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Risk Factors for Urinary Incontinence Among Women with Type 1 Diabetes: Findings from the Epidemiology of Diabetes Interventions and Complications Study

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Abstract

Objectives—To determine risk factors for and long-term effects of glycemic control on urinary incontinence among women with type 1 diabetes enrolled in the Epidemiology of Diabetes Interventions and Complications (EDIC) study.

Methods—The Diabetes Control and Complications Trial (1982 to 1993) cohort follow-up, EDIC, began in 1994. In 2004, women participants (N=550), completed a self-administered questionnaire on incontinence. Our primary outcome was $\geq$ weekly incontinence, overall and by type. Multivariable regression models were used to determine independent predictors of weekly UI, both overall and by type.

Results—Overall, 38% of women reported any incontinence and 17% reported $\geq$ weekly incontinence. Increasing body mass index (Odds Ratio (OR) 1.1 per kg/m², 95% Confidence Interval (CI) 1.1–1.2) was significantly associated with weekly incontinence, overall and by type. Advancing age and two or more urinary tract infections in the prior year were associated with weekly urge incontinence (OR 1.4, 95% CI 1.0–2.0 per 5 years; OR 4.9, 95% CI 1.8–13.5, respectively). There was weaker evidence for increased risk with age for overall weekly incontinence (22% per 5 years, $p=0.06$) and stress incontinence (21 % per 5 years, $p=0.08$)

Conclusions—Urinary incontinence is common among women with type 1 diabetes and risk factors including advancing age, increased weight, and prior urinary tract infection are important.

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Weight reduction and treatment of urinary tract infections may have the additional benefit of preventing incontinence or reducing its severity.

Keywords

Risk Factors; Urinary Incontinence; Type 1 Diabetes

Introduction

Urinary incontinence is estimated to affect 30–40% of middle-aged women, leading to significant distress and poorer quality of life.¹ Recent evidence suggests that urinary incontinence is more common among women with type 2 diabetes and that diabetes is an independent risk factor for urinary incontinence.^{2–4} However, there has been limited research among middle-aged women with type 1 diabetes (T1DM).

Many studies of incontinence in women with diabetes were conducted in small samples from selected populations; included mostly women with type 2 diabetes or did not differentiate between type 1 and type 2 diabetes; and did not assess severity of diabetes in terms of duration, glycemic control, treatment history, or associated complications.^{5,6} These studies were observational and most were analyzed without adjustment for potential confounding variables such as age, body weight, and childbirth history. Consequently, there are no well-established risk factors for incontinence among women with T1DM and no clinical trials of interventions to reduce the risk or severity of incontinence among women with T1DM.

We analyzed data from the Urologic Complications of Epidemiology of Diabetes Interventions and Complications (UroEDIC) Study to determine the risk factors for, and the long-term effects of intensive glycemic therapy on urinary incontinence among women with T1DM.

Materials and Methods

UroEDIC Study Sample

The Diabetes Control and Complications Trial (DCCT) was a randomized controlled clinical trial that enrolled 1,441 subjects with T1DM between 1983 and 1989 who at baseline were 13 to 39 years of age, with T1DM duration for 1 to 15 years, and in generally good health.⁷ The DCCT consisted of two cohorts: the primary prevention cohort had T1DM for 1–5 years, no retinopathy and urinary albumin excretion < 40 mg per 24 hours at baseline; the secondary intervention cohort had T1DM for 1–15 years, and very mild-to-moderate non-proliferative retinopathy, and urinary excretion ≤ 200 mg per 24 hours at baseline. A total of 711 participants were randomly assigned to receive intensive treatment, which consisted of insulin administered three or more times per day by injection or by continuous subcutaneous infusion with an external pump. The conventional therapy group (730 participants) received one or two daily insulin injections with a goal of freedom from symptoms of hyperglycemia and/or hypoglycemia and frequent or severe hyperglycemia and/or hypoglycemia. At the end of the trial in 1993, after 6.5 years of mean follow-up, the DCCT proved that intensive treatment significantly reduced the risks of several diabetic complications compared with conventional treatment and intensive therapy was recommended for all subjects and they returned to their own health care providers for diabetes care. In 1994, 1,375 (96%) (655 women, 720 men) of the surviving members volunteered to participate in the Epidemiology of Diabetes Intervention and Complications (EDIC) observational follow-up study.⁸

