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Diabetes, glycemic control, and urinary incontinence in women

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Abstract

OBJECTIVES—To estimate the association between urinary incontinence and glycemic control in women ages 20 to 85.

METHODS—We included 7,270 women from the 2005–2010 National Health and Nutrition Examination Survey, stratified into three groups of glycemic control defined by hemoglobin A1c (HbA1c): i) those below the diagnostic threshold (HbA1c<6.5%), ii) those with relatively controlled diabetes (HbA1c 6.5–8.5%), and iii) those with poorly controlled diabetes (HbA1c>8.5%) to allow for a different relationship between glycemic control and urinary incontinence within each group. The primary outcomes were the presence of *any*, *only stress*, *only urgency*, and *mixed* urinary incontinence. We calculated adjusted risk ratios using Poisson regressions with robust variance estimates.

RESULTS—The survey-weighted prevalence was 52.9% for *any*, 27.2% for *only stress*, 9.9% for *only urgency*, and 15.8% for *mixed* urinary incontinence. Among women with relatively controlled diabetes, each one-unit increase in HbA1c was associated with a 13% (95% CI: 1.03–1.25) increase for *any* urinary incontinence and a 34% (95% CI 1.06–1.69) increase in risk for *only stress* incontinence but was not significantly associated with *only urgency* and *mixed* incontinence. Other risk factors included body mass index, hormone replacement therapy, smoking, and physical activity.

CONCLUSIONS—Worsening glycemic control is associated with an increased risk for stress incontinence for women with relatively controlled diabetes. For those either below the diagnostic threshold or with poorly controlled diabetes, the risk may be driven by other factors. Further prospective investigation of HbA1c as a modifiable risk factor may motivate measures to improve continence in women with diabetes.

Keywords

Diabetes; Glycemic control; Mixed urinary incontinence; Stress incontinence; Urgency incontinence

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INTRODUCTION

Urinary incontinence and diabetes mellitus are two morbid and prevalent conditions in the United States, affecting 25–50% and 10% of women, respectively, resulting in substantially reduced quality of life.^{1–4} While urinary incontinence has been shown to be more common in women with diabetes,^{5,6} there is a dearth of literature regarding the influence of glycemic control on urinary incontinence.

Diabetes may contribute to urinary incontinence through glycosuria and microvascular damage similar to processes involved in retinopathy and peripheral neuropathy. However, the fact that women with pre-diabetes (who generally lack these severe diabetic complications) also have increased rates of urinary incontinence suggests that unknown processes may contribute.^{7,8} Likewise, little is known about modifiable risk factors for urinary incontinence among women with diabetes. Intensive lifestyle therapy and weight loss may be effective but the value of conventional treatments for urinary incontinence in women with diabetes has been questioned.^{7,9,10} While glycemic control may make intuitive sense as a modifiable risk factor, the data in the literature has been inconclusive.^{11–13}

Using nationally representative data, we hypothesized that the risk of urinary incontinence would increase with worsening glycemic control, but the strength of this relationship may vary based on the type of urinary incontinence and the extent of glycemic control. Our primary aim was to evaluate glycemic control as a modifiable risk factor in the setting of different types of urinary incontinence. In order to evaluate glycemic control fully, we also evaluated other potential risk factors for urinary incontinence as a secondary aim. Our other secondary aims were to examine the relationship between glycemic control and urinary incontinence among women with pre-diabetes, both due to incontinence and effect on daily living, as well as the relationship between weight loss and urinary incontinence among women with diabetes. We believe that these results will motivate further investigation regarding glycemic control as a possible modifiable factor in preventing and managing the risk of urinary incontinence among women, as well as raise awareness about the risk of urinary incontinence among women with diabetes.

MATERIALS AND METHODS

National Health and Nutrition Examination Survey (NHANES) collects cross-sectional data using surveys, physical examinations, and blood and urine samples from a nationally representative sample of the resident civilian non-institutionalized U.S. population.¹⁴ All demographic information and medical history were collected using standardized instruments.¹⁵

We used hemoglobin A1c (HbA1c) levels obtained from blood specimens as a measure of glycemic control. As we had hypothesized that the strength of the association between glycemic control and urinary incontinence may be different for a population with HbA1c below the diagnostic threshold for diabetes than for a population with HbA1c well above the level indicative of well-controlled diabetes and a population with HbA1c between these two extremes, we stratified women based on their HbA1c level. An HbA1c <6.5% defined the

sample below the diagnostic threshold for diabetes; relatively controlled diabetes was defined by an HbA1c of 6.5%–8.5%; and poorly controlled diabetes was defined as HbA1c >8.5%.

