Glycemic Control and Urinary Tract Infections in Women with Type 1 Diabetes: Results from the DCCT/EDIC

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Purpose: We examined the relationship between glycemic control and urinary tract infections in women with type 1 diabetes mellitus.

Materials and Methods: Women enrolled in the Epidemiology of Diabetes Interventions and Complications study, the observational followup of the Diabetes Control and Complications Trial, were surveyed to assess the rate of physician diagnosed urinary tract infections in the preceding 12 months. The relationship between glycated hemoglobin levels and number of urinary tract infections in the previous 12 months was assessed using a multivariable Poisson regression model.

Results: A total of 572 women were evaluated at year 17. Mean age was 50.7 ± 7.2 years, mean body mass index was 28.6 ± 5.9 kg/m^2, mean type 1 diabetes duration was 29.8 ± 5.0 years and mean glycated hemoglobin was 8.0% ± 0.9%. Of these women 86 (15.0%) reported at least 1 physician diagnosed urinary tract infection during the last 12 months. Higher glycated hemoglobin levels were significantly associated with number of urinary tract infections such that for every unit increase (1%) in recent glycated hemoglobin level, there was a 21% (p=0.02) increase in urinary tract infection frequency in the previous 12 months after adjusting for race, hysterectomy status, urinary incontinence, sexual activity in the last 12 months, peripheral and autonomic neuropathy, and nephropathy.

Abbreviations and Acronyms

AER = albumin excretion rate

BMI = body mass index

DCCT = Diabetes Control and Complications Trial

EDIC = Epidemiology of Diabetes Interventions and Complications

HbA1c = glycated hemoglobin

MNSI = Michigan Neuropathy Screening Instrument

UI = urinary incontinence

UroEDIC = Urologic Complications of Diabetes Study

UTI = urinary tract infection

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Conclusions: The frequency of urinary tract infections increases with poor glycemic control in women with type 1 diabetes. This relationship is independent of other well described predictors of urinary tract infections and suggests that factors directly related to glycemic control may influence the risk of lower urinary tract infections.

Key Words: urinary tract infections, diabetes mellitus, risk factors

URINARY tract infections affect millions of women each year.[1] Diabetes mellitus is a comorbidity that predisposes patients to more frequent and complex UTIs.[2] Several epidemiological studies support this tenet, demonstrating a 1.2 to 2.2-fold increased risk of lower UTIs in subjects with diabetes compared to those without diabetes.[3–6] However, the relationship between traditional measures of diabetes severity such as duration of disease, level of glycemic control and presence of diabetic complications among women with diabetes and the risk of UTI is not clear. Glycated hemoglobin, and diabetic microvascular and neuropathic complications have not been associated with symptomatic UTIs, while duration of diabetes and insulin use have been variably correlated.[4,7,8] These studies were limited by their inclusion of women with primarily type 2 diabetes and single measurement of glycemic control. Consequently, data on factors associated with symptomatic UTIs for women with type 1 diabetes mellitus are limited.

We examined the relationship between HbA1c and UTIs in women with type 1 diabetes using data from the DCCT and its observational followup, the EDIC study. This study has collected detailed information on women with type 1 diabetes since 1983. Information regarding UTIs was collected in 2010 (EDIC year 17) as part of an ancillary study of urological complications of diabetes (UroEDIC). We hypothesized that worse glycemic control, as measured by HbA1c levels, in type 1 diabetes was associated with an increased rate of UTIs.

MATERIALS AND METHODS

Population and Setting

The DCCT was a multicenter, randomized clinical trial designed to compare the effects of intensive and conventional diabetes therapy on the development and progression of early microvascular complications of type 1 diabetes.[9,10] From 1983 to 1989, 1,441 subjects (680 women) age 13 to 39 years were recruited. The DCCT included a primary prevention cohort and a secondary intervention cohort. The primary prevention cohort consisted of 348 women with no retinopathy, a urinary AER less than 40 mg per 24 hours and diabetes duration of 1 to 5 years at baseline. The secondary intervention cohort consisted of 332 women who, at baseline, had nonproliferative retinopathy, urinary AER 200 mg or less per 24 hours and diabetes duration of 1 to 15 years. Individuals were excluded from analysis if they had hypertension, a history of symptomatic ischemic heart disease or symptomatic peripheral neuropathy. At the end of the trial in 1993 the DCCT proved that intensive therapy significantly reduced the risk of diabetic microvascular complications compared with conventional treatment.[11] Intensive treatment was subsequently recommended for all subjects.

In 1994 of the surviving 680 women 655 (96%) volunteered to participate in EDIC. Mean age of these women was 35 ± 7 years. During 2010, EDIC year 17, 580 of 618 active female participants (94%), mean age 51 ± 7 years, agreed to participate in UroEDIC, an ancillary study to examine the presence of urological complications, including urinary incontinence, lower urinary tract symptoms, UTIs and sexual dysfunction. Among the 580 women 575 had UTI information. Three individuals reported 4, 6, and 9 UTIs, and HbA1c levels of 8.5, 8.0 and 8.2, respectively. Given the single observation for these counts and influential status (inclusion altered association estimate), they were excluded from study, resulting in 572 women for the current analyses (fig. 1). All DCCT/EDIC procedures were reviewed and approved by institutional review boards at the participating center and all participants provided written informed consent.

UTI Measurements

Urinary tract infections were quantified by the response to the question, "How many times in the last 12 months were you diagnosed by a physician with a bladder infection?" This question is the same as that used in the third National Health and Nutrition Examination Survey.[12]

Diabetes Measurements

Each EDIC subject underwent an annual history, physical examination and laboratory evaluation including HbA1c, which was measured at baseline and quarterly during DCCT and annually in EDIC.[13] For the purposes of this analysis recent glycemic control was the HbA1c measured at the EDIC year 16 visit (1 year before UTI assessment), and long-term glycemic control was the time weighted mean of all HbA1c values obtained during DCCT and through EDIC year 16. Retinopathy was established by fundus photographs that were obtained periodically and graded centrally using the Early Treatment Diabetic Retinopathy Study scale.[14,15] AER was measured in alternate years during EDIC. Nephropathy was defined as microalbuminuria (AER 30 to 300 mg per 24 hours) or albuminuria (AER greater than 300 mg per 24 hours). Peripheral neuropathy was determined at year 17 using the MNSI, and defined as greater than 6 positive responses on the MNSI questionnaire or a score of greater