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# Lower urinary tract symptoms in older children with and without diabetes mellitus

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## Summary

Lower urinary tract symptoms (LUTS) are an under-recognized complication of diabetes mellitus (DM) in adults and have undergone limited investigation in children. We estimated the prevalence of LUTS in 120 older children (11–17 years) with and without DM and identified patient factors associated with LUTS in logistic regression. Older children (11–17 years) completed a validated LUTS measure and questions about age, ethnicity, gender, BMI and degree of bother secondary to LUTS. The unadjusted prevalence of LUTS was 20.87% in the overall cohort, and LUTS was twice as prevalent in children with DM (33.3% vs. 16.7%) than children without DM. In logistic regression, Hispanic/Latino ethnicity was positively associated with LUTS (OR 8.45, p= 0.011). LUTS may be a prevalent but under-recognized condition, which is more prevalent in Hispanic/Latino and diabetic children.

### Keywords

Pediatric; Diabetes; Lower urinary tract symptoms; Children

## Introduction

Diabetes mellitus (DM) is a major risk factor for developing urinary problems in adults, in part due to diabetic bladder dysfunction (DBD), but this complication has not been well studied in the pediatric population.[1–4] Rates of DM are rapidly increasing, particularly in children. From 2001 to 2009, there was a 21.1% and 30.5% increase in prevalence of Type 1 and Type 2 DM, respectively, among children in the United States.[5] As of 2017, 193,000 Americans under age 20 were estimated to have been diagnosed with DM.

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DBD can progress from lower urinary tract symptoms (LUTS) to urinary tract infections, pyelonephritis, and nephrolithiasis, and can contribute to the development of chronic kidney disease and end stage renal disease.[1] LUTS are common in the adult DM population with an estimated occurrence rate between 37–70%, [1,2,6–9] but the prevalence of LUTS in children has not been examined. A recent systematic review of prevalence and risk factors for nocturnal enuresis and daytime urinary incontinence in healthy older children (10–18 years old) revealed that 1–2% have nocturnal enuresis and 1% have daytime urinary incontinence. [10] Globally, rates of nocturnal enuresis have been reported to affect up to 25% of 5–8 year olds and persists in 1–2% of adolescents.[10–20] Similarly, the prevalence of urge incontinence was recently reported from Finland in up to 45% of 4–7 year olds and 10% of 13–17 year olds.[17] However, many of the previous studies of LUTS did not use the most recent terminology from the International Children's Continence Society.[21]

The complications attributed to LUTS in children go beyond physical expressions, and are associated with decreased quality of life, increased school absences, bullying, social isolation, and depression.[22,23] Forty-eight percent of enuretic children were found to have poor school performance in a recent study of healthy Turkish school children. [22] Further, a high proportion of pediatric urology clinic visits involve management of lower urinary tract problems.[24]

It is imperative to identify risk factors for LUTS in older children and determine if children with DM are at an increased risk for developing LUTS compared to their peers. Such an association would support clinical practice changes to screen patients with DM for LUTS. In this study, we sought to determine if the prevalence of LUTS in older children and whether there is an increased prevalence of LUTS in pediatric patients with DM.

## Methods

### Patient Cohort and Recruitment

Children aged 11–17 years were recruited from pediatric primary care and endocrinology clinics at our institution between June and November 2017. Patients were excluded if they had a known anatomical anomaly of the gastrointestