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Original Research Article

Clinical and microbiological profile of type 2 diabetic patients with urinary tract infections

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ABSTRACT

Background: Diabetes Mellitus is reported to increase the risk of Urinary Tract Infection (UTI) with higher probability of drug resistant organisms. Understanding the burden, microbiological profile and antibiotic sensitivity pattern is vital for effective prevention and management. To assess the microbiological profile and antibiotic sensitivity pattern of Urinary Tract infections among type 2 diabetes mellitus patients.
Methods: The study was A prospective observational study done on 117 type 2 diabetic subjects aged above 18 years presenting with symptoms of UTI in a tertiary care hospital Urine was analyzed for urine routine examination, culture and antibiotic sensitivity using standard testing methods on a midstream urine sample. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables.
Results: The mean age of the study population was 57 years. Females constituted 62.39% of participants. Burning micturition (52.99%) was the most common presenting symptom. The prevalence of culture positive UTI was 51.28%. Among gram-negative bacilli, *Escherichia coli* (20.51%), *Klebsiella* (6.85%) dominated the culture reports. *Enterococcus* (4.27%) and *Staphylococcus aureus* (2.6%) were the common gram-positive organisms isolated. Meropenem was the most effective antibiotic against *E. coli* (87.5%) and *Klebsiella* (95%) Vancomycin had 100% sensitivity against *Enterococci* and *S. aureus*.
Conclusions: More than half of diabetic patients presenting with symptoms of UTI had culture positive UTI, predominantly caused by gram negative organisms. There is a need for comparative studies of Diabetes and controls to explore the key differences in the pattern of UTI.

Keywords: Antibiotic sensitivity, Culture positive, Drug resistance, *Escherichia coli*, Microbiological profile, Urinary tract infection

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by increased levels of blood glucose leading to damage all over the body especially resulting in retinopathy, neuropathy, nephropathy and cardiac complications. In the past few decades, there has been a dramatic increase in the prevalence of diabetes mellitus. According to the IDF Diabetic atlas, it was estimated that in 2017 there were 451 million people aged between 18 to 99 years suffering from diabetes worldwide and these figures were estimated to increase to 693 million by 2045.[1] The global diabetes prevalence was estimated to be 8.8% with 95% confidence interval of 7.2-11.3% in 2017, standardized for the age group of 20 to 79 years.[2] According to ICMR -Indian study, the overall prevalence of diabetes in all 15 states of India was 7·3% (95% CI 7·0-7·5).[3] It varied from 4·3% in Bihar to about 10·0% in Punjab. It was

higher in urban areas than in rural areas.[3] In diabetic subjects, there is a greater risk of acquiring serious ascending infections of the urinary tract.[4,5] The higher amounts of glucose excreted in urine help in the growth of bacteria in these individuals. In diabetes, there is disturbance in the intracellular insulin signaling pathways along with defects in the defensive system against the microbes due to the reduced expression of the effectors of innate immune system.[6] Altered bacterial adhesion to uroepithelium and granulocyte dysfunction plays a major role in the pathogenesis of UTI in diabetic population.[7] The probability of antibiotic-resistant organisms causing UTI is high in subjects with Diabetes. Compared to subjects without diabetes, in diabetic patients, the prevalence of pyelonephritis is significantly higher. The most common organism isolated was *E. coli*.[8] Elevated Glycosylated Hemoglobin (HbA1c) predisposes people with diabetes to UTI.[8] In Diabetic subjects, the severity of UTI is high, caused by more resistant pathogens and the outcome in these group of subjects is also poor compared to normal subjects without diabetes.[4] Hence, screening for UTI in diabetic patients is very important to enable bacteriuria to be properly treated and prevent further complications. But controversies exist with regards to prevalence of culture-positive UTI in diabetic population.[9-12] Indiscriminate use of antibiotics often results in the increased resistance of urine pathogens to most commonly used antimicrobial agents.13. Hence the current study was conducted to assess the prevalence of culture-positive Urinary Tract Infection (UTI) among the people with type 2 diabetes mellitus, presenting with symptoms suggestive of UTI and analyze the microbiological profile and antibiotic sensitivity pattern among type 2 diabetic population.

METHODS

The current study was a prospective observational study conducted in the department of general medicine, RL Jalappa Hospital, Kolar, Karnataka. The study was conducted between December 2018 to November 2019.

Inclusion criteria

- The study population included adults aged above 18 years, belonging to both genders, known cases of type 2 diabetes mellitus for at least last 1 year, presenting with symptoms suggestive of UTI.

Exclusion criteria

- People who had a history of any surgical procedure involving the genito-urinary tract, people with a history of hospitalization in last 1 month with urinary catheterization, people with type 1 diabetes mellitus were excluded from the study.

The study was approved by the institutional human ethical committee. After obtaining the informed written consent, all the study participants were evaluated by thorough clinical history, physical examination. History regarding the duration of diabetes and other co-morbidities was collected. A mid-stream urine sample was collected from all the study participants in a sterile container and sent for urine routine examination, culture and antibiotic sensitivity. About 10 ml of venous blood was collected under aseptic conditions and transported for the assessment of FBS, PPBS, HbA1c, blood urea, serum creatinine, hemoglobin and total leucocyte counts.

Sample size was calculated assuming the proportion of UTI as 21% as per the study by Simkhada R et al.[12] The other parameters considered for sample size calculation were 8% absolute precision and 95% confidence level. The following formula was used for sample size calculation. Based on the previous hospital records, the approximate number of potential anterior uveitis cases to be attending the study setting during the data collection period were considered as 200. Hence a finite population correction was applied for 200. The minimum required number of subjects as per the above-mentioned calculation was 112. To account for a non-participation rate of 5%, we needed 117 minimum sample size.

Statistical analysis

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non-normally distributed quantitative variables were summarized by the median and Interquartile Range (IQR). Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.

p value <0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

RESULTS

A total of 117 people was included in the final analysis. The mean age was 57.13±12 years. Among the study population, 44 (37.61%) participants were male and remaining 73 (62.39%) participants were female. Among the study population 62 (52.99%) had burning micturition, 48 (41.03%) had to fever, 45 (38.46%) had frequency, 26 (22.22%) had suprapubic pain, 23 (19.66%) had urgency, 19 (16.24%) had Incontinence, 17 (14.53%) had hematuria, 10 (8.55%) had back pain and 7 (5.98%) had flank pain. The mean duration of diabetes in years was 9.37±4.95. Among the study population, 32 (27.35%) had diabetes less than 5 years of duration. 57 (48.72%) had diabetes 5 to 10 years of duration, and 28 (23.93%) had diabetes more than 10 years of duration. Among the study population 40 (34.19%) were taking Insulin, 37 (31.62%) were taking OHA, 26 (22.22%) were taking both insulin and OHA (Table 1).

The mean pulse was 87.19±16.95 beats per minute. The mean systolic BP was 117.78±20.6 mm of Hg. The mean diastolic BP was 76.85±15.03 mm of Hg. The mean GHB

was 8.55±2.53%. The mean FBS was 172.38±73.67 mg/dl. The mean PPBS was 225.35±103.91 mg/dl. The mean Urea was 49.38±32.27 mg/dl. The mean Creatinine was 1.41±1.1 mg/dl. The mean haemoglobin was 10.3±2.39 g/dl. The mean WBC was 14.8±7.16 T/cumm. The mean platelets were 249.03±114.84 T/cumm. Among the study population 32 (27.35%) had good diabetic control (GHB<6.5), 20 (17.09%) had fair diabetic control (GHB-6.5 to 7), 26 (22.22%) had Sub-optimal diabetic control (GHB-7 to 9) and 39 (33.33%) had Poor diabetic control (GHB>9). Among the study population 7 (5.98%) had severe anaemia, 36 (30.77%) had moderate anaemia, 36 (30.77%) had mild anaemia and 38 (32.48%) were normal. Among the study population 22 (18.80%) people had tachycardia (Table 2).

Table 1: Descriptive analysis of demographic parameters in the study population (n=117).

Parameter		Summary
Age (mean±sd)		57.12±12.0
Gender	Male	44 (37.61%)
	Female	73 (62.39%)
Symptoms	Burning micturition	62 (52.99%)
	Fever	48 (41.03%)
	Frequency	45 (38.46%)
	Suprapubic pain	26 (22.22%)
	Urgency	23 (19.66%)
	Incontinence	19 (16.24%)
	Hematuria	17 (14.53%)
	Back pain	10 (8.55%)
	Flank pain	7 (5.98%)
Duration diabetes (years)		9.37 ± 4.95
Duration of DM category	<5 years	32 (27.35%)
	5 to 10 years	57 (48.72%)
	>10 years	28 (23.93%)
Treatment	Insulin	40 (34.19%)
	Oha	37 (31.62%)
	Both	26 (22.22%)
	No treatment	14 (11.97%)

Among the study population, all 117 (100%) had acidic urine PH. Among the study population 75 (64.10%) had proteinuria. Of these, 45 (38.46%) had grade 1 proteinuria, 18 (15.38%) had grade2, 9 (7.69%) had grade 3, only one subject had grade 4, and 2 (1.71%) had traces of protein in urine. Among the study population 53 (45.3%) had glycosuria.

Of these, 18 (15.38%) had grade 1 glycosuria, 16 (13.68%) had grade 2, 2 (1.71%) had grade 3, and 17 (14.53%) had traces of glucose in urine. Among the study population 56 (47.86%) had up to 6 cells of WBC in urine and 61 (52.14%) had more than 7 cells of WBC in urine. Among the study population 43 (36.75%) had hematuria. Of these, 21 (17.95%) had grade 1 hematuria, 12 (10.26%) had grade 2, 10 (8.55%) had grade 3 hematuria (Table 3).

Table 2: Descriptive analysis of clinical parameters in the study population (N=117).

Parameter		Mean±sd
Hba1c		8.55±2.53
FBS (mg/dl)		172.38±73.67
PPBS (mg/dl)		225.35±103.91
Urea	(Up to 39.99)	58 (49.6%)
	(40 and above)	59 (50.4%)
Creatinine	Up to 1.2	74 (63.2%)
	>1.2	43 (36.8%)
Haemoglobin (g/dl)		10.3±2.39
WBC		14.8±7.16
Hba1C	Good diabetic control (<6.5)	32 (27.35%)
	Fair diabetic control (6.5 to 7)	20 (17.09%)
	Sub optimal diabetic control (7 to 9)	26 (22.22%)
	Poor diabetic control (>9)	39 (33.33%)
Anaemia	Severe (<6)	7 (5.98%)
	Moderate (6.01 to 9)	36 (30.77%)
	Mild (9.01 to 11)	36 (30.77%)
	Normal (more than 11	38 (32.48%)
Tachycardia	Normal (up to 100)	95 (81.20%)
	Tachycardia (more than 100)	22 (18.80%)

Table 3: Descriptive analysis of urine components in the study population (N=117).

	Parameter	Summary
Proteinuria	Yes	75 (64.10%)
	No	42 (35.90%)
Proteinuria grade	1+	45 (38.46%)
	2+	18 (15.38%)
	3+	9 (7.69%)
	4+	1 (0.85%)
	Nil	42 (35.90%)
	Traces	2 (1.71%)
Glycosuria	Yes	53 (45.3%)
	No	64 (54.70%)
Glycosuria grade	1+	18 (15.38%)
	2+	16 (13.68%)
	3+	2 (1.71%)
	Nil	64 (54.70%)
	Traces	17 (14.53%)
Urine WBCs	Normal	56 (47.86%)
	Increased pus cells	61 (52.14%)
Hematuria	Yes	43 (36.75%)
	No	74 (63.25%)
Hematuria grade	1+	21 (17.95%)
	2+	12 (10.26%)
	3+	10 (8.55%)
	Nil	74 (63.25%)

Majority of the study population 24 (20.51%) yielded E. *coli* in their urine culture, 9 (7.7%) had Insignificant Bacteriuria, 8 (6.85%) had *Klebsiella* and 5 (4.27%) had *Enterococcus*. Among the study population, 60 (51.28%) had positive culture and remaining 57 (48.72%) had negative culture (Table 4).

Table 4: Descriptive analysis of organisms isolated and culture in the study population (N=117).

Parameter	Frequency
Organisms isolated	
E. Coli	24 (20.51%)
Klebsiella	8 (6.85%)
Enterococcus	5 (4.27%)
Staphylococcus aureus	3 (2.6%)
Candida albicans	3 (2.6%)
Candida tropicalis	3 (2.6%)
Pseudomonas aeruginosa	2 (1.71%)
Acinetobacter	1 (0.90%)
Proteus mirabilis	1 (0.90%)
Culture	
Positive	60 (51.28%)
Negative	57 (48.72%)

Among the people with *E. Coli* 41.7% were sensitive to Tobramycin, 64.2% were sensitive to Amikacin, 33.3% were sensitive to Cotrimoxazole, 79.2% were sensitive to Nitrofurantoin, 87.5% were sensitive to Meropenem, 70.8% were sensitive to Piperacillin-tazobactam, 33.5% were sensitive to Ceftazidime, 4% were sensitive to amoxicillin-clavulanate. 50% were sensitive to Gentamicin, 80% were sensitive to Imipenem, 82.5% were sensitive to Ertapenem, 4.2% were sensitive to Ciprofloxacin, 12% were sensitive to Levofloxacin, 4.2% were sensitive to Norfloxacin. 24% were sensitive to Ceftriaxone, 12% were sensitive to Chloramphenicol. Among the people with *Klebsiella* 32.5% were sensitive to Tobramycin, 71.2% were sensitive to Amikacin, 32.5% were sensitive to Cotrimoxazole, 65.0% were sensitive to Nitrofurantoin, 95.0% were sensitive to Meropenem, 63.5% were sensitive to Piperacillin-tazobactam, 36% were sensitive to Ceftazidime, 50% were sensitive to Gentamicin, 92.5% were sensitive to Imipenem, 72% were sensitive to Ertapenem, 25.0% were sensitive to Ciprofloxacin and 37.5% were sensitive to Norfloxacin.

Among the people with enterococcus culture 60.0% were sensitive to Nitrofurantoin, 40.0% were sensitive to Piperacillin-tazobactam, 100% were sensitive to Vancomycin, and 100% were sensitive to Linezolid. Among the people with *Staphylococcus aureus* 52.5% were sensitive to Cotrimoxazole, 100.0% were sensitive to Nitrofurantoin, 20.0% were sensitive to Piperacillin-tazobactam, 50% were sensitive to Ceftazidime, 80% were sensitive to Gentamicin, 25.0% were sensitive to Ciprofloxacin and 37.5% were sensitive to Norfloxacin (Table 5).

DISCUSSION

In subjects with diabetes mellitus, the UTI spectrum can range from asymptomatic bacteriuria to pyelonephritis, renal abscess and severe urosepsis. Type 2 diabetes mellitus is a risk factor for both Community-acquired UTI and Hospital-acquired UTI.4, 14, 15 The prevalence of culture-positive UTI in this study was 51.28%. Similar to this study, Sharma S et al. reported a prevalence of 43% in their study on diabetic subjects aged over 60 years in south India.[16] The prevalence of culture-positive Urinary Tract Infection in diabetic subjects was only 21% in the study by Simkhada R et al, in Nepal.[12] They conducted their study on 100 patients in which 53 were females.

This study was carried out on 117 subjects with majority (62.39%) being females. This difference could be due to the fact that their study was done in a different demographic group in Nepal which was aged 80 and above. The mean age of this study population was 57 years. Burning micturition (52.99%) was the most common presenting symptom followed by Fever (41.03), increased frequency of urination (38.46%), suprapubic pain (22.22%), urgency (19.66%), Incontinence (16.24%) and hematuria (14.53%). Simkhada R et al, observed that burning micturition (90%), increased frequency of micturition (80%), suprapubic pain (60%), urgency (70%), loin pain (30%), and fever (20%) were the most common symptoms similar to this study.[12] The mean duration of diabetes in this study was 9.37 years, and majority (48.72%) had diabetes for 5 to 10 years.

