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Comparison of the frequency of bacteriuria in diabetic and non-diabetic patients without symptoms of urinary tract infection

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ABSTRACT

Introduction: Urinary tract infections (UTIs) are the most common infections among either community or hospital-acquired infections. UTIs are common in diabetes mellitus, with glycosuria and neurogenic bladder being the predisposing factors.

Methods: This was a retrospective observational study. The study population consisted of 100 diabetic and 40 non-diabetic patients. The rates of bacteriuria and pyuria were investigated in diabetic and non-diabetic patients who had been hospitalized and who did not have any complaints of UTI. Urine samples of patients were collected and each sample was tested through microscopy and culture. Furthermore, the urine samples were inoculated on blood agar and eosin methylene blue agar medium and incubated for 18–24 h at 37°C. Diabetic patients were evaluated to obtain data on age, gender, duration and type of diabetes, body mass index, retinopathy, nephropathy, glycated hemoglobin (HbA1c) level, and fasting plasma glucose (FPG) level.

Results: A higher rate of bacteriuria was detected in diabetic patients (21%) than in non-diabetic patients (5%) ($p = 0.02$). Infections were detected more frequently in patients with high HbA1c level ($p = 0.001$), those in the advanced age group ($p = 0.014$), and those with nephropathy ($p < 0.01$).

Conclusion: Asymptomatic bacteriuria was more prevalent in diabetic than in non-diabetic patients, with poor glycemic control, age, and nephropathy being significant risk factors. *Escherichia coli* is the most common organism that causes bacteriuria in diabetic patients.

Keywords: Asymptomatic bacteriuria; diabetes mellitus; urinary tract infection

INTRODUCTION

Urinary tract infections (UTIs) are the most common infectious diseases that impose a significant health and financial burden on society. The risk of UTI and whether it is symptomatic depends on the virulence of the organism (1). The presence of bacteria in the urine of a patient who has no symptoms or signs of UTI is defined as asymptomatic bacteriuria (ASB) (2). One possible mechanism could be that strains with low virulence can colonize the urine rather than causing symptomatic infection (3).

Diabetes mellitus is a disease that affects multiple organ systems (4). It negatively affects neutrophil function and humoral immunity. In addition, it makes the body susceptible to infections in all organ systems by damaging the antioxidant system (4-6). The urinary tract is the most common site for these infections, which are caused by both hyperglycemia and neuropathy that create a glucose-rich environment in the urine. This milieu favors pathogen growth and increases bacterial resistance, predisposing diabetics to UTI (7).

Urinary tract infections are an important problem commonly observed in diabetics, with a several-fold increased risk compared to non-diabetics. UTI complications are also common in diabetic patients. ASB is a risk factor for pyelonephritis and renal dysfunction in these patients (8,9).

In this study, the incidence of ASB was investigated in diabetic and non-diabetic patients. In addition, parameters that may be associated with ASB such as age, sex, duration and type of diabetes, body mass index (BMI), retinopathy, nephropathy, and glycated hemoglobin (HbA1c) and fasting plasma glucose (FPG) levels were studied.

METHODS

This was a retrospective observational study conducted at Şişli Etfal Training and Research Hospital, İstanbul, Turkey.

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Demographic and clinical data, microscopic examination of urine, and urine cultures from patient records were evaluated. The study included 100 patients (65 women and 35 men) hospitalized at the Internal Medicine Clinic of Şişli Etfal Training and Research Hospital for regulation or complications of diabetes and 40 nondiabetic patients (24 women and 16 men) hospitalized for other internal medicine reasons. The mean age of the patients was 57 ± 12 (20-82) and 55 ± 10 (34-74) years, respectively.

Patients who did not exhibit any signs and symptoms of UTI were included in our study.

All symptomatic UTI patients, children, pregnant women, patients who had used antibiotics in the last 2 months, and patients with urinary catheters were excluded from the study.

ASB is diagnosed either on the basis of the presence of 100,000 colony-forming units (CFU)/mL in a midstream urine specimen sample (2). Pyuria and urine culture were performed in both groups. Pyuria was considered positive in patients with > 10 leukocytes per field under a magnification of ×40 following urine centrifugation at 2000 rpm for 5 min. In accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines, midstream urine samples were collected from all patients. For microbiological testing, the patients' midstream urine was collected in a sterile container and processed in the microbiology laboratory of our hospital within half an hour at the latest. The collected urine was prepared for Gram staining and the presence of bacteria was determined under the microscope. The urine was inoculated onto blood agar and eosin methylene blue agar using a standard loop (0.01 mL). After 18-24 hours of incubation at 37°C, the number of colony-forming units per milliliter of urine (CFU/mL) was calculated. Organisms were identified by colony morphology and biochemical reactions (10). Antibiotic susceptibility testing for positive organisms was performed using the Kirby-Bauer disk diffusion method according to CLSI guidelines.

In diabetic patients, demographic and clinical data such as age, sex, duration of diabetes and type of treatment, fundus examination, BMI, and HbA1c level were recorded as parameters to be studied. Fundus examinations in diabetic patients were performed in the ophthalmology clinic of our hospital and the presence of diabetic retinopathy was detected. Patients with proteinuria were considered positive for nephropathy. Epi Info 7 was used for statistical analysis. $p < 0.05$ was considered significant.

