DOI: https://doi.org/10.53350/pjmhs22169956

ORIGINAL ARTICLE

Urinary Tract Infection due to Extended-Spectrum Beta-Lactamase Producing Organisms is a risk Factor for Acute Kidney Injury among Patients diagnosed with Diabetes Mellitus Type 2

NAIMAT ULLAH[1], TALAL ALI[2], OBAID UR RAHMAN[3], SHEERAZ AHMED[4], MUHAMMAD HAMZA[5], MUHAMMAD ZAIN NOORANI[6]
[1]*CMO, Women and Children Hospital MTI Bannu*
[2]*CMO (Casualty Medical Officer), Al Nafees Medical College and Hospital, Islamabad*
[3]*Federal Medical College Islamabad*
[4]*Senior Registrar, Al Noor Specialist Hospital Makkah, Saudi Arabia*
[5, 6]*Medical Officer, Al-Nafees Medical College and Hospital Islamabad*
Corresponding author: Naimat Ullah, Email: naimatislamian@gmail.com, Mobile: 0332 7070880

ABSTRACT

Background: UTI is one of the most prevalent bacterial infection in the adults. It is reported that the risk of ESBL-positive UTI are greater in the diabetic patients with the poor glycemic control. Acute kidney damage (AKI) and sepsis may complicate the cases of UTI.

Objective: This study was carried out to find whether the UTI caused by Extended-Spectrum Beta-Lactamase Producing Organisms is a risk Factor for Acute Kidney Injury among Patients diagnosed with Diabetes Mellitus Type 2.

Study design: It is a case control study conducted at the nephrology department of Al-Nafees medical college and hospital Islamabad for the duration of six months from January 2022 to June 2022.

Material and Material: This study was conducted on 98 patients suffering from diabetes mellitus, included majority were female members (n=55) and there were (n=43) male. The patients who had proven UTI infection were consider as the subjects for this study from their culture testing.

Results: The average age of patients was 57.5 years. The diabetes mellitus mean duration was 8.77±5.77. It was seen that age, sex and duration of diabetes mellitus has no impact on the condition as no significant difference was seen.

Conclusion: It was found that the UTI caused due to ESBL Producing Organisms like *E. coli* and *K. pneumonia*. The risk of developing UTI in diabetes mellitus type II is higher in case of ESBL producing organism infection. It is also a risk factor for acute kidney infection.

Keywords: *E. coli* and acute kidney infection.

INTRODUCTION

UTI are the most common bacterial infections. The patients diagnosed with diabetes mellitus are more prone to this infection. *Escherichia coli* is the commonly reported pathogens that cause urinary tract infections (UTIs) around the globe[1-2]. The other most commonly observed pathogen is *Klebsiella pneumonia.* The bacteria's that generate ESBL are of high concern nowadays. These continues to grow in vagina. The report have suggested that the risk of ESBL-positive UTI are greater in the diabetic patients with poor glycemic control. Acute kidney damage (AKI) and sepsis may complicate cases of UTI. UTI are prevalent bacterial infection. The bacteremia and sepsis complicate the UTI particularly pyelonephritis. Antimicrobials are considered as very effective for treatment of UTI. The major concern about such treatment is antimicrobial resistance, it is common especially among organisms that produce extended-spectrum beta-lactamase (ESBL)[3-4].

ESBL-positive organisms have naturall resistant to penicillin. Therefore, UTIs resulted from ESBL-positive organisms require injectable agents such as carbapenems and aminoglycosides. Few UTI causing organisms also have resistance to oral agents. According to clinical observations, diabetes mellitus increased the severity and complication associated with infections. According to the reported literature the scientist has concluded that the long-term sequelae and metabolic abnormalities are the determinants of infectious morbidity. Although how precisely these variables contribute to the infection is not well-understood still[5-6]. Moreover, the variability of diabetic populations hinders efforts to comprehend the relationships between diabetes and infection. It is commonly concluded that the greater frequency of complications and severity is observed in diabetic individuals. The 8 to 26% of diabetic women have asymptomatic bacteriuria. A number of the diabetic patients remain poorly characterized. The bladder dysfunction is reported in almost 50% of the population suffering from diabetes mellitus. The age, diabetes duration and metabolic control play important role in developing this dysfunction. This ultimately leads to UTI infection. The UTI infection leads to acute kidney injury in many patients. It is observed to be 2 to 3 times higher in diabetic women as compared to non-diabetic women. The diabetic patients with the long-duration complications are at the higher risk of developing UTI[7-8].