During the tenth study visit of EDIC (September 1, 2002 - April 30, 2004), 550 of the 652 (84%) women remaining in the EDIC study agreed to participate in the Urologic Complications of Diabetes (UroEDIC) study and responded to questions about urinary incontinence and

potentially associated factors. These women are the subjects of this cross-sectional study. Figure 1 shows the flow of the women participants from entry into DCCT to EDIC year 10 and the completion of the UroEDIC questionnaire.

Urinary Incontinence Measurements

Urinary incontinence was assessed by a self-administered questionnaire based on validated instruments used in previous studies.^{9,10} The sequence of incontinence questions began with “During the past 12 months how often have you leaked even a small amount of urine...”. Frequency of incontinence was ascertained as every day, one or more times per week, one or more times per month, or less than once per month. The primary outcome of interest was weekly or more frequent incontinence, which we consider clinically significant. Among women with weekly incontinence, type of incontinence over the past seven days was classified by the addition of questions “.... during activities like coughing, sneezing, lifting, or exercise?” (stress incontinence) and “.... with an urge to urinate and couldn't get to the bathroom fast enough?” (urge incontinence).

Other Measurements

Each EDIC subject had an annual history, physical examination, and laboratory testing, including serum creatinine and hemoglobin A1c, determined using the same methods as during the DCCT.^{7,8,11} Albumin excretion rate using 4-hour urine collections were obtained in alternate years during EDIC.⁸ For these analyses albumin excretion rate was measured during EDIC years 9 and 10.

Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, or documented treatment with anti-hypertensive agents. Coronary calcification was measured by computed tomography between November 2000 and March 2003. The average Agatston score from two scans was employed in the analysis.¹²

The number of urinary tract infections (UTIs) and episodes of pyelonephritis in the last year were determined by self-report. Participants were asked how many times they were diagnosed with a “bladder infection” and “kidney infection.”

Statistical Analysis

Characteristics of the UroEDIC sample were summarized using median values and proportions as appropriate. Multivariable logistic regression models were used to assess the independent predictors of weekly UI, both overall and by type, among the diabetic women in the UroEDIC cohort. All factors associated with incontinence at $p < 0.2$ in unadjusted analyses were included in the multivariable models. All analyses were conducted using SAS Version 9.13 (SAS Institute, Cary NC).

Results

At DCCT baseline, UroEDIC women ($n=550$) were similar to the remainder ($n=130$) of the original DCCT women, with the exception that the UroEDIC women had a lower triglyceride level (83.7 vs. 74.9 mg/dl, $p=0.04$), lower HbA1c (9.6 vs. 9.1%, $p=0.003$), and were less likely to smoke (25.4% vs. 15.3%, $p=0.006$). At year 10, there were no significant differences in participant characteristics (i.e. sociodemographic, diabetes-related, health measures) between the 550 UroEDIC women who completed the self-reported questionnaire on incontinence and the 102 women who did not participate in UroEDIC. The mean age for women in UroEDIC was 44 ± 7 years.

Seventeen percent of UroEDIC women reported clinically significant (weekly or more frequent) urinary incontinence during the past year, with daily incontinence reported by 4%, weekly incontinence by 13%, and monthly incontinence by 21%. (Table 1) When asked about urinary incontinence during the past 7 days, 22.5% (n=124) overall reported any urinary incontinence with 21.6% (n=116) reporting stress incontinence and 10.4% (n=49) reporting urge incontinence. (Table 1)

Table 2 presents factors potentially associated with incontinence among women in the UroEDIC cohort. In this unadjusted analysis, age, diabetes duration, hemoglobin A1c, body mass index (BMI), change in BMI from DCCT baseline, current smoking, waist circumference, postmenopausal, prior hysterectomy, retinopathy, nephropathy, coronary calcification, hypertension, and urinary tract infections were associated with overall weekly incontinence or one type of incontinence at $p < 0.2$.