In order to address our primary aim, within each of these three populations, we modeled the association between glycemic control and our primary outcomes of interest, defined as the presence of *any* urinary incontinence, *only stress* incontinence, *only urgency* incontinence, and *mixed* urinary incontinence.¹⁶ The type of urinary incontinence was determined by questionnaires based on validated instruments used in previous studies.^{17–19} *Stress* incontinence was defined as responding yes to the question, “During the past 12 months, have you leaked or lost control of even a small amount of urine with an activity like coughing?” *Urgency* incontinence was defined as responding yes to the question, “During the past 12 months have you leaked or lost control of even a small amount of urine with an urge or pressure to urinate and you could not get to the toilet fast enough?” Any urinary incontinence was defined as answering yes to either question, and *mixed* urinary incontinence was defined as answering yes to both questions.

Other possible risk factors for urinary incontinence that we analyzed, including parity, history of hysterectomy, and hormone replacement therapy (HRT) use, were defined as per NHANES. Smoking was defined as having ever smoked at least 100 cigarettes.

Our other secondary analyses included modeling the association between HbA1c and urinary incontinence among women with pre-diabetes, between incontinence and quality of life in terms of bother and affected daily life, as well as between weight loss and urinary incontinence as a previously reported management option. Pre-diabetes was defined as having HbA1c from 5.7% to <6.5%. We defined bother and affected daily living as a response of somewhat, very much or greatly to the following questions: 1) “During the past 12 months, how much did your leakage of urine bother you?” 2) “During the past 12 months, how much did your leakage of urine affect your day-to-day activities?” Weight loss was defined as reported weight loss over the past 10 years.

All statistical analyses were conducted with STATA, version 12. Sample weights were used when calculating all estimates. Descriptive data are presented as mean $\pm$ standard deviation or proportion. Data were compared with Pearson’s chi-squared test and analysis of variance as appropriate. We used Poisson regression with robust variance estimates to estimate the risk ratios and 95% confidence intervals (CI) for the effect of glycemic control on the outcomes of interest. We considered as potential confounders those variables that we believed would influence both glycemic control and risk of urinary incontinence, such as age, body mass index (BMI), race/ethnicity, physical activity and measures of socioeconomic position. We also included variables known to be strong risk factors for urinary incontinence, such as parity, smoking, hysterectomy and HRT. Variables that altered the risk ratio by more than 10% were considered confounders and retained in the model. We also used Poisson regression with interaction terms to evaluate whether the relationship between glycemic control and urinary incontinence was different across the three HbA1c groups and confirmed our hypothesis that the relationship differed across the groups.

Participants provided written informed consent for the National Health and Nutrition Examination Survey and study procedures were approved by the National Center for Health Statistics Research Ethics Review Board. The analysis presented in this article does not meet the definition of human subject research because it was based on de-identified, public-use data.

RESULTS

Among the sample of 8,829 women 20 years of age or older from NHANES 2005–2010, we excluded 1,257 who had not completed the urinary incontinence information and then 302 who did not have blood drawn, resulting in a final sample of 7,270 (82.3%) women. Compared with women missing data for urinary incontinence or HbA1c, those in our study population were more likely to be non-Hispanic white, non-Hispanic black or other race; had a higher income-to-poverty ratio and educational attainment; had lower rates of HRT use and smoking; and were more often married. The sample-weighted mean HbA1c among the women excluded due to missing urinary incontinence data was $5.5\% \pm 0.73\%$.

Of our analytical sample, 6,548 (90.1%) were below the diagnostic threshold for diabetes with a sample-weighted mean HbA1c of $5.4\% \pm 0.48\%$, while 550 (7.6%) were classified as having relatively controlled diabetes with a sample-weighted mean HbA1c of $7.1\% \pm 0.63\%$ and 172 (2.4%) were classified as having poorly controlled diabetes with a sample-weighted mean HbA1c of $10.3\% \pm 2.17\%$. The sample-weighted prevalence of any incontinence was 52.9%, of *only stress* incontinence was 27.2%, of *only urgency* incontinence was 9.9%, and of *mixed* urinary incontinence was 15.8%. Women below the diagnostic threshold for diabetes tended to be younger, had a lower BMI, and were more likely to be non-Hispanic white (all $P < 0.001$, Table 1). With the exception of marital status and history of smoking, all other variables differed significantly across the groups (all $P < 0.021$, Table 1).

