

**OBSERVATIONS**

**Diabetes and the Course of Febrile Urinary Tract Infection**

Diabetes is considered a risk factor for acquisition of febrile urinary tract infection (UTI) (1,2), but there is a lack of information on the association of diabetes with the subsequent course of disease and its outcome. We performed a prospective observational multicenter cohort study including consecutive adults with community-onset febrile UTI presenting at 7 emergency departments and 35 primary care centers. The effect of pre-existing diabetes on presentation and microbiological and clinical outcome was assessed and multivariable logistic regression performed to establish whether diabetes was an independent risk factor for a complicated course.

Of 858 patients, 140 had diabetes (93% type 2 diabetes), of whom 41 (30%) used insulin, 19 (14%) were managed by diet only, and the remaining were managed by a combination of metformin, insulin, and diet. Patients with diabetes were older (median age 73 years [interquartile range (IQR) 46–78] vs. 64 [IQR 42–77], P < 0.001), were more frequently male (48 vs. 35%, P = 0.006), and had a higher rate of cardiovascular and urinary tract comorbidities (28 vs. 12%, P < 0.001, and 34 vs. 23%, P = 0.005). Clinical symptoms did not differ between diabetic and nondiabetic patients (Table 1), except that diabetic patients less frequently experienced flank pain, as reported previously (3). *Escherichia coli* was the most common isolated uropathogen in both diabetic and nondiabetic patients. Diabetes was not associated with a longer duration of fever (median 2 days in both groups) or prolonged hospital admission (both median 6 days). Patients with diabetes more often had bacteremia at presentation (30 vs. 22%, P = 0.037), intensive care unit admission (6 vs. 3%, P = 0.065), recurrent UTI (9 vs. 3%, P = 0.017), asymptomatic bacteriuria (13 vs. 9%, P = 0.247), and mortality during 30 days of follow-up (6 vs. 2%, P = 0.007). However, when adjusted for possible confounders such as underlying cardiovascular disease, diabetes was not an independent risk factor for any of these complications—bacteremia odds ratio (OR) 1.2 (95% CI 0.8–1.8), 30-day mortality OR 2.0 (0.7–5.8), recurrent UTI OR 2.2 (95% CI 0.7–6.8), and asymptomatic bacteriuria after 1 month OR 1.1 (0.5–2.5)—although women with diabetes were at increased risk of asymptomatic bacteriuria after 1 month (15 vs. 4%, P = 0.003, OR 4.3 [95% CI 1.5–11.9]).

| Table 1—Baseline characteristics of 858 patients presenting with febrile UTI |
|---------------------------------|-----------------|--------------------|-----------------|
|                                | All             | Diabetes           | No diabetes     | P             |
| n                               | 858             | 140                | 718             |               |
| Age (years), median (IQR)       | 66 (46–78)      | 73 (60–81)         | 64 (42–77)      | <0.001        |
| Male sex                        | 320 (37)        | 67 (48)            | 253 (35)        | 0.006         |
| Antibiotic pretreatment         | 254 (30)        | 48 (34)            | 206 (29)        | NS            |
| Urologic history                |                 |                    |                 |               |
|Urinary tract disorder*          | 210 (24)        | 48 (34)†           | 162 (23)        | 0.005         |
|Indwelling urinary catheter      | 58 (7)          | 16 (11)            | 42 (6)          | 0.016         |
|Recurrent UTI†                   | 269 (31)        | 54 (39)            | 215 (30)        | 0.044         |
|Comorbidity                      |                 |                    |                 |               |
|Malignancy                       | 91 (11)         | 19 (14)            | 72 (10)         | NS            |
|Heart failure                    | 128 (15)        | 39 (28)            | 89 (12)         | <0.001        |
|Cerebrovascular disease          | 112 (13)        | 25 (18)            | 87 (12)         | NS            |
|Chronic renal insufficiency      | 78 (9)          | 26 (19)            | 52 (7)          | <0.001        |
|Chronic obstructive pulmonary disease | 118 (14) | 28 (20)            | 90 (13)         | 0.023         |
|Presentation                     |                 |                    |                 |               |
|At emergency department          | 662 (77)        | 120 (86)           | 542 (76)        | 0.008         |
|Shaking chills                   | 489/783 (63)    | 79/125 (63)        | 410/658 (62)    | NS            |
|Dysuria§                         | 613 (76)        | 102 (83)           | 511 (75)        | NS            |
|Flank pain                       | 526/837 (63)    | 66/132 (50)        | 460/705 (65)    | <0.001        |
|Fever duration at presentation (h), median (IQR) | 30 (12–60) | 36 (15–72)         | 29 (12–60)      | NS            |
|Heart rate >90 bpm               | 448/850 (53)    | 73/139 (53)        | 375/711 (53)    | NS            |
|Systolic blood pressure (mmHg), mean ± SD | 130 ± 23      | 138 ± 25           | 129 ± 22        | <0.001        |
|Diastolic blood pressure (mmHg), mean ± SD | 72 ± 14        | 72 ± 16            | 72 ± 14         | NS            |

Data are presented as n (%) unless otherwise indicated. *Defined as any functional or anatomical abnormality of the urinary tract except urinary catheter and history of nephrolithiasis. †Prostatic hypertrophy (n = 20), malignancy of the urinary tract (n = 6), neurogenic bladder (n = 5), status after nephrectomy (n = 3), and other anatomical or functional disorders of the urinary tract (n = 14). ‡Defined as ≥3 UTIs in the past 12 months or ≥2 UTIs in the past 6 months. §Not recorded in patients with an indwelling urinary catheter.
The higher prevalence of complications in patients with diabetes was mainly explained by an increased prevalence of cardiovascular comorbidity and higher age.

Although it is widely held that patients with diabetes more often have a complicated course of infections, our prospective multicentre cohort study shows that diabetes is not independently associated with a complicated course in an unselected population of patients with febrile UTI. The prevalence of complications was higher in diabetic patients but attributable to concurrent illnesses, especially cardiovascular comorbidities, and a higher age of the diabetic population. Our study does not lend support for the increased duration of antimicrobial treatment of febrile UTI in diabetic compared with nondiabetic patients, since clinical and microbiological outcomes after 1 month did not differ significantly between both groups and diabetic and nondiabetic patients were treated alike.

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W.E.V.d.S. was responsible for the original design and data management, carried out the statistical analysis, wrote the initial draft, was involved in patient recruitment and data collection, and contributed to and approved the final version of the manuscript. H.B. was responsible for data management, carried out the statistical analysis, wrote the initial draft, was involved in patient recruitment and data collection, and contributed to and approved the final version of the manuscript. A.M.V. supervised the writing of the initial draft, critically revised the manuscript, and contributed to and approved the final version of the manuscript. J.T.v.D. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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