In the multivariable logistic models, higher body mass index (BMI) was significantly associated with weekly incontinence, both overall and by type. (Table 3) For each unit (per kg/m²) increase in BMI, incontinence risk increased about 10%. We did not include waist circumference in the multivariable logistic models because of its high correlation with BMI. In exploratory analyses, we found that change in BMI from DCCT baseline also independently predicted weekly incontinence as well as weekly stress incontinence, but was not significantly associated with weekly urge incontinence; these models did not control for year 10 BMI. The mean change in BMI from DCCT baseline for subjects without weekly incontinence both overall and by type was 4.1 ± 4.0 .

Report of two or more UTIs in the prior year was associated with a 5-fold increased risk of weekly urge incontinence. ($p=0.01$). Urge incontinence was also associated with advancing age (risk increased 42% per 5 years, $p=0.03$) and there was evidence of less risk among women with very mild retinopathy. There was weaker evidence for increased risk with age for overall weekly incontinence (22% per 5 years, $p=0.06$).

Of note, we did not find evidence that DCCT cohort stratum or treatment assignment was associated with weekly incontinence, overall or by type, in either unadjusted or adjusted comparisons.

Comment

In UroEDIC, a cohort of young and middle-aged women with T1DM followed for over 20 years, we found urinary incontinence to be highly prevalent with 38% reporting any urinary incontinence and 17% reporting weekly or more frequent incontinence. Importantly, we found increasing weight was significantly associated with weekly incontinence, both overall and by type.

The association of increased weight and incontinence has been demonstrated among women without diabetes.¹ Weight reduction has also been shown to improve incontinence in moderately obese women.¹³ The likely mechanism is that decreasing weight reduces intra-abdominal and intravesicular pressure, as well as urethral mobility. We have previously found that intensive lifestyle change among women with pre-diabetes resulting in weight loss decreased prevalence of incontinence among women enrolled in the Diabetes Prevention Program.¹⁴ We are currently investigating whether weight loss among women with type 2 diabetes is also associated with decreased incontinence in the Look AHEAD (Action for Health in Diabetes) study.¹⁵ Among women with T1DM, weight reduction may also have the additional benefit of preventing incontinence or reducing its severity.

In our cohort, advancing age and prior UTIs were identified as significant risk factors for urge incontinence, as has been previously seen among women without diabetes.¹⁶ Among women with T1DM, increased prevalence of UTIs and asymptomatic bacteriuria have also been described.^{17,18} The causal relationships between urinary tract infection and urge incontinence may be bidirectional.¹⁹ It would be of interest to determine whether treatment of UTIs in women with T1DM would improve urge incontinence, or treatment of urge incontinence would decrease risk of UTIs.

Several mechanisms by which diabetes might promote incontinence have been proposed, including the hypothesis that microvascular complications might damage innervation of the bladder or alter bladder muscle function.²⁰ Although the prevalence of incontinence in UroEDIC was similar to that of known microvascular complications of diabetes, including neuropathy, nephropathy, and retinopathy, incontinence in UroEDIC was not associated with nephropathy or neuropathy, and there was evidence for less incontinence among women with very mild retinopathy. Furthermore, while the DCCT showed that intensive treatment reduced the risk of retinopathy, nephropathy, and neuropathy, and EDIC demonstrated that the benefit extended well beyond the initial trial,²¹ we did not find any decreased risk of incontinence in groups assigned to intensive treatment, either overall or within the primary prevention or secondary intervention strata, nor among women with better current glycemic control. The reason for a lack of treatment effect of glycemic control on incontinence among women with T1DM is not apparent. In type 1 diabetic rat models, diabetes associated bladder complications are multifactorial and most likely a result an alteration of the detrusor smooth muscle cell, neuronal dysfunction, and/or urothelial dysfunction.^{20,22} Recent evidence suggests treatment may not be effective in reversing bladder dysfunction.²³

Among women without diabetes, parity is a well-known and major risk factor for development of urinary incontinence in middle-aged women, and that risk increases with the number of births.^{24,25} However, among women in UroEDIC, we found no significant difference in the rate of UI overall or by type by number of births. This is likely due to the fact that approximately a third of the population was nulligravid (n=165, 30%). Although this suggests that other factors, potentially those associated with diabetes, may explain the increased prevalence of incontinence in this cohort, we were unable to detect differences in risk according to many diabetes-specific factors, including duration, insulin use, and HbA1c.

