

Clinical and Laboratory Profile of Urinary Tract Infections in Type 2 Diabetics Aged over 60 Years

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ABSTRACT

Introduction: Urinary tract infections are frequently encountered among diabetic patients and the incidence rate increases with age. There have been growing research to identify the clinical profile of urinary tract infections in diabetic patients. However, such studies on elderly patients are rare.

Aim: To determine the risk factors, clinical/laboratory profiles, causative organisms and antimicrobial susceptibilities in type 2 diabetics aged over 60 years.

Materials and Methods: This prospective single centre study was conducted at NRI Medical College and General Hospital, Guntur, India, between November 2012 and November 2014. A total of 100 consecutive patients with type 2 diabetes mellitus, aged over 60 years, with symptoms suggestive of urinary tract infection were examined. Subsequently, the demographic characteristics, detailed medical history, signs/symptoms of urinary tract infections, laboratory investigations for blood and urine samples, ultrasound abdomen findings were compared between bacteriuric and non bacteriuric patients. In addition, the organisms in urine cultures and antibiotic sensitivity patterns were investigated for bacteriuric patients. Two groups were compared using the Mann-Whitney test for continuous variables

and the Chi-square or the Fisher's exact test for categorical respectively.

Results: Bacteriuria was found in 43% of type 2 diabetic patients aged over 60 years. Comparative analysis revealed that bacteriuria was more common among patients with female gender ($p=0.028$), diabetes duration of >15 years ($p=0.011$) and diabetes complications such as neuropathy ($p=0.027$) and diabetic foot ($p=0.003$). Age and uncontrolled fasting blood sugar or HbA1c levels did show an increased propensity for developing urinary tract infections. Increased frequency (76.7%), and urgency (67.4%), dysuria (65.1%) were significantly more common among bacteriuric patients than that in nonbacteriuric patients ($p<0.05$). Urine culture analysis revealed that *E. coli* (69.8%) was the most common causative organism, followed by *Klebsiella* (16.3%). Majority of isolated organisms were sensitive to antimicrobial agents like nitrofurantoin and imipenem.

Conclusion: Bacteriuria was very common in elderly patients with diabetes. The observed trends in risk factors, clinical profile, laboratory profile, causative organism patterns, and antimicrobial susceptibilities will help to add the growing literature on this topic.

Keywords: Bacteriuria, Diabetes mellitus, *Escherichia coli*, Risk factor

INTRODUCTION

Diabetes mellitus is the most common endocrine disease of this century [1]. Changing lifestyle and urbanization has caused an increase in the incidence in developing countries, including India [1]. It has been estimated that India has the largest number of diabetics in the world, with a prevalence of about 40.9 million individuals [2]. Diabetes can slow down the body's ability to fight against pathogens by weakening the immune system, which may lead to a greater frequency and severity of certain infections, especially foot infections, yeast infections, surgical site infections and urinary tract infections [3]. Of these, urinary tract infections are of major concern as many recent studies have shown an increased prevalence of urinary tract infection in diabetics [4]. Poor circulation in diabetics, reduced ability of white blood cells to fight infection, dysfunctional bladders that contract poorly may contribute to the increased prevalence of urinary tract infections among diabetic individuals [4]. Diabetic complications like neuropathy and glycosuria can also predispose such infections [3]. Of note, elderly diabetics are found to have a five fold higher mortality risk due to urinary tract infections than elderly non diabetics [4]. The major factors that may predispose the development of urinary tract infection in elderly diabetic patients may include longer duration of diabetes, high levels of glycated haemoglobin (HbA1c), comorbidities of glycosuria/pyuria, and increased ability of pathogens to adhere to urinary tract mucosa [5]. In recent years, there have been growing

research to identify the clinical profile of urinary tract infections in diabetic patients [6]. However, such studies on elderly patients are rare. With this background, the present study was conducted to examine the clinical and laboratory profile of urinary tract infections in type II diabetic elderly patients.