Simkhada R et al, observed that UTI was common among subjects with prolonged duration of diabetes (p=0.039) and among those receiving insulin as compared to those under oral medications (p=0.08).[12] The majority (34.19%) of the study subjects were on Insulin in this study while 31.62% were on OHA. Aswani SM et al, in their study observed that majority of the people with diabetes with UTI (87.14 per cent) had HbA1c >6.5 per cent with p<0.001.[8] The mean HbA1c levels were also increased (8.55±2.53) in this study, 22.22% had Sub-optimal diabetic control (HbA1c of 7 to 9) while 33.33% had Poor diabetic control (HbA1c >9). The mean WBC count was increased ([14.8±7.16] X 103 cells/ cubic mm) in this study. Sharma S et al, in their study also observed 30.2% patients in the bacteriuric group and 12.3% patients in the non-bacteriuric group had leukocytosis.[16]

In this study, Majority (20.51%) had *E. coli* in their urine culture. 7.7% had Insignificant Bacteriuria. Gram-negative bacilli such as *E. coli* (20.51%), *Klebsiella* (6.85%) dominated the culture reports. In Gram-positive organisms, *Enterococcus* (4.27%) was the most cocci observed followed by *Staphylococcus aureus* (2.6%). Among the fungi, *Candida albicans* and *Candida tropicalis* were observed in 2.6% of the subjects respectively. Similar to this study, other studies also reported that *E. coli* was the most common isolated

organism in culture.[11,12,16] In the study by Sharma S et al, *E. coli* (69.8%) was the most common causative organism in urine culture analysis, followed by *Klebsiella* (16.3%).[16] Sharma S et al, in their study observed that majority of isolated organisms were sensitive to antimicrobial agents like nitrofurantoin and imipenem.[16] Simkhada R et al, also observed that *Escherichia-coli* was most common organism followed by *Klebsiella*, proteus and pseudomonas.[12] Simkhada R et al, also observed that most of the urinary isolates were sensitive to ciprofloxacin, cotrimoxazole and ceftriaxone, whereas resistance was high for ampicillin.[12] In Sudan, Hamdan HZ et al, in their study observed that *E. coli* was the most frequent isolate organism in diabetic subjects followed by *K. pneumoniae*.[11]

They also observed that *E. coli* was 100% sensitive to gentamicin and cephalexin. The antibiotic of choice against gram negative organisms according to this study results was Meropenem followed by Nitrofurantoin. For gram positive organisms, Vancomycin had 100% sensitivity against *Enterococci* and *S. aureus*. In this study, Meropenem was the most effective antibiotic against *E. coli* (87.5%) and *Klebsiella* (95%). The next best was Nitrofurantoin with sensitivity of 79.2% against *E. coli*, 65% against *Klebsiella*, 60% against *Enterococcus* and 100% against *S. aureus*. Tobramycin had a sensitivity of 41.7% against *E. coli*, 37.5% against *Klebsiella*.

Hence, Meropenem and Nitrofurantoin could be the preferred choice of antimicrobial agents in the treatment of urinary tract infections. In developing countries, with increasing antimicrobial drug resistance, it is important to identify factors that place patients at increased risk for a multidrug-resistant infection, so that broad-spectrum antibiotics can be reserved for use in these patients. Limiting broad-spectrum empiric antibiotics to patients with proven risk factors can help slow the prevalence of resistance to these antibiotics.

This study was only a hospital-based study, limited by its small sample size and observational study design, denying the temporal relationship of causative organisms in diabetic patients. Hence this study results cannot be extrapolated to other populations. But this study findings are an important step in this area where literature is scarce considering its usefulness in day to day management of UTI in diabetic subjects. Large scale community-based studies are the need of the hour for determining the causative organisms, antibiotic sensitivity pattern and further management.

CONCLUSION

More than half (51.28%) of the diabetic patients with suspected UTI had culture positive UTI. It is important to identify factors leading to increased risk for a multidrug-resistant infection in diabetic subjects so that broad-spectrum antibiotics can be reserved only for them.

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