RESULTS

ASB was determined in 21 (21%) of 100 diabetic patients and 2 (5%) of 40 non-diabetic patients; the difference was statistically significant ($p = 0.0226$). While pyuria was detected in all patients with positive urine cultures, it was not observed in any patient with negative urine cultures. The demographic and clinical characteristics of diabetic patients are presented in Table 1 and the characteristics of diabetic patients according to the urine culture result in Table 2.

The mean age and duration of diabetes, as well as HbA1c and FPG levels of patients with positive urine culture were found to be higher than those of patients with negative culture; moreover, the difference in age and HbA1c level was statistically significant. Although the BMIs of culture-positive patients were lower than those of culture-negative ones, the difference was not statistically significant ($p = 0.756$).

It was observed that nephropathy developed in 15 (71.4%) of 21 culture-positive patients and 23 (29.1%) of 79 culture-negative ones in the diabetic group, and the difference was statistically significant ($p < 0.01$). Nine (42%) of 21 culture-positive patients and 17 (21.5%) of 79 culture-negative patients had retinopathy and the difference was not statistically significant ($p = 0.088$).

There was also no statistically significant difference between culture positivity and gender in the diabetic group ($p = 0.8570$). The distribution of culture positivity by gender is presented in Table 3. Culture positivity was observed in 14 (21.5%) of 65 female patients in the diabetic group and in 2 (8.3%) of 24 female patients in the control group, and the difference was not statistically significant ($p = 0.2172$).

TABLE 1. The characteristics of diabetic patients

Parameter	Mean
Age (years)	57±12 (20–82)
Duration of diabetes (years)	8.9±7.0 (1–35)
HbA1c	8.0±2.2 (5.2–20.4)
BMI	27.3±4.0 (16–38)
FPG (mg/dl)	168.0±53.6 (72–383)
Type of diabetes	Number of patients
Type 1	8
Type 2	92
Type of treatment	
OAD	69
Insulin	26
Diet	2
OAD+Insulin	3
Retinopathy	
Negative	74
Positive	26
Nephropathy	
Negative	62
Positive	38

BMI: Body mass index, HbA1c: Glycated hemoglobin, FPG: Fasting plasma glucose, OAD: Oral anti-diabetics

TABLE 2. Distribution and comparison of the mean age, duration of diabetes, HbA1c level, BMI, and FPG level of the patients according to the urine culture results

Culture results	Age	Duration of diabetes (year)	HbA1c	BMI	FPG (mg/dl)
Negative (*n*=79)	56±12	8±7	7.5±1.5	27.4±4.2	165±52
Positive (*n*=21)	64±8	11±7	10.0±3.1	26.8±3.2	176±58
p-value	0.014	0.095	<0.001	0.756	0.153

BMI: Body mass index, HbA1c: Glycated hemoglobin, FPG: Fasting plasma glucose

TABLE 3. Distribution of culture positivity by gender

Culture	Female (%)	Male (%)	Total
Positive	14 (66.6)	7 (33.3)	21
Negative	51 (64.5)	28 (35.4)	79

There was no significant relationship between the type of received treatment and the presence of UTI ($p = 0.4455$). Urine culture was positive in seven patients receiving insulin, 12 patients receiving oral anti-diabetics (OAD), one patient receiving insulin + OAD, and one patient receiving diet therapy.

Enterobacteriaceae (62%) were the most frequently isolated organisms in the study group; coagulase-negative staphylococci (19%), *Candida* spp. (14%), and alpha-hemolytic streptococci (5%) were also isolated.

Considering the susceptibility pattern of the most frequent uropathogen, *Escherichia coli*, the highest resistance rate was observed for trimethoprim/sulfamethoxazole (TMP/SXT) and ampicillin, whereas it was most sensitive to cefepime, amikacin, and imipenem.

DISCUSSION

ASB is the presence of bacteria in the urine of a patient without UTI symptoms. It is not well understood why the same uropathogens responsible for UTI are less virulent in such patients. Decreased uroepithelial compliance and often reduced host response in diabetes may explain this lack of symptoms (11). ASB can have severe consequences in pregnant women; children; patients with obstructive uropathy, chronic renal failure, or kidney transplant; and diabetic and neutropenic patients as well as before urological intervention.

In our study, the rate of positive urine culture was statistically different between the diabetic and non-diabetic patients (21% and 5%, respectively; $p = 0.0226$). The prevalence of ASB was determined to be between 9% and 27% in diabetic patients in various studies, and this rate is higher when compared with those of healthy individuals (12). In a study from Turkey, ASB was detected in 14.7% of female diabetic patients (13). In the study by Njunda et al. from Cameroon, the prevalence of ASB was found to be 47.2% in diabetic patients (14), whereas in one study from India, similar to our study, ASB was found to be 21.25% in Type 2 diabetic patients (11). In a meta-analysis, the ASB prevalence was found to be 12.2% versus 4.5% in Type 2 diabetic patients compared with that in the healthy control group (15). Moreover, in another study from Southern India, the ASB prevalence was 32% versus 6% (16). In other studies from India, it was found to be 28.2% in diabetic patients and 7.5% in the healthy control group ($p = 0.001$) (17) as well as 17.5% in diabetic patients and 10% in non-diabetic ones ($p = 0.015$) (18).