MATERIALS AND METHODS

Study Design and Patient Population

In this prospective single centre study, diabetic patients who were admitted at NRI Medical College and General Hospital, Guntur, India, between November 2012 and November 2014 were selected for the study. Inclusion criteria were: (a) age >60 years; (b) diagnosis of type 2 diabetes; (c) fasting blood glucose levels ≥ 126 mg/dl and post-prandial blood glucose level ≥ 180 mg/dl; and (d) clinical or microbiological features of urinary tract infections. Patients with a history of diabetes and those who were on treatment for the same were also eligible for the study. On the other hand, patients who had a history of receiving antibiotics within two weeks prior to culture and those on continuous indwelling catheter were excluded. Accordingly, 100 consecutive patients were enrolled irrespective of their sex, duration of diabetes, treatment, and adherence to treatment. Informed consent was obtained from each patient at the time of enrollment. The study protocol was approved from the Institutional Review Board.

Data Collection

A detailed history was taken for each patient, with special reference to age, gender, duration of diabetes, type of anti-diabetic treatment, adherence to treatment, and complications of diabetes. Common symptoms related to urinary tract infection like frequent urination, urinary urgency, burning micturition, dysuria, haematuria, pyuria, suprapubic pain, flank pain, and fever were noted. Blood samples were collected for the estimation of haemoglobin levels, leukocytes levels, fasting blood sugar levels, and HbA1c levels. Abdominal ultrasonography was performed to evaluate various urinary tract infections including Benign Prostatic Hyperplasia (BPH), cystitis, and pyelonephritis. Post-void residual urine volume was also estimated in each patient. Midstream urine samples were collected under sterile conditions and were estimated for pH and specific gravity. For culture analysis, urine samples were incubated at 37°C for 24–48 hours in blood agar and MacConkey agar plates and the organisms were identified based on colony characteristics, lactose fermentation, and biochemical tests. Sensitivity to common antibiotics was tested in all positive cultures.

Study Groups

Based on the findings of urine culture analysis, patients were divided into two groups: (a) patients with bacteriuria; and (b) patients without bacteriuria. Here, patients with bacteriuria were characterized by uncentrifuged gram-stained urine containing at least one organism per oil immersion field, correlating with a colony count of $>10^5$ CFU/ml. Subsequently, the clinical and laboratory profiles were compared between these two groups.

STATISTICAL ANALYSIS

All data were analysed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 17.0. Continuous variables are presented as mean \pm standard deviation, while categorical variables are presented as frequency and percentages. For the statistical comparison between the two groups, the non-parametric Student's t-test (i.e., the Mann-Whitney test) was used for continuous variables and the Chi-square test or the Fisher's-exact test was used for categorical variables. A p-value <0.05 was used to identify statistically significant difference between two groups.

RESULTS

Baseline Demographics of Elderly Diabetic Patients

A total of 100 elderly diabetic patients with clinical or microbiological evidence of urinary tract infection were enrolled in the study. Of them, 57 (57%) patients had no evidence of bacteriuria, while 43 (43%) patients had bacteriuria. The baseline demographics for these two groups of patients are given in [Table/Fig-1]. In brief, the mean age of patients in the bacteriuria and non bacteriuria groups were 70.95 ± 7.3 and 69.35 ± 5.46 respectively ($p=0.22$). Further, there was a significant female preponderance in bacteriuria group ($p=0.028$). The mean duration of diabetes was significantly more for non bacteriuric patients than for bacteriuric patients (17.90 vs. 14.82 years; $p=0.011$). No difference was observed between two groups with regard to the type of treatment for diabetes. However, treatment adherence was significantly more among patients in the non bacteriuria group than that in the bacteriuria group (31.6 vs. 16.3%; $p<0.001$). Various diabetic complications were more common among bacteriuric patients than non bacteriuric patients, with statistically significant differences for peripheral neuropathy ($p=0.027$) and diabetic foot ($p=0.003$). Comorbidities like hypertension and ischemic heart disease were comparable between two groups.

