OBSERVATIONS

Diabetes and the Course of Febrile Urinary Tract Infection

iabetes 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 preexisting 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	Р
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 \pm 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.

Online Letters

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 an 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. N.M.D. was involved in patient recruitment and data collection, critically revised the manuscript, and contributed to and approved the final version of the manuscript. J.W.v.W. was involved in patient

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References

- Jackson SL, Boyko EJ, Scholes D, Abraham L, Gupta K, Fihn SD. Predictors of urinary tract infection after menopause: a prospective study. Am J Med 2004;117:903–911
- 2. Muller LMAJ, Gorter KJ, Hak E, et al. Increased risk of common infections in patients with type 1 and type 2 diabetes mellitus. Clin Infect Dis 2005;41:281–288
- Horcajada JP, Moreno I, Velasco M, et al. Community-acquired febrile urinary tract infection in diabetics could deserve a different management: a case-control study. J Intern Med 2003;254:280–286