There is an increase in the incidence of asymptomatic bacteriuria in diabetic males. In the National Survey at Dutch it was concluded that the risk of developing UTI infections are 1.96 times higher in the patients with diabetes mellitus type I while the risk of developing UTI infections are 1.24 times higher in the patients with diabetes mellitus type II. Diabetes is considered as independent risk factor for pyelonephritis. When bacteria or fungi populate the urethra in women, the vagina ascend into the bladder and kidney that leads to urinary tract infection. Normal host defense mechanisms prevent bacteria from entering or persisting in the UT. Urine is a source of nutrients for the most of bacteria. The glycosuria inn urine accelerate the rate of bacterial and fungal development in urine[9-10]. This study was carried out to find whether the ESBL generating bacteria that caused UTI are a risk Factor for Acute Kidney Injury among patients diagnosed with Diabetes Mellitus type 2.

MATERIAL AND METHODS

It is a case-control study carried out at the nephrology department of Al-Nafees medical college and hospital Islamabad for the duration of six months from January 2022 to June 2022.This study was conducted on 98 patients suffering from diabetes mellitus, included majority were female members (n=55) and there were (n=43) male. The participating individuals had complete knowledge about the study and written permission was taken from them. The study was approved by the ethical committee and review board of the hospital. These patients had proven UTI infection considering from their culture studies. Patients with type 2 diabetes and a culture-proven UTI were the subjects of this study. Patients who had UTIs that were complicated by AKI were considered to be cases, while patients who did not have AKI were used as controls. A risk factor for AKI was determined to be the presence of ESBL-positive bacteria in the isolated organisms. The average age of patients was 57.5 years. The average duration of diabetes mellitus was 8.77±5.77 overall. The control group contained patients with UTI but no AKI and the diabetes mellitus mean duration was

8.92±15.66 in that case. The colony and culture characteristics of the bacteria were also studied to look for the growth and other characteristics. Triple sugar iron test was used for this purpose. The samples were sub-cultured. The antibiotic sensitivity was measured. The data was tabulated and then stratified. SPSS software was used for statistical analysis of the data recorded. The value of p less than 0.05 was considered as significant value.

RESULTS

This study conducted on 98 patients suffering from diabetes mellitus, included majority were female members (n=55) and there were (n=43) male. The participating individuals had complete knowledge about the study and written permission was taken from them. These patients had proven UTI infection considering from their culture studies. The average age of patients was 57.5. The diabetes mellitus was mean duration was 8.77±5.77 overall. The control group contained patients with UTI but no AKI and the diabetes mellitus mean duration was 8.92±15.66 in that case. It was seen that sex, age and diabetes mellitus duration has no impact on the condition as no significant difference was seen.

Table 1: Basic features of study participants

Features	Overall N=98	UTI with AKI cases n=56	UTI without AKI cases n=42	P-value
Average age	57.5± 13.2	55.3±14.4	56.44±12.22	0.765
Male: female	1:2:64	20:43	16:55	0.231
Average duration of DM	8.77±5.77	9.24±5.66	8.92±15.66	0.323
Average HbA1c	8.98±1.99	9.87±156	8.77±122	0.667

The basic features of the study group were also analyzed. It was observed that the commonest prevalence was seen in case of *E. coli* with 43 cases reported the presence of *E. coli.* Almost 43 cases of *E. coli* were ESBL positive and 16 were non-ESBL. There were 6 cases of *K. pneumoniaea* that were ESBL positive and 8 were ESBL non-positive.

Table 2: Etiological features of study group (n=131)

Organism	ESBL-positive	Non-ESBL	Sum
E.coli	43	16	59
K. pneumoniaea	6	7	13
Enterobacter Tota	3	2	5
Pseudomonas spp.	-	1	1
Citrobacter	2	5	7
Staphylococcus	-	1	1
*MRSA Staph	-	6	6
Enterococcus	-	6	6
Acinetobacter	-	-	-
Streptococcus	-	-	-
Total	54	44	98

The UTI in case of 54 patients was due to ESBL positive organisms and in 44 cases it was seen that the UTI was because of any non-ESBL organism. ESBLE positivity was seen as a major factor that triggered AKI in most of the cases.