	Bacteriuria (n=43)	Non bacteriuria (n=57)	p-value
Gender			
Male	16 (37.2%)	34 (59.6%)	0.028
Female	27 (62.8%)	23 (40.4%)	
Age (years)	70.95 ± 7.3	69.35 ± 5.46	0.22
60–69 years	17 (39.5%)	23 (40.4%)	0.308
70–79 years	20 (46.5%)	31 (54.3%)	
>80 years	6 (14.0%)	3 (5.3%)	
Duration of Diabetes	14.82 ± 6.63	17.90 ± 6.95	0.011
1–5 years	6 (13.9%)	5 (8.7%)	0.060
6–10 years	10 (23.3%)	7 (12.3%)	
11–15 years	2 (4.5%)	13 (22.8%)	
16–20 years	17 (39.5%)	17 (29.8%)	
>20 years	8 (18.8%)	15 (26.4%)	
Treatment taken for diabetes			
Insulin	11 (25.6%)	17 (29.8%)	0.661
Oral hypoglycaemic agents	22 (51.2%)	26 (49.7%)	0.833
Both	7 (16.2%)	8 (14%)	0.784
No treatment	3 (7.0%)	6 (10.5%)	0.728
Adherent to treatment	7 (16.3%)	18 (31.6%)	<0.001
Adherent to follow up	4 (9.3%)	8 (14.0%)	0.119
Complications of diabetes			
Retinopathy	17 (39.5%)	16 (28.1%)	0.284
Peripheral neuropathy	25 (58.1%)	20 (35.1%)	0.027
Nephropathy	11 (25.6%)	9 (15.8%)	0.313
Diabetic foot	16 (37.2%)	6 (10.5%)	0.003
Hypertension	16 (37.2%)	16 (28.1%)	0.389
Ischemic heart disease	7 (16.3%)	14 (25.0%)	0.336
Others	0 (0)	4 (7.0%)	0.132

[Table/Fig-1]: Demographic details of elderly diabetic patients with and without bacteriuria.

Signs/symptom	Bacteriuria (n=43)	Non bacteriuria (n=57)	p-value
Asymptomatic	0 (0%)	14 (24.6%)	<0.001
Fever	14 (32.6%)	12 (21.1%)	0.251
Dysuria	28 (65.1%)	18 (31.6%)	0.001
Increased frequency	33 (76.7%)	26 (45.6%)	0.046
Urgency	29 (67.4%)	7 (12.3%)	<0.001
Haematuria	12 (27.9%)	8 (14.0%)	0.129
Pyuria	0 (0%)	1 (1.7%)	1.000
Flank pain	11 (25.6%)	6 (10.5%)	0.628
Suprapubic pain	20 (46.5%)	16 (28.1%)	0.062
Suprapubic tenderness	14 (32.6%)	11 (19.3%)	0.163
Renal angle tenderness	11 (25.6%)	9 (15.8%)	0.313

[Table/Fig-2]: Clinical characteristics of urinary tract infection symptoms in elderly diabetic patients with bacteriuria and without bacteriuria.

Finding	Bacteriuria (n=43)	Non bacteriuria (n=57)	p-value
Normal	21 (48.8%)	50 (87.7%)	<0.001
Benign Prostatic Hyperplasia (BPH)	2 (4.7%)	7 (12.3%)	0.293
Cystitis	8 (18.5%)	0 (0%)	<0.001
Pyelonephritis	12 (28%)	0 (0%)	<0.001

[Table/Fig-3]: Findings of abdominal ultrasound in elderly diabetic patients with bacteriuria and without bacteriuria.

Organisms with colony count of >10 ⁵ CFU/mL	Total patients with Bacteriuria (n=43)	Males with Bacteriuria (n=16)	Females with Bacteriuria (n=27)
<i>Candida</i>	1 (2.3%)	0 (0%)	1 (3.7%)
<i>E. coli</i>	30 (69.8%)	10 (62.5%)	20 (74.1%)
Enterococci	4 (9.3%)	2 (12.5%)	2 (7.4%)
<i>Klebsiella</i>	7 (16.3%)	3 (18.8%)	4 (14.8%)
<i>Pseudomonas</i>	1 (2.3%)	1 (6.2%)	0 (0%)

[Table/Fig-4]: Analysis of causative organisms isolated from urine cultures of elderly diabetic patients with bacteriuria.