The UroEDIC women had participated in the DCCT and subsequently in the EDIC study, and thus may not be representative of T1DM patients. Among participants in the DCCT assigned to usual care, diabetic management was very good, perhaps better than the standard at the time, possibly limiting our power to detect effects of glycemic control on incontinence. However, we have no reason to believe that the risk factors that we did identify in this sample would not be similar in other groups of women with T1DM.

Conclusions

In summary, we found evidence that young and middle aged women with T1DM have a high prevalence of weekly incontinence but no suggestion that intensive glycemic therapy is likely to prevent or reduce incontinence in this population. The association of incontinence with increasing weight and prior urinary tract infections suggests that weight reduction and treatment of urinary tract infections among women with T1DM may have the additional benefit of preventing incontinence or reducing its severity.

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Figure 1.
Flow of Female participants through DCCT and EDIC to UroEDIC

Table 1

Urinary incontinence in the past 12 months among women with type 1 diabetes in the UroEDIC cohort (N=550)

Frequency of incontinence	None	191 (35)
	Less than Monthly	152 (28)
	Monthly	113 (21)
	Weekly	69 (13)
	Daily	24 (4)
Type of Incontinence[†]	Any	124 (23)
	Stress [‡]	116 (22)
	Urge [‡]	49 (10)

Note: DCCT=Diabetes Control and Complications Trial

EDIC= Epidemiology of Diabetes Intervention and Complications Study

UroEDIC=Urological Component of EDIC; completed at EDIC year 10

[†] Among women with incontinence during past seven days[‡] Stress UI defined as $\geq$ weekly UI during activities like coughing, sneezing, lifting, or exercise; Urge UI defined as $\geq$ weekly urge to urinate with inability to reach toilet.

Table 2

Univariate risk factors of weekly urinary incontinence (UI), overall and by type among UroEDIC women at EDIC Year 10, 2002–2004 (N=550)

	N (%)	N (%)	p-value	N (%)	p-value	N (%)	p-value
Primary Prevention							
Conventional	132(48)	30(23)	0.5	30(23)	0.3	11(10)	0.5
Intensive	146(53)	28(19)		25(18)		9(7)	
Secondary Intervention							
Conventional	138(51)	33(24)	0.9	32(24)	0.9	14(12)	0.8
Intensive	134(49)	33(25)		29(23)		15(13)	
Retinopathy*							
None	18(3)	1 (6)	0.3 [†]	1(6)	0.4 [†]	0(0)	0.14 [†]
Microaneurysm only	143(26)	37(26)	0.9 [‡]	33(24)	0.8 [‡]	18(15)	0.9 [‡]
Very mild NPDR	215(39)	47(22)		45(21)		14(8)	
> Moderate NPDR	174(32)	39(22)		37(22)		17(11)	
Diabetes Duration, years							
≥median (21.75)	290(53)	73(25)	0.12	67(24)	0.17	31(13)	0.09
<median (21.75)	260(47)	51(20)		49(19)		18(8)	
HbA1c							
First quartile(4.4<HbA1c≤7.0)	126(23)	26(20)	0.08	24(19)	0.08	11(10)	0.07
Second quartile(7.0<HbA1c≤7.6)	149(28)	30(20)	0.6 [‡]	30(20)	0.7 [‡]	9(7)	0.6 [‡]
Third quartile (7.6<HbA1c≤8.6)	128(24)	40(31)		37(30)		18(18)	
Fourth quartile(8.6<HbA1c≤13.6)	135(25)	27(20)		24(19)		11(9)	
Attained Age							
20–29	8(2)	3(38)	0.02 [†]	3(38)	0.04 [†]	0(0)	0.13 [†]
30–39	169(31)	26(15)	0.003 [‡]	25(15)	0.01 [‡]	9(6)	0.004 [‡]
40–49	248(45)	59(24)		55(23)		25(12)	
50–59	125(23)	36(29)		33(27)		15(14)	
Current Smoking							
Yes	74(14)	14(19)	0.4	14(19)	0.5	3(5)	0.10
No	466(86)	109(23)		101(22)		46(12)	
Hypertension[§]							
			0.009		0.007		0.08