Table 3: Analysis of UTI with ESBL positive bacteria considering as risk factor for AKI

Bacterial-Speciemen	ESBL-positive	Non ESBL
ESBL-positive (54)	30	24
Non-ESBL (44)	28	16

DISCUSSION

This study was conducted on 98 patients among these, there were 55 females and 43 males. The definition of acute kidney infection is diverse and has changed over the course of time. As per studies there are mostly three criteria that tells us about the occurrence of AKI. If there is absolute increase in level of creatinine in the body, and if the value exceeds 0.3 mg/dl over a 2 days period it could be one sign of acute kidney disease, another sign is when the serum creatinine level rises to 1.5 times more than the normal in one week that is a clear sign of acute kidney infection. If the urine formation is decreased to 0.5ml/kg/h that also indicates towards acute kidney disease. These are some of the most commonly used criteria for the definition of acute kidney disease. Most of the time first two criteria are used for serum creatinine level measurement[11-12] AKI is very common condition found in people specially that use public washrooms more often. The patients that are suffering from diabetes mellitus are at more risk of having urinary tract injection. If patient reports about the past history of CKD and AKI, then these are considered as risk factors for urinary tract infection[13]. As per studies urinary tract infection becomes worse if you have diabetes mellitus. Older age, diabetes mellitus, and urinary tract infection are all risk factors that can lead to acute kidney infection[14]. In this study the ESBL positivity of the organisms that are causing urinary tract infection in diabetes mellitus patients was studied as it is a risk factor for acute kidney disease. As per studies the ESBL positive organisms are more commonly found that cause UTI in diabetes patients. The diabetic females that have less glycemic control are more prone to develop acute kidney failure. Similar results were reported by other studies as well[15-16].

In this study it was found that the total 54 ESBL positive organisms were playing role in causing urinary tract infection and ultimately acute kidney disease among diabetes patients. Among these patients there were 43 cases reported due to *E. coli* strain that were ESBL positive then it was followed by *K. penumonaea*. As per studies in the ESBL positive organisms case, the patients reported about prior hospitalization and use of high doses of antibiotics. ESBL positive organisms causes urinary tract infection that can get worse with the passage of time[17-18-19]. Urinary tract infection damages kidney function. As per studies patients with UTI infection were studied and it was found that the rate of kidney damage was quite high in those patients. in patients that have done kidney transplants the risk of developing kidney failure increases with UTI[20-22]. However, there were some potential limitations in this study as the study was only carried out by taking data from single center. The study period was also not so long enough to report other complications that could have resulted because of ESBLE positive urinary tract infection. In this study the other risk factors and their link with the acute kidney failure was also not studied. The base line kidney function was also needed to be evaluated.

The colony and culture characteristics of the bacteria were also studied to look for the growth and other characteristics. Triple sugar iron test was used for this purpose. The samples were sub-cultured. The antibiotic sensitivity was measured. The data was tabulated and then stratified. SPSS software was used for statistical analysis of the data recorded. The value of p less than 0.05 was considered as significant value. The treatment by using angiotensin blockers like ACEIs and other blockers could have provided help to look into the matter with more precision. The use of antibiotics for nephrotoxic agents and their effect on urinary tract infection was also missing. Taking in consideration of all these results the multicenter study can be carried out in future that can give detailed analysis about Extended-Spectrum Beta-Lactamase Producing Organisms and their effect on urinary tract infection and acute kidney infection.

CONCLUSION

This study comprised analysis of ESBL Producing Organisms and their role in causing urinary tract infection among diabetes mellitus patients as it is a risk factor for acute kidney infection. *Escherichia coli* is the commonly reported pathogens that cause urinary tract infections (UTIs). The other most commonly observed pathogen is *Klebsiella pneumonia.* It is also a risk factor for acute kidney infection. There is need of good glycemic control and effective preventive measures so that UTI can be avoided due to ESBL positive organisms as it will further reduce the risk of acute kidney infection.

REFERENCES

1. Rahim MA, Zaman S, Jahan I, Habib SH, Samad T, Chowdhury TA, Saha SK, Latif A, Khoda MM, Billah MM, Ananna MA. Urinary Tract Infection due to Extended-spectrum Beta-lactamase Producing Organisms is a Risk Factor for Bacteraemia Among Patients with Type 2 Diabetes Mellitus. Bangladesh Journal of Medicine. 2020;31(1):9-12.
2. Rodríguez-Baño, J., Navarro, M.D., Retamar, P., Picón, E., Pascual, Á. and Extended-Spectrum Beta-Lactamases–Red Española de Investigación en Patología Infecciosa/Grupo de Estudio de Infección Hospitalaria Group, 2012. β-Lactam/β-lactam inhibitor combinations for the treatment of bacteremia due to extended-spectrum β-lactamase–producing Escherichia coli: a post hoc analysis of prospective cohorts. *Clinical Infectious Diseases*, *54*(2), pp.167-174.

