In the present study, almost two-fifths of the study participants had UTI due to ESBL-positive organisms which is lower than a previous report from Bangladesh.⁸ Patients with diabetes mellitus and specially those with poor glycaemic control are at increased risk for infection with ESBL-positive organisms.^{2,15-17} The percentage of ESBL-positive

organisms was higher in our study compared to some other international reports.^{16,18} Inadvertent and non-judicious use of antimicrobials may be one of the most important contributory factors for such findings in the present study.

Community acquired UTI cases are generally treated at outpatients with oral fluoroquinolones, cephalosporins and nitrofurantoin. ESBL-positive organisms are resistant to penicillins and cephalosporins.² One-third of our patients had chronic kidney disease, but nobody was on renal replacement therapy in any form. Patients with chronic kidney disease are not suitable for prescriptions with nitrofurantoin or aminoglycosides. So, carbapenems remain the option, thus increasing treatment cost by many folds.⁶

Bacteremia itself implies severe disease. Published reports varied regarding outcome of UTI cases complicated by sepsis; some authors found worse outcome while others did not.^{4,19-21} Morbidity and mortality evaluation was beyond the scope of the present study but we feel outcome evaluation in UTI complicated by bacteremia remains area for further exploration in our setting.

Published literatures indicated urinary obstruction like enlarged prostate, indwelling catheters, stone disease and lithotripsy as risk factors for bacteremia and sepsis in UTI.^{5,12,22-24} We excluded all these confounders in our study during selection of study participants. We assume duration of diabetes and status of glycaemic control could be further confounders in our study, which could be adjusted during analysis. Moreover, small sample size, short term study in a single center—all these remain as limitations of present study.

In conclusion, almost two-fifths of UTI cases were due to ESBL-positive organisms in this study and ESBL-positivity of the causative organisms for UTI was a significant risk factor for bacteremia among type 2 diabetic subjects.

Conflict of interest: Nothing to declare.

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