Organisms (n=43)	<i>E. coli</i> (n=30)	<i>Enterococcus</i> (n=4)	<i>Klebsiella</i> (n=7)
Nitrofurantoin	52.4%	32.8%	-
Piperacillin	20.7%	-	89.7%
Certrioxone	12.7%	12.5%	13.5%
Levofloxacin	30.4%	-	15.4%
Amikacin	40.7%	20.4%	-
Acid	6.1%	23.7%	16.7%
Imipenem	41.1%	60.7%	17.8%

[Table/Fig-5]: Analysis of antibiotic sensitivity of various organisms isolated from urine cultures of elderly diabetic patients with bacteriuria.

Clinical Characteristics of Urinary Tract Infections among Elderly Diabetic Patients with and without Bacteriuria

The findings of clinical characteristics of urinary tract infections among elderly diabetic patients are given in [Table/Fig-2]. Analysis of individual symptoms in bacteriuric and non bacteriuric patients revealed that increased frequency and dysuria were the most common symptoms in both the groups. There was a significant difference between two group for the symptoms of urgency ($p<0.001$), frequency ($p=0.046$), and dysuria ($p=0.001$). Frequency of symptoms like fever, haematuria, pyuria, flank pain, suprapubic pain, suprapubic tenderness and renal angle tenderness showed no significant difference between two groups.

Laboratory Examinations of Elderly Diabetic Patients with and without Bacteriuria

The evaluation of fasting blood glucose levels revealed that all 43 (100%) patients in the bacteriuric group and 53 out of 57 (93%) patients in the non-bacteriuric group had fasting blood glucose levels >126 mg/dl ($p=0.181$). Similarly, all 43 (100%) patients in the bacteriuric group had HbA1c levels >7% as compared to 54 out of 57(94.7%) patients in the non-bacteriuric group ($p=0.080$). Moreover, 37 (86.0%) and 39 (68.5%) patients in the bacteriuric and non-bacteriuric groups had HbA1c levels >10% respectively.

Anaemia, as defined by haemoglobin levels <12 gm/dl, was reported in 21 patients each in the bacteriuric and non-bacteriuric groups ($p=0.306$). Leucocytosis, as defined by leukocyte count >12,000/cu mm, was present in 13 (30.2%) patients in the bacteriuric group and 7 (12.3%) patients in the non-bacteriuric group ($p=0.042$). Further, laboratory investigations of urine samples revealed that the mean urine pH was 6.59 ± 0.63 for bacteriuric patients and 6.10 ± 0.55 for non-bacteriuric patients. The pH values were significantly higher in the bacteriuric group ($p<0.001$). There was no significant difference between both groups for specific gravity of urine.

Ultrasound Examination of Elderly Diabetic Patients with and without Bacteriuria

The findings of abdominal ultrasound are described in [Table/Fig-3]. The evaluation of post-voidal residue did not show any statistically significant difference between bacteriuric and non-bacteriuric patients ($p=0.237$). Ultrasound abdomen of all patients revealed that BPH was present in 7 (12.3%) patients in the non-bacteriuric group and 2 (4.7%) patients in the bacteriuric group ($p=0.293$). In

addition, 12 cases of pyelonephritis ($p<0.001$) and eight cases of cystitis ($p<0.001$) were noted in the bacteriuric group of patients. No patients required ICU admission.

Urine Culture among Elderly Diabetic Patients with Bacteriuria

Analysis of urine cultures of causative organisms of bacteriuria revealed that the most predominant bacteria isolated was *Escherichia coli* ($n=30$), followed by *Klebsiella spp.* ($n=7$), *Enterococci* ($n=4$), *Pseudomonas* ($n=1$), and *Candida* ($n=1$). Gender based evaluation also showed *E. coli* as the most common causative organism in both males and females [Table/Fig-4]. Antibiotic sensitivity of isolated urine cultures [Table/Fig-5] revealed that *E. coli* cultures were sensitive to nitrofurantoin, imipenem, and amikacin; *Enterococcus* cultures were sensitive to imipenem and nitrofurantoin; while *Klebsiella spp.* was sensitive to piperacillin.