In our study, the mean age, duration of diabetes, and HbA1c and FPG levels of patients with positive urine culture were found to be higher than those with negative culture, and age and HbA1c levels were statistically significant. Although the BMIs of culture-positive patients were lower than those of culture-negative ones, the difference was not statistically significant. As in our study, the HbA1c level and advanced age were found to be significantly correlated with ASB in both studies (19,20). In one study, while there was no significant difference between the groups in terms of age and BMI, a significant difference was observed in terms of HbA1c level and duration of diabetes ($p < 0.05$) (8). In one study from India, age and final glycemic status were not correlated, whereas bacteriuria patients with higher HbA1c level were at a higher risk of UTI (11). In another study from India, the main risk factors for ASB were advanced age, longer duration of diabetes, and poor glycemic control (17). HbA1c measurements enable assessment of glucose control, with high HbA1c level indicating hyperglycemia, thus resulting in an increased risk of developing ASB.

In our study, nephropathy developed in 71.4% of culture-positive and 29.1% culture-negative diabetic patients, and the difference was statistically significant ($p < 0.01$). As in our study, in a meta-analysis, albuminuria was found to be more common in diabetic patients with ASB than in those without ASB (15). In the study by Ishay et al., the important risk factors for ASB were macroalbuminuria and serum creatinine level (9). In the study by Papazafiropoulou et al., an increased prevalence of ASB was observed in diabetic patients with microalbuminuria compared with those without microalbuminuria (21% vs. 8%, $p < 0.001$) (21). Albuminuria may cause structural damage in the kidney and so may increase vulnerability to bacterial attacks, thus resulting in an increased risk of developing ASB (22).

In our study, the rate of patients with retinopathy was statistically different between patients with positive urine culture and those with negative urine culture (42% and 21.5%, respectively; $p = 0.088$). In the study by Raz, the prevalence of ASB was increased in patients with diabetic retinopathy (3), whereas in the study by Ishay et al., no significant relationship was observed (9).

In our study, there was no statistically significant difference between culture positivity and gender in the diabetic group ($p = 0.8570$). The culture positivity rate was higher in a statistically significant level in female diabetic patients than in female non-diabetic patients (21.5% and 8.3%, respectively; $p = 0.2172$). Similar to our study, women with Type 2 diabetes were not found to be at a higher risk of developing ASB compared with non-diabetic women in the study from Israel (9). Contrary to our study, in one meta-analysis, the ASB prevalence was higher in women than in men (15). While several researchers found a threefold higher prevalence of ASB in diabetic women than in non-diabetic women, diabetic men did not exhibit higher ASB prevalence rates than non-diabetic ones (3). In the study from North India, the prevalence was significantly higher in diabetic women (39.1%) than in controls (10.8%) ($p = 0.003$) (18).

Enterobacteriaceae (62%) were the most frequently isolated organisms in the diabetic groups followed by coagulase-negative staphylococci (19%), candida spp. (14%), and alpha-hemolytic streptococci (5%). *E. coli* was the predominant strain that had phenotypically antimicrobial resistance to TMP/SXT and ampicillin. As in our study, the most frequently isolated microorganism in other studies was *E. coli* (8,16,19-21,23). *E. coli* expressing Type 1 fimbriae was found to adhere more freely to the uroepithelial cells of diabetic women than those isolated from non-diabetic women. Increased adhesion of *E. coli* with Type 1 fimbriae to diabetic uroepithelial cells as well as lower urinary cytokine secretion and leukocyte count may partly explain this increased prevalence (24). In one study from India, female diabetic patients with ASB due to *E. coli* were found to have a significantly higher risk of developing UTIs within 1 year (11). A study from Canada found that *E. coli* bacteriuria persisted for a long time in diabetic women (25). On the contrary, a study from India demonstrated that coagulase-negative staphylococci were isolated as the dominant organism (36.36%) from the urine of both diabetic and non-diabetic patients; *Klebsiella* spp., *Candida* spp., and *E. coli* were more frequent in diabetic patients (26). In one study from Srinagar, India, ASB was found to be significantly associated with symptomatic UTI at the 6-month follow-up without deterioration in renal parameters (18).

This study has few limitations. First, it was conducted at a single tertiary care hospital. Second, the aspects of sexual hygiene, socioeconomic status, immunocompromised patients, and patients in the intensive care unit were not considered in our analysis.

CONCLUSION

Bacteriuria was more common in diabetic patients without symptoms of UTI than in non-diabetic patients. The most frequently isolated microorganism was *E. coli*. In diabetic patients, advanced age, high HbA1c level, and nephropathy were found to be risk factors for developing ASB. These risk factors indicate the severity of diabetes; therefore, one would expect that diabetes management will reduce the incidence of these complications.

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STATEMENT OF INTEREST

Author declares no conflict of interest.

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