ORIGINAL ARTICLE

MOST COMMON PATHOGENIC ORGANISMS CAUSING URINARY TRACT INFECTION IN DIABETIC VERSUS NONDIABETIC PATIENTS AND THEIR ANTIBIOTIC SENSITIVITY PATTERNS

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ABSTRACT

Background: Emerging antibiotic resistance to commonly encountered urinary tract infections are the leading cause of treatment failure in our population. This study aims to identify the most common pathogen causing urinary tract infection in diabetics versus nondiabetics and their antibiotic susceptibility.

Material and Methods: This case control study was conducted Combined Military Hospital Mardan, August 2022 - January 2023. Using a stratified sampling technique 90 patients were divided into Group DM and Group NDM with 45 participants in each group. History, demographic characteristics, symptomatology and empirical treatment prescribed was recorded for each patient and midstream urine sample was collected. Urine culture and sensitivity was performed to identify the organisms and antibiotic susceptibility of the causative agent. Recorded variables included the organisms identified and their sensitivity patterns.

Results: Gender distribution revealed males were 17(37.8%) versus 12(26.7%) from Group DM and Group NDM with a mean age of the participants was 54.64 ± 9.74 years. Clinical features like history of UTI, history of catheterization, asymptomatic bacteriuria was seen more in diabetics as compared to non-diabetics with a p value of < 0.05. *Escherichia coli* was the most common causative organism found in 44 (48.5%) out of 90 patients in both diabetic and non-diabetic patients. Antibiotic susceptibility revealed increased sensitivity of *Escherichia coli* to Fosfomycin (88.6%) followed by nitrofurantoin (81.8%) and meropenem (75%).

Conclusion: *Escherichia coli* is the most common isolate causing urinary tract infection in diabetic and non-diabetic patients which shows greatest sensitivity to Fosfomycin, nitrofurantoin and meropenem.

Key Words: Antibiotic susceptibility, Culture, Pathogen, Sensitivity.

BACKGROUND

Urinary tract infection (UTI) is one of the most common infections encountered in lifetime with a greater prevalence observed in females and diabetics as compared to males and non-diabetics.[1]

Invasion and active multiplication by a variety of organisms can cause inflammatory changes in the epithelium of the urinary tract causing infection. These organisms can travel up the urinary tract into the kidneys resulting into a more complicated infection. A variety of bacteria, viral or fungal organisms can lead to infection of the urinary tract, but the most common infection is caused by bacterial pathogens of which the common invading agents include *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae* and others.[2]

Diabetes is a common metabolic disorder leading to changes in microvasculature and macrovasculature. The decrease response of the immune system, increased blood sugar levels, neuropathy, incomplete bladder emptying and damage to other organ systems leads to greater chances of urinary tract infection. The higher chances of urinary tract infection can be partially explained by impaired function, decreased chemotaxis and suppressed phagocytic activity of the white blood cells in addition to decreased activity of Killer T cells. Several environmental factors, instrumentation of the bladder, decreased hydration and urinary continence are the risk factors which can precipitate the infection.[3]

Keeping in view the hot temperatures, poverty and poor hygiene in our country, the general population are

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more prone to develop urinary tract infection. The treatment of urinary tract infection is not as simple as it was once thought. Prompt recognition of the infection, early commencement of the right empirical antibiotics and adequate hydration are required to decrease the complications.[4]

Treatment of the urinary tract infection in both diabetics and non-diabetics is challenging as the emerging pathogens colonizing the urinary tract infection cannot be eradicated by prescribing a simple antibiotic.[5] Increase in the development of resistance against antimicrobial drugs is a global issue which needs to be addressed. A number of antibiotics have been in use empirically for treatment of urinary tract infection but none to date has been considered as gold standard. Knowledge about the evolving pathogens in our population in diabetics and non-diabetics is the need of hour.[6] The aim of this cross-sectional trial was to identify the most common isolate found in urine specimen of diabetics and non-diabetic patients presenting to our institute and to assess their antimicrobial drug sensitivity patterns.[7]

MATERIAL AND METHODS

This case control study was done at Combined Military Hospital Mardan after obtaining approval from the hospital's ethical review board under ERB no 2010/Estb/EC/02/2022. Who sample size calculator was used for the calculation of sample size. Previous research shows that the presence of urinary tract infection in diabetics was 25% as compared to 2% in non-diabetic patients.[8] With a 90% power of study and a level of significance taken as 5% the calculated sample size was 90. These 90 participants were divided in two groups i.e., Group-DM (Diabetes myelitis) and Group-NDM (non-diabetes myelitis) with 45 patients assigned to each group.

Patients of either gender who were older than 18 years with or without the history of diabetes diagnosed as cases of urinary tract infection, not taking any antibiotics willing to participate in the research were included in the study. Participants who were terminally ill or having a history of genitourinary tuberculosis, females with active menstrual cycles, pelvic inflammatory disease, tubal ovarian pathology, appendicitis colitis, male patients with epididymitis and orchitis were excluded from the trial.