DISCUSSION

We investigated the clinical profile of urinary tract infection in type 2 diabetic patients aged over 60 years. Findings of the present study will help to add the growing literature on this topic. In our study, bacteriuria was prevalent in 43% patients. In one of the earliest studies in this regard, Huvos A et al., observed bacteriuria in 26% of diabetic patients ($n=50$) and 22% of non diabetic patients. ($n=50$) [7]. A recent study by Jha BK et al., showed that 9.43% of diabetic patients with age >40 years had bacteriuria [8]. We believe that the increased prevalence noted in our study might be attributed to elderly population.

It has been established that women with diabetes are about two to three times more likely to have urinary tract infections than women without diabetes [4]. Interestingly, the same does not appear true for men. This gender based difference may be because of shorter urethra and closer proximity to the anus among women [4]. In our study, incidence of bacteriuria was significantly higher among female patients, which is in agreement with almost all previous studies [9-11]. We observed no correlation between bacteriuria and patients stratified according to age nor between bacteriuria and patients stratified according duration of diabetes, which is in contrast to earlier studies [6,12,13]. However, patients with diabetes for >15 years displayed increased chances for developing bacteriuria. It is reported that prevalence of bacteriuria increase by 1.9 fold for every 10 years of duration of diabetes [14]. In our study, incidence of bacteriuria was comparatively higher among patients taking oral hypoglycaemic alone as compared to those taking insulin or combined (insulin and oral hypoglycaemic) treatment, which is similar to observations made in earlier study [9].

We observed that patients with neuropathy or diabetic foot had significantly higher chances for developing bacteriuria. Patients with other complications like retinopathy, nephropathy, and hypertension also showed non significantly higher risk for developing bacteriuria. Similar observations regarding bacteriuria and long standing diabetic complications are reported in literature [15]. We also observed that various symptoms of urinary tract infection were higher among bacteriuric patients than among non bacteriuric patients.

Vaishav B et al., had demonstrated higher incidence of bacteriuria in uncontrolled diabetic patients [6], while Sewify M et al., indicated no link between control of diabetes and incidence of bacteriuria [12]. In our study, laboratory investigations revealed uncontrolled fasting blood sugar levels and high HBA1c levels in both group of patients. Urine pH was significantly higher in the bacteriuric group, while specific gravity was comparable between two groups. This is in agreement with well established finding that urinary pH is a valuable tool in the diagnosis and management of urinary tract infections [16]. Urine culture analysis revealed that *E. coli* (69.8%) was the commonest organism, followed by *Klebsiella* (16.3%). This finding is similar to earlier studies involving diabetic patients with bacteriuria

[6,12-14]. Further, most of these organisms were susceptible to nitrofurantoin and imipenem, indicating that they could be the preferred choice of antimicrobial agents in the treatment of urinary tract infections.

LIMITATION

The major limitations of our study include observational study design, which denies any conclusion on causation of bacteriuria in elderly diabetic patients. In addition, the role of common antibiotic medications in the management of these patients was not considered in the analysis. Our study also lacks subgroup comparisons of clinical and laboratory profiles for men vs. women, early vs. late elderly, or young, middle, and late elderly due to the small sample size. The small sample size of our study population and non parametric nature of the data may limit the generalization of the results. Despite these limitation, we strongly believe that present study provides important insights about urinary tract infections in 'elderly', for which data are rare. We recommend a large scale community based study on 'elderly' diabetic patients investigating the trends in risk factors, clinical and laboratory profiles, causative organism patterns, and antimicrobial susceptibilities that will help in understanding the aetiology and early management of these patients to avoid potential complications.

CONCLUSION

In the present study, bacteriuria was prevalent in 43% of type 2 diabetic patients aged over 60 years. Patients with female gender, diabetes duration of >15 years, and diabetes complications such as neuropathy and diabetic foot were found to have an increased preponderance for developing urinary tract infections. On the other hand, age, uncontrolled fasting blood sugar levels, and uncontrolled HbA1C levels did not show an increased propensity for developing urinary tract infections. *E. coli* was the most common causative organism and majority of isolated organisms were sensitive to antimicrobial agents like nitrofurantoin and imipenem, supporting their role in the treatment of urinary tract infections.

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