Short Communication

Frequency, Risk Factors, and Responsible Pathogenic Microorganisms of Asymptomatic Bacteriuria in Patients with Type 2 Diabetes Mellitus

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(Received August 8, 2007. Accepted April 4, 2008)

SUMMARY: Urinary tract infection is a serious problem in diabetic patients, and asymptomatic bacteriuria (ASB) in these patients is a risk factor for pyelonephritis and renal dysfunction. In the present study, we investigated the relationships between age, body mass index, duration of diabetes, HbA1c level, glucosuria, glomerular filtration rate and microalbuminuria in type 2 diabetic patients with ASB. One hundred and twenty-three patients with type 2 diabetes mellitus were included in the study. The patients were divided into two groups according to ASB; Group I consisted of 22 patients with ASB, and Group II of 101 patients without ASB. There were no significant differences between the groups in regard to body mass index, creatinine clearance or microalbuminuria, while there were significant differences in HbA1c, duration of diabetes mellitus, glucosuria and pyuria ($P < 0.05$). The most commonly isolated microorganism was *Escherichia coli*. The present study identified the duration of diabetes, high HbA1c, glucosuria and pyuria as risk factors for ASB in type 2 diabetic patients.

The risk of infection is higher and urinary tract infections are serious clinical problem in patients with diabetes mellitus (1,2). Both symptomatic and asymptomatic urinary tract infection are reported to occur with increased frequency in women with diabetes (3,4). The biological explanation for this increased occurrence has not been defined. It has been suggested that asymptomatic bacteriuria (ASB) may lead to symptomatic urinary infection, as well as increase in the frequency of renal failure as one of the long term adverse effects (5). Serious complications of urinary infection, such as emphysematous cystitis, pyelonephritis, renal and perinephric abscess, bacteremia and renal papillary necrosis are most commonly seen in diabetic patients. On a population basis, diabetic women, depending on age, are 6 - 24 times more likely than non-diabetic women to be admitted for acute pyelonephritis, and diabetic men are 3.4 - 17 times more likely than their non-diabetic counterparts to be admitted for the same condition (6). Most of the urinary tract infections are asymptomatic, especially in women. Previous studies have shown that the prevalence of ASB is three times higher in diabetic women than non-diabetic women (7). The prevalence of ASB in previous studies ranged between 6.1 and 26.6% (3,6,8-14). Age, sexual activities, duration of diabetes, metabolic control of the disease and the state of diabetic complications have been implicated as risk factors for ASB in diabetic patients (9,15,16). The most commonly isolated pathogen in males and females alike is *Escherichia coli*, whether or not they have diabetes. However, some other studies have reported that this microorganism was not more frequently seen the pathological agent in urinary tract infections in diabetic patients when compared to non-diabetic ones (17-21).

In the present study, we investigated the relationships between age, body mass index (BMI), duration of diabetes, HbA1c level, glucosuria, glomerular filtration rate and microalbuminuria in type 2 diabetic patients with ASB.

One hundred and twenty-three out-patients with type 2 diabetes mellitus, between 26 and 80 years of age (mean age, 56.7 ± 10.21; 91 females), were included in the study. Patients who were pregnant, had recently been hospitalized or operated upon, had urinary system anomaly and/or indwelling catheter, had used antibiotics for any reason in the past 14 days, or showed symptoms of urinary tract infection, including dysuria, pollakiuria, urgency, suprapubic tenderness and fever, were not included in the study. Patients were questioned to determine their age and duration of diabetes. The diagnosis of ASB was established based on the criteria defined by the Centers for Disease Control and Prevention (Atlanta, Ga., USA). That is, none of the patients had an indwelling urinary catheter within 7 days of the first positive culture, and ASB was diagnosed when a patient had at least two positive urine cultures (i.e., 10³ microorganisms per cm³ of urine) with repeated isolation of the same microorganism and no more than two species of microorganisms, and no symptoms of infection, such as fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness (22).

A clean-catch, midstream urine specimen was collected for urine analysis, microscopy, culture and antimicrobial susceptibility tests. Urine analysis was performed using a URISYS 2400 and UF 100 (Roche®) auto-analyzer. Uncentrifuged urine was examined on a Thoma microscope slide. A leukocyte count of ≥10/mm³ was considered to indicate pyuria (23). Blood agar and eosine methylene blue agar were used for routine urine cultures. Plates were incubated aerobically for 24 h at 37°C. Routine identification methods were followed for assessment of urine isolates. If the Gram stain test gave a Gram-negative result, identification of microorganism was performed with biochemical tests (the triple sugar iron agar test, citrate utilization test, urease production test, methyl red test, indole production test, decarboxylation of lysine test, and other tests).
was no significant difference in BMI between the groups studies exploring the relation between BMI and ASB there with and without ASB. In line with our study, in two recent statistically significant difference in BMI between the groups (26). There was no statistically significant difference between BMI and ASB (10). In the present study, however, there was no significant relation between glomerular filtration rate and microalbuminuria. HbA1c was measured by the spectrophotometric method (Abbot Aeroset®).