3. Fünfstück R, Nicolle LE, Hanefeld M, Naber KG. Urinary tract infection in patients with diabetes mellitus. Clinical nephrology. 2012 Jan 1;77(1):40.
4. Landaluce-Triska E, Dominguez-Torres P, Shabaka A. Emphysematous Cystitis in a Hemodialysis Patient. The American Journal of the Medical Sciences. 2021 Oct 1;362(4):e33-4.
5. Pal S, Kumar S, Ghosh RR, Bandyopadhyay M, Chatterjee M. Clinico-bacteriological Profile of Urinary Tract Infection in Selected Patients of Type 2 Diabetes Mellitus in a Tertiary Care Hospital, Eastern India: An Observational Study.
6. Medina-Polo J, Sopeña-Sutil R, Benítez-Sala R, Lara-Isla A, Alonso-Isa M, Gil-Moradillo J, Justo-Quintas J, García-Rojo E, González-Padilla DA, Passas-Martínez JB, Tejido-Sánchez Á. Prospective study analyzing risk factors and characteristics of healthcare-associated infections in a Urology ward. Investigative and Clinical Urology. 2017 Jan 1;58(1):61-9.
7. Medina-Polo J, Naber KG, Johansen TE. Healthcare-associated urinary tract infections in urology. GMS Infectious Diseases. 2021;9.
8. Kamei J, Yamamoto S. Complicated urinary tract infections with diabetes mellitus. Journal of Infection and Chemotherapy. 2021 Aug 1;27(8):1131-6.
9. ONWUEZOBE IA. CORRELATING ANTIBIOTIC CONSUMPTION RATE WITH ANTIMICROBIAL RESISTANCE PATTERN OF UROPATHOGENS IN THE LAGOS UNIVERSITY TEACHING HOSPITAL. Faculty of Pathology. 2007.
10. Chaudhary AA. Evaluation and Quantification of Resistant Gene in Antibiotic Resistant ESBL Producing E. coli in UTI Samples with Diabetes Mellitus: A Molecular Study. Journal of Pharmaceutical Research International. 2022 Feb 5:48-60.
11. Slettengren M. *Evaluation of an automatic urinometer including use of silicone oil to decrease biofilm formation due to proteinuria, hemoglobinuria and bacterial growth* (Doctoral dissertation, Karolinska Institutet (Sweden)).
12. Carrondo CM. Health Risk Adjustment: Urinary Tract Infection Rates in Diabetic Women In-Hospital. Clin Surg. 2021;5(14):1-6.
13. Pipili C, Grapsa E. Risk Factors. Clinical Nephrogeriatrics: An Evidence-Based Guide. 2019 Aug 13:87.
14. de Cuetoa M, Aliagab L, Alósc JI, Canutd A, Los-Arcose I, Martínezf JA, Mensaf J, Pintadog V, Rodriguez-Pardoe D, Ramon J, Yusteh CP. Diagnosis and treatment of urinary tract infection. Clinical guidelines of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC).
15. AL-Hamdawee AM, AL-Zeydi AJ. Diagnosis of Klebssiella pneumonia Isolated from Clinical Cases of Hospital-Acquired Infection in Al-Dewaniyah Teaching Hospital. Al-Qadisiyah Medical Journal. 2019 Aug 26;15(1):52-60.
16. Abd AlMayahi FS. Antimicrobial Susceptibility Pattern of Klebsiella pneumonia from Various Clinical and environmental Samples in Diwaniyah hospitals. Al-Qadisiyah Journal of Pure Science. 2021 May 10;26(2):44-54.
17. Raheem AA, Mohammed GJ. Molecular Detection of Some Capsulargenes of Klebsiella pneumoniaeIsolated from Clinical Samples. Al-Qadisiyah Journal of Pure Science. 2021 Jul 16;26(4):138-45.
18. Nima M, Al-Ramahi SK. Isolation and identification Klebsiella pneumoniae bacteria from different clinical sources of human in Al-Diwaniyah city. Al-Qadisiyah Journal of Pure Science. 2020 Jul 15;25(3):1-6.
19. Ktab FK. Bacterial Species associated with appendicitis. AL-QADISIYAH MEDICAL JOURNAL. 2011;7(12):66-75.
20. Ali AK, Abdul-Kareem L, Rashed EJ. Identification of bacterial agentsand antimicrobial susceptibility of neonatal sepsis with patient, s outcome. Al-Qadisiyah Medical Journal. 2014;10(17):148-61.
21. Naher HS, Al-Mrzoq JM, Hasson SO. Gram-positive bacteremia in febrile children under two years of age in babylon province. Al-qadisiyah medical journal. 2012;8(13):1-9.
22. Al-Azawi IH. Detection of Extended Spectrum Beta Lactamase (ESBL) in Klebseilla pneumoniae Isolated from Urinary Tract Infections. Al-Qadisiyah Medical Journal. 2014;10(18):168-73.