	N (%)	N (%)	p-value	N (%)	p-value	N (%)	p-value
Yes	172(32)	51(30)		48(29)		20(15)	
No	369(68)	72(20)		67(19)		29(9)	
Body Mass Index (kg/m²)			<0.001		<0.001		0.03
<25	183(34)	25(14)	<0.001 [‡]	22(12)	<0.001 [‡]	12(7)	0.002 [‡]
25 to <30	222(42)	53(24)		51(24)		18(10)	
≥30	130(24)	43(33)		40(32)		18(17)	
Body Mass Index (kg/m²) Change from DCCT Baseline	4.4 (4)	5.6(4)	<0.001	5.5(4)	<0.001	5.5(4)	0.02
Waist Circumference (cm)			<0.001		<0.001		<0.001
≥median (82.2)	260(50)	83(32)		79(31)		33(16)	
<median (82.2)	259(50)	35(14)		31(12)		13(6)	
Coronary Calcification //			0.02		0.02		0.7
Yes	98(20)	30(31)		29(30)		9(12)	
No	399(80)	80(20)		75(19.)		36(10)	
Nephropathy (AER[§])			0.8		0.8		0.11 [‡]
Normal (AER<40)	415(76)	92(22)	0.9 [‡]	88(22)	0.6 [‡]	31(9)	0.15 [‡]
Microalbuminuria (40≤AER<300)	110(20)	27(25)		24(23)		15(16)	
Albuminuria (AER≥300)	25(5)	5(20)		4(17)		3(13)	
Peripheral Neuropathy ever during DCCT and EDIC[#]			0.9		0.9		0.6
Yes	374 (68)	84 (23)		79 (22)		35 (11)	
No	176 (32)	40 (23)		37 (22)		14 (9)	
Postmenopausal^{**}			0.13		0.13		0.02
Yes	124(23)	35(28)		33(27)		18(17)	
No	407(77)	88(22)		82(21)		31(9)	
Hysterectomy^{††}			0.11		0.09		0.05
Yes	66(12)	20(30)		19(30)		10(18)	
No	484(88)	104(22)		97(20)		39(9)	
Parity (# of live births)			0.65		0.56		0.45
0	165(30)	34 (21)	0.4 [‡]	30 (19)	0.3 [‡]	14 (10)	0.3 [‡]
1	112(21)	24 (22)		23 (21)		7 (7)	
≥2	273(50)	66 (24)		63 (23)		28 (12)	
Kidney Infections (within last year)			0.8 [†]		0.8 [†]		1.000 [†]

	N (%)	N (%)	p-value	N (%)	p-value	N (%)	p-value
0	491(97)	110(22)	0.3 [‡]	104(22)	0.4 [‡]	42(10)	0.7 [‡]
1	14(3)	2(14)		2(152)		1(8.)	
≥2	2(0)	0(0)		0(02)		0(0.)	
Urinary tract infections (within last year)							
0	449(85)	98(22)	0.10 [‡]	91(21)	0.17 [‡]	35(9)	0.07 [‡]
1	44(8)	8(18)		8(19)		2(5)	
≥2	35(7)	11(31)		11(31)		7(23)	

* Determined by Early Treatment Diabetic Retinopathy Study.

[†] Fisher Exact test.

[‡] Wilcoxon test of trend on 1 df.