Patients presenting to our hospital with symptomology were interviewed and screened. On the basis of detailed history, clinical examination and laboratory investigations patients with diagnosis of urinary tract infection were recruited in the study after obtaining a written informed consent. On the basis of comorbids, 45 diabetic patients were recruited as cases in Group DM and 45 non-diabetic patients were recruited as controls in Group-NDM. Comorbidities, demographic characteristics and clinical features of each participant were recorded on a predesigned Performa.

Urine samples were collected after providing clear instructions to the patients using aseptic technique obtaining a midstream urine sample. The specimen was inoculated on Blood agar plates and Cysteine lactose electrolyte deficient media (CLED) plates and incubated for 35 degrees Celsius ± 2 under aerobic conditions in ambient air for 48 hours. Cultures yielding growth of $>10^5$ colony forming unit were identified and further processed using microbiological tests. Modified Kirby Bauer method was used for antimicrobial sensitivity. Zone sizes were measured using latest clinical and laboratory standards institute (CLSI) guidelines 2022.[8] Pathogens identified on urine culture and their antibiotic sensitivity patterns were recorded.

RESULTS

The number of patients included in the trial were 90 which were divided into two groups with equal participants in each group. 45 patients with diabetes were assigned to Group DM and 45 patients to Group NDM. Male participants were 17 (37.8%) from group DM and 12 (26.7%) from group NDM however female patients from group DM were 28(62.2%) and 33 (73.3%) from group NDM. Mean age of participants was 62.04 ± 5.59 years in group DM and 47.24 ± 6.99 years in group NDM. Clinical characteristics among both the groups revealed significant difference in regard to previous history of UTI, previous history of catheterization, asymptomatic bacteriuria and fever as shown in Table-I. *Escherichia coli* 44(48.9%) was the most common isolate found in both the groups as a causative organism of urinary tract infection followed by *Enterococcus* 18(20%) and *Klebsiella* 11(12.2%) as shown in table II. Antibiotic susceptibility revealed increased sensitivity of *Escherichia coli* to Fosfomycin

(88.6%) followed by nitrofurantoin (81.8%) and meropenem (75%). Ampicillin, amoxicillin, ceftriaxone and ciprofloxacin showed highest resistance against *E.coli* as shown in Table-III. Ceftriaxone and ciprofloxacin was the most common empirical antibiotic prescribed to patients in both groups as shown in Table-IV.

Table-I: Clinical characteristics of the two groups.

Clinical Characteristics	Group 'DM' n (%)	Group 'NDM' n (%)	p- value
Asymptomatic bacteriuria	16 (35.6%)	04 (8.9%)	0.002
Fever	25 (55.6%)	42 (93.3%)	0.000
Dysuria	08 (17.8%)	06 (13.3%)	0.561
Urinary retention	05 (11.1%)	02 (4.4%)	0.238
Increased frequency of micturition	07 (15.6%)	06 (13.3%)	0.764
Abdominal Pain	04 (8.9%)	06 (13.3%)	0.502
Vomiting	07 (15.6%)	07 (15.6%)	1.00
Pyuria	09 (20%)	11 (24.4%)	0.612
History of UTI	18 (40%)	02 (4.4%)	0.000
History of catheterization	13 (28.9%)	01 (2.2%)	0.000
Hydronephrosis	02 (4.4%)	01 (2.2%)	0.557
Pyelonephritis	03 (6.7%)	00 (0%)	0.078

Table-II: Causative organisms among groups.

Organisms	Group 'DM' n (%)	Group 'NDM' n (%)	Total n (%)
Escherichia coli	25 (55.6%)	19(42.2%)	44(48.9%)
Enterococcus spp	07(15.6%)	11 (24.4%)	18(20%)
Klebsiella pneumoniae	07(15.6%)	04 (8.9%)	11(12.2%)
Pseudomonas aeruginosa	03(6.7%)	04(8.9%)	07(7.8%)
Enterobacter cloacae	02(4.4%)	04(8.9%)	06(6.7%)
Candida	01(2.2%)	03(6.7%)	04(4.4%)

Table-III: Urine isolates and their % resistance to antimicrobials.

Antibiotics	*Escherichia coli* 44 (48.9%)	*Enterococcus spp* 18(20%)	*Klebsiella pneumoniae* 11(12.2%)	*Pseudomonas aeruginosa* 07(7.8%)	*Enterobacter cloacae* 06(6.7%)
Ampicillin	96	61.1	100	100	100
Amoxicillin clavulanate	91	61.1	82	100	100
Ceftriaxone	91	100	82	100	100
Cefepime	75	Not tested	82	71	67
Piperacillin tazobactam	71	Not tested	73	71	67
Trimethoprim sulfamethoxazole	68	Not tested	73	100	67
Ciprofloxacin	93	89	82	71	83
Levofloxacin	84	78	82	71	67
Imipenem	30	61	55	43	50
Meropenem	25	100	36	29	33
Nitrofurantoin	18	22	27	100	50
Fosfomycin	11	11	9	100	00
Vancomycin	Not tested	33	Not tested	Not tested	Not tested

Table-IV: Empirical treatment prescribed among groups.