We found that urinary incontinence was associated with many factors in our univariable analyses. Modifiable risk factors associated with an increased risk of any incontinence for women below the diagnostic threshold for diabetes included higher BMI, HRT use, and history of smoking, while physical activity was associated with decreased risk. Higher BMI also was a risk factor among women with relatively controlled diabetes. Of note, HRT use was not only a risk factor among women in all groups, but also had the greatest magnitude of effect (15–41% increase in risk). Full results are presented in Table 2.

Our main findings are that among women with relatively controlled diabetes, each one percentage increase in HbA1c was associated with a significant 13% (95% CI: 1.03–1.25) increase in the risk of any incontinence, and a significant 34% (95% CI: 1.06–1.69) increase in the risk of *only stress* incontinence after adjusting for age and BMI (Table 3). Although the risk ratio for *mixed* urinary incontinence also was elevated among women with relatively controlled diabetes, this association was not significant, and no increased risk was observed for *only urgency* urinary incontinence. Somewhat similar, though uniformly non-significant, associations were seen in women below the diagnostic threshold for diabetes and with poorly controlled diabetes. The adjusted estimates for the association between glycemic control and risk of urinary incontinence are presented in Table 3.

As part of our secondary analyses, we found that women with pre-diabetes (n=1,351) had a higher sample-weighted prevalence of any incontinence (63.8%), *only urgency* incontinence (13.1%), and *mixed* urinary incontinence (21.7%), compared to those below the threshold for pre-diabetes ($P<0.001$). However, for each one-unit increase in HbA1c, there was no statistically significant association with any of the types of urinary incontinence in women with pre-diabetes (data not shown). For each one-unit increase in HbA1c, we also did not find a statistically significant association with being bothered by incontinence (data not shown). Our results did demonstrate that, adjusted for age and BMI, worsening glycemic control was associated with an increased risk of urinary incontinence at least “somewhat” affecting daily living for those with poorly controlled diabetes (RR 1.23 for each 1-unit increase in HbA1c; 95% CI: 1.00–1.52, $P=0.04$). In addition, each 10 pounds of weight loss was associated with a 10% (RR 0.90; 95% CI: 0.82–0.99) decrease in the risk of *only stress* incontinence among women with poorly controlled diabetes ($P=0.025$); however, weight loss was not significantly associated with adjusted risks for other types of urinary incontinence.

DISCUSSION

The level of glycemic control as measured by HbA1c is significantly associated with the risk of any urinary incontinence and especially *only stress* incontinence among women with relatively controlled diabetes. In these women, each percentage increase in HbA1c was associated with a 34% increase in the risk of *only stress* incontinence after controlling for age and BMI.

Previously reported risk factors for urinary incontinence among women include white race, higher BMI, higher parity, smoking, lower physical activity, current postmenopausal hormone use, diuretic use, hysterectomy, vascular disease, longer duration of diabetes, and urinary tract infections.^{3,8,11,20–22} We identified many of the same risk factors, though only age and BMI confounded the association between glycemic control and urinary incontinence.

Our results support glycemic control as a potentially modifiable risk factor for any urinary incontinence and especially *only stress* incontinence among some women with diabetes. In previous studies, neither Jackson et al. nor Phelan et al. found an association between HbA1c and urinary incontinence among women;^{11,13} however, Lee et al. found that higher HbA1c was associated with more limitations due to urinary incontinence.¹² Although our study cannot establish a causality, the association between the level of glycemic control and urinary incontinence for some women with diabetes highlights the need for awareness among these patients. This may be important given traditional treatments for urinary incontinence have been found to be less effective in women with diabetes,¹⁰ and furthermore, one study found that women with diabetes were less likely to discuss urinary incontinence with physicians.²⁶