[§] Hypertension is defined as sitting systolic BP≥140 mm Hg and/or diastolic BP≥90 mm Hg or the use of antihypertensive medication.

^{||} Coronary Calcification is defined as No if equal to zero and Yes if greater than zero, Agaston unit.

[¶] Albumin Excretion Rate (mg/24hr).

[#] Defined in DCCT by the presence of definite clinically evident distal symmetrical polyneuropathy and an abnormal nerve conduction study or in EDIC by Michigan Neuropathy Screening Instrument (MNSI) >6 positive responses on the questionnaire or a score >2 on the examination.

** Postmenopausal is defined as a subject's menstrual periods ceasing and it being considered permanent.

^{††} Hysterectomy is defined as a subject's history of menstrual period ceasing and it being considered permanent due to surgery.

^{‡‡} 537 women answered the question regarding stress UI and 470 women answered the question regarding urge UI.

Risk factors associated with weekly incontinence among UroEDIC women with type 1 diabetes in UroEDIC at Year 10, 2002–2004

Table 3

	OR	95% CI	p-value*	OR	95% CI	p-value*	OR	95% CI	p-value*
Age (per 5 years)	1.22	0.99–1.50	0.06	1.21	0.97–1.50	0.08	1.42	1.04–1.96	0.03
Body Mass Index (per 1 kg/m ²)	1.10	1.05–1.15	<0.001	1.10	1.05–1.16	<0.001	1.08	1.01–1.16	0.03
Primary vs secondary cohort	1.21	0.62–2.38	0.6	1.21	0.60–2.44	0.6	0.63	0.22–1.76	0.4
Treatment group (Conventional vs Intensive)	1.24	0.79–1.96	0.3	1.40	0.88–2.25	0.2	1.20	0.56–2.57	0.6
Postmenopausal	0.75	0.36–1.57	0.4	0.76	0.36–1.63	0.5	0.59	0.19–1.80	0.3
Prior hysterectomy	1.68	0.76–3.75	0.2	1.81	0.80–4.08	0.2	1.42	0.42–4.81	0.6
Coronary calcification	1.36	0.79–2.36	0.3	1.41	0.80–2.48	0.2	---	---	---
Hypertension	1.19	0.73–1.95	0.5	1.24	0.75–2.05	0.4	1.11	0.52–2.38	0.8
Diabetes duration (per 5 years)	1.14	0.81–1.59	0.5	1.15	0.81–1.62	0.4	1.00	0.61–1.65	0.99
Current smoking	---	---	---	---	---	---	0.43	0.12–1.53	0.16
HbA1c	0.98	0.81–1.17	0.8	0.95	0.78–1.15	0.6	0.99	0.76–1.31	0.96
Nephropathy	---	---	---	---	---	---	---	---	0.19
Microalbuminuria (40 ≤ AER < 300) vs. AER < 40	---	---	---	---	---	---	2.17	0.96–4.91	---
Albuminuria (AER ≥ 300) vs. AER < 40	---	---	---	---	---	---	1.62	0.31–8.53	---
Retinopathy	---	---	---	---	---	---	---	---	0.06
Very mild NPDR vs. No retinopathy or Micro-aneurysm only	---	---	---	---	---	---	0.34	0.14–0.84	---
>=Moderate NPDR vs. No retinopathy or Micro-aneurysm only	---	---	---	---	---	---	0.46	0.16–1.31	---
Urinary tract infections (within last year)	---	---	---	---	---	---	---	---	0.01
1 vs 0	---	---	---	---	---	---	0.74	0.16–3.40	---
≥2 vs 0	---	---	---	---	---	---	4.88	1.76–13.53	---

OR = odds ratio; CI = confidence interval

Odds ratio and confidence intervals are derived from multivariate logistic models used to assess the independent predictors of weekly UI, both overall and by type. All factors associated with incontinence at p < 0.2 in the unadjusted analysis were included in the multivariable model comparing weekly urinary incontinence with no incontinence.

* p-values based on Likelihood Ratio Test.