All analyses were conducted using SPSS 9.0 software (SPSS for Windows 9.0; Chicago, Ill., USA). Chi-square statistics were used to assess differences between categorical variables and a P value of less than 0.05 was considered statistically significant.

The patients were divided into two groups according to ASB: Group I consisted of 101 ASB (–) patients and Group II contained 22 ASB (+) patients. The demographic characteristics of the groups are shown in Table 1. There was no significant difference between the groups regarding age, BMI, duration of diabetes, the amount of glucosuria and pyuria significantly differed between the groups. ASB was detected in 18.6% of female and 15.6% of male patients.

The most common pathogen in patients with ASB was E. coli (68%), followed by Klebsiella pneumoniae (23%), Enterobacter aerogenes (4.5%) and group B beta-hemolytic streptococci (4.5%).

In the present study, we found ASB in 22 of 123 (17.8%) type 2 diabetes mellitus patients. The frequency of ASB varied between 6.1 and 26.6% in previous studies (3,6,8-14,24). These rates are generally the ones reported in female diabetic patients. Our result is comparable to the rates reported in diabetic patients.

Age is a well-known risk factor for bacteriuria in non-diabetic females (25). Advanced age has been proposed as a risk factor for ASB in patients with type 2 diabetes mellitus (10). In the present study, however, there was no significant age difference between the groups with and without ASB. This result is in agreement with the results of some previous studies (12-14).

In a previous study on non-diabetic patients, no relation was found between BMI and ASB (26). There was no statistically significant difference in BMI between the groups with and without ASB. In line with our study, in two recent studies exploring the relation between BMI and ASB there was no significant difference in BMI between the groups (10,14).

We found a significant relation between high HbA1c level, indicating that the metabolic control of the disease is compromised, and ASB. There are conflicting results in the literature with regard to the relation between high HbA1c level and ASB. While Geerlings et al. (10), Boroumand et al. (13), and Ishay et al. (14) did not find a significant relation, Bonadio et al. (12) and Kelestimur et al. (27) argued that a high HbA1c level may be a risk factor for ASB. The results of these studies suggest that a high level of HbA1c in diabetic patients can be defined as a risk factor for ASB. In the present study, we also found a significant relation between glucosuria and ASB. Similarly, Boroumand et al. (13) found a significant relation between bacteriuria and glucosuria. In vitro studies have also demonstrated that glucosuria increased the growth of various E. coli spp. (28).

Microalbuminuria is an early marker of diabetic nephropathy. With regard to diabetic nephropathy in the present study, however, there was no significant relation between glomerular filtration rate or microalbuminuria and ASB. Recent studies have reported that there were no significant relations between ASB and microalbuminuria or renal dysfunction in type 2 diabetic patients (10,12,29). However, we found that there was a statistically significant relation between the duration of diabetes and ASB. In agreement with our results, some previous studies have shown that patients with long-lasting diabetes mellitus had increased risk of ASB (3,6), even though studies that could not confirm this argument also exist (12-14).

The most common pathogenic microorganism isolated in patients with ASB is E. coli (68%). E. coli is also the most commonly isolated microorganism in community-acquired urinary tract infections. One study investigating the agents of ASB in diabetic patients reported that E. coli was the most common agent (12-14,30), while other studies have reported that Klebsiella was more common (13,19,31,32).

In conclusion, different risk factors for ASB in patients with type 2 diabetes have been reported in previous studies. Based on the results of the present study, we suggest that duration of diabetes, high HbA1c level, glucosuria and pyuria are risk factors for ASB in patients with type 2 diabetes. E. coli and K. pneumoniae are the most frequently isolated bacteria in these patients with ASB. Routine urine culture might be recommended in diabetic patients who show no urinary symptoms but who have one or more of the risk factors identified in this study.

REFERENCES

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>ASB (–) (n = 101)</th>
<th>ASB (+) (n = 22)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>55.9 ± 10.2</td>
<td>60.8 ± 9.5</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>73.2</td>
<td>77.2</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.8 ± 4.9</td>
<td>32.5 ± 5.8</td>
<td>NS</td>
</tr>
<tr>
<td>Glycohemoglobin level (%)</td>
<td>7.37 ± 2.1</td>
<td>8.7 ± 2.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Glomerular filtration rate (mL/min)</td>
<td>90.0 ± 37.9</td>
<td>77.4 ± 30.5</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of diabetes (y)</td>
<td>6.0 ± 7.0</td>
<td>10.9 ± 6.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Microalbuminuria (0-300 mg/day)</td>
<td>68.3 ± 247.7</td>
<td>34.0 ± 42.9</td>
<td>NS</td>
</tr>
<tr>
<td>Glucosuria (mg/dL)</td>
<td>62.4 ± 207.5</td>
<td>352.2 ± 456.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Pyuria (1000 cell/mm³)</td>
<td>36.97 ± 169</td>
<td>363.5 ± 458</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

ASB, asymptomatic bacteriuria; BMI, body mass index.