Our analyses also suggest that the risk for mixed and urgency incontinence appears unaffected by glycemic control, whereas the risk for stress incontinence does appear to be affected. In stress incontinence, worsening glycemic control may cause progressive

microvascular injury leading to gradually worsening connective tissue support, or cause worsening dysfunction at the pudendal nerve endings leading to gradually compromised voluntary urethral sphincter function. Worsening glycemic control also leads to greater glycosuria with a higher volume load, and may lead to decreased bladder contractility, baseline maximum flow rates, and voided volume,²⁴ leading some women with overflow incontinence to present with symptoms mimicking stress incontinence. However, in urgency incontinence, the neurovascular damage from diabetes may lead to inappropriate micturition reflex signals, which may approximate an all-or-nothing response that is not significantly affected by the level of glycemic control. Notably, glycemic control does not appear to be associated with urinary incontinence among patients with poorly controlled diabetes. Pathophysiologically, this may be due to these patients having reached a severity of diabetes where incremental changes in glycemic control may not significantly affect neurologic function and therefore urinary incontinence.

Our study has several limitations. Urinary incontinence is self-reported; however, incontinence affects quality of life, where subjective measures are valid and have been recognized as more useful than objective ones.^{27,28} HbA1c represents blood glucose levels over approximately 3 months and does not capture the duration of disease or other diabetic complications. To the extent that HbA1c does not capture longer-term glycemic control, which may affect urinary incontinence, our results would be biased towards the null. By our classification, the group below the diagnostic threshold for diabetes may include women who have diabetes but have excellent control, while the groups with relatively and poorly controlled diabetes may include some women who have undiagnosed diabetes. This would not be a misclassification insofar as the association between urinary incontinence and diabetes is mediated by the physiological manifestations of diabetes, and any potential misclassifications would bias our results towards the null. In addition, the excluded and the analytic samples differed in some respects. However, these characteristics were not selected in the final analyses due to their small contributions to explaining the risk of the outcomes. Furthermore, the excluded participants tended to have characteristics that would predict a lower risk of urinary incontinence, as well as lower HbA1c levels, and likely would have supported our findings if included. The smaller sample sizes among groups with poorly controlled diabetes limit the power to detect significant differences. Finally, although cross-sectional results cannot establish causality, confounding likely would not explain our findings as we evaluated many possible confounders. Nevertheless, longitudinal and randomized controlled trials are needed to determine whether improving glycemic control can improve urinary incontinence symptoms.

Despite these limitations, our study has several strengths. Our results are generalizable given the nationally representative sample used, large sample size, and relatively limited missing data. In addition, validated questions were used to define urinary incontinence, and HbA1c was used for exposure rather than self-reported diagnosis of diabetes.

Our study indicates that the extent of glycemic control, even among those with relatively controlled diabetes, is significantly associated with the risk for urinary incontinence and especially stress incontinence. Further study is needed to determine if improved glycemic control can modify the risk of urinary incontinence for women with moderately elevated

HbA1c levels. Our results also suggest a need for greater awareness regarding the risk of urinary incontinence among women with diabetes.

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Table 1

Summary Statistics^a

	Below diagnostic threshold (n=6548)	Relatively Controlled Diabetes (n=550)	Poorly Controlled Diabetes (n=172)	P	All participants (n=7270)
Age (years)	46.7 ± 18.6	61.9 ± 17.0	51.7 ± 17.5	<0.001	47.6 ± 18.9
Race					
Mexican American	465 (7.1)	50 (9.0)	29 (17.1)	<0.001	538 (7.4)
Other Hispanic	282 (4.3)	22 (4.1)	17 (9.7)	0.03	320 (4.4)
Non-Hispanic White	4754 (72.6)	324 (59.0)	72 (41.8)	<0.001	5198 (71.5)
Non-Hispanic Black	688 (10.5)	111 (20.2)	43 (25.2)	<0.001	814 (11.2)
Other	354 (5.4)	43 (7.8)	11 (6.2)	0.24	407 (5.6)
Body mass index	28.3 ± 8.6	34.4 ± 10.7	35.0 ± 9.9	<0.001	28.7 ± 8.9
Parity	2.4 ± 1.7	3.4 ± 2.5	2.8 ± 2.2	<0.001	2.4 ± 1.8
History of hysterectomy	1384 (23.9)	209 (39.4)	50 (32.1)	<0.001	1616 (25.0)
Hormone replacement therapy	1509 (23.2)	170 (31.1)	38 (22.3)	0.01	1716 (23.6)
History of smoking	2690 (41.1)	233 (42.4)	76 (44.0)	0.79	3068 (41.2)
Moderate to vigorous physical activity	2933 (44.8)	197 (35.8)	51 (29.8)	<0.001	3206 (44.1)
Income to poverty ratio	3.0 ± 2.0	2.5 ± 2.1	2.5 ± 2.5	<0.001	3.0 ± 2.0
Health insurance coverage	5449 (83.3)	480 (87.2)	132 (76.9)	0.02	6058 (83.4)
Educational attainment					
<9 th grade	322 (4.9)	71 (12.8)	34 (20.0)	<0.001	404 (5.6)
9–11 th grade	773 (11.8)	114 (20.8)	21 (12.2)	<0.001	893 (12.3)
High school graduate/GED	1528 (23.3)	150 (27.3)	32 (18.5)	0.12	1707 (23.5)
Some college	2096 (32.0)	161 (29.3)	61 (35.7)	0.47	2320 (31.9)
College graduate or above	1824 (27.9)	53 (9.7)	23 (13.7)	<0.001	1940 (26.7)
Marital status (married)	3603 (55.0)	287 (52.2)	74 (43.2)	0.05	3977 (54.7)