Antibiotics prescribed empirically	Group 'DM' n(%)	Group 'NDM' n(%)	Total n (%)
Ceftriaxone	18 (40%)	17(37.8%)	35(38.9%)
Ciprofloxacin	07(15.6%)	05 (11.1%)	12(13.3%)
Meropenam	02(4.4%)	03 (6.7%)	05(5.6%)
Tazobactem piperacillin	10(22.2%)	08(17.8%)	18(20%)
Amikacin	01(2.2%)	02(4.4%)	03(3.3%)
Nitrofurantoin	04(8.9%)	05(11.1%)	09(10%)

DISCUSSION

This case control study was conducted to evaluate the most common pathogen responsible for causing UTI in diabetics and non-diabetic patients. The isolates received from all the patients in the trail revealed that *Escherichia coli* was the most common isolate identified in all the specimen collected from participants of both groups. Such patients presenting to outpatient clinics and emergency reception of our hospital were treated empirically with conventional antibiotics by attending doctors. Increase in the resistance of organisms against antimicrobials can lead to failure of treatment. Ceftriaxone was prescribed to 35(38.9%) of the patients while ciprofloxacin to 12(13.3%) of the patients however the antibiotic susceptibility patterns revealed higher resistance of 91% and 93% by *E.coli* respectively.

Similar to our study another trial performed in diabetic patients in Ethiopia revealed that the most common organism causing UTI was *Escherichia coli* (63.6%) followed by *Klebsiella pneumoniae* (13.6%).[9] History of previous urinary tract infection and duration of diabetes mellitus were the leading risk factors leading to infection in diabetics.[10]

Similar to the results achieved from our trial, Raya et al found that Diabetic patients are more prone to urinary tract infections as compared to non-diabetic patients. The most common pathogen responsible for UTI in both diabetics and non-diabetics was *Escherichia coli*. Similarly, the antibiotic susceptibility revealed that the pathogen carry a high resistance against quinolones, penicillin and cephalosporin as found in our trial.[11]

A local trial performed at a tertiary care hospital in Northwest General Hospital and Research Centre, Pakistan also revealed that *Escherichia coli* was the most common pathogen responsible for causing UTI in 71% of diabetic patients and drugs similar to our study including Fosfomycin, nitrofurantoin and imipenem were the most sensitive drugs against the pathogen.[12]

A comparative study conducted in diabetics versus nondiabetics in Nepal revealed that gram negative rods were the most common isolates causing urinary tract infection including *E.coli* and *Klebsiella pneumoniae*.[13] Female gender and diabetes were the predominant risk factors which can cause UTI.[14]

The emergence of resistant strains has led to treatment failure leading to increased morbidity. The usual empirical treatment prescribed to patients presenting with UTI is usually not effective as proved by a study done by et al. This trial suggested to modify the empirical antibiotics for the treatment of UTI for better outcomes.[15]

Diabetics were found to be twice as prone to UTI as in comparison with a nondiabetic patient. Female gender increased the risk up to 5 folds. Asymptomatic bacteriuria was found in 31.4%[16] of the patients as compared to 35.6% in our trial. *Pseudomonas* was identified in 16% of the urine cultures as compared to a lower percentage of 6.7% in our patients.[17]

The increase in prevalence of diabetes among our population leads to increased chances of urinary tract infection.[18] Empirical treatment of antibiotics cannot eradicate the organisms which can result in multiple complications in patients presenting with urinary tract infections.[19] Similar to several trials our study proves that diabetic patients are more prone to develop urinary tract infection and the most common organism responsible for UTI in both diabetics and nondiabetic patients remains *Escherichia coli* which shows greater sensitivity to Fosfomycin followed by nitrofurantoin and meropenem. Empirical treatment given to such patients requires modification and addition of more sensitive drugs for better outcome.

CONCLUSION

Escherichia coli is the most common isolate causing urinary tract infection in diabetic and non-diabetic patients which shows greatest sensitivity to Fosfomycin, nitrofurantoin and meropenem.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Sundas Shaukat: Conception, Research Analysis and Manuscript Drafting.

Ashfaq Hussain: Data collection, Research Supervision.

Mazhar Shaukat: Research analysis and final approval of the version to be published.

Laila Shaukat: Research supervision and analysis

Nayab Zamir: Data interpretation and drafting.

Haseeba Arif: Research analysis and final approval of the draft.

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