^aData are weighted means ± standard deviation or weighted n (%). Percentages may not add up to 100% due to rounding.

Table 2Risk factors associated with any urinary incontinence.^a

	Below Diagnostic Threshold (n=6548) RR (95% CI)	Relatively Controlled Diabetes (n=550) RR (95% CI)	Poorly Controlled Diabetes (n=172) RR (95% CI)
Age (per one year)	1.01 (1.01–1.01)	1.00 (0.99–1.00)	1.01 (1.00–1.02)
Race (reference: Non-Hispanic White)			
Mexican American	1.00 (0.94–1.06)	0.96 (0.84–1.10)	0.97 (0.72–1.30)
Other Hispanic	0.95 (0.87–1.03)	0.84 (0.68–1.04)	1.14 (0.84–1.56)
Non-Hispanic Black	0.87 (0.81–0.93)	0.82 (0.71–0.94)	0.76 (0.54–1.07)
Other	0.78 (0.68–0.90)	0.80 (0.59–1.10)	0.36 (0.11–1.24)
Body mass index	1.02 (1.01–1.02)	1.01 (1.00–1.01)	1.01 (0.99–1.02)
Parity (per additional child)	1.05 (1.04–1.06)	0.99 (0.97–1.02)	1.01 (0.97–1.05)
Hysterectomy	1.27 (1.21–1.34)	1.07 (0.95–1.19)	1.24 (0.97–1.58)
Hormone replacement therapy	1.40 (1.34–1.47)	1.15 (1.03–1.28)	1.38 (1.10–1.72)
Smoking	1.09 (1.04–1.14)	1.05 (0.94–1.17)	1.19 (0.94–1.49)
Physical activity	0.95 (0.91–1.00)	1.01 (0.90–1.13)	0.95 (0.73–1.24)
Income-to-poverty ratio	1.01 (1.00–1.03)	1.00 (0.96–1.04)	0.91 (0.82–1.02)
Health insurance coverage	1.07 (1.01–1.13)	1.04 (0.89–1.22)	1.15 (0.88–1.51)
Educational attainment (per level of education ^b)	0.97 (0.95–0.98)	1.03 (0.98–1.07)	0.97 (0.89–1.06)
Marital status (reference: single)	1.13 (1.08–1.18)	1.14 (1.03–1.27)	1.17 (0.93–1.48)

^aUnivariable models are used to assess the risk factors in this table^bLevels of education ordered by: less than 9th grade, 9–11th grade (includes 12th grade with no diploma), high school grad/GED or equivalent, some college or AA degree, and college graduate or above.

Table 3

Risk of urinary incontinence for each one-unit increase in HbA1c adjusted for age and BMI.

	Below Diagnostic Threshold (n=6548) RR (95% CI)	Relatively Controlled Diabetes (n=550) RR (95% CI)	Poorly Controlled Diabetes (n=172) RR (95% CI)
Any urinary incontinence	1.06 (1.00–1.12)	1.13 (1.03–1.25)	1.03 (0.96–1.12)
Only stress urinary incontinence	1.06 (0.94–1.19)	1.34 (1.06–1.69)	1.04 (0.89–1.23)
Only urgency urinary incontinence	1.05 (0.88–1.25)	0.88 (0.62–1.24)	0.84 (0.62–1.15)
Mixed urinary incontinence	1.09 (0.94–1.26)	1.11 (0.87–1.41)	1.14 (0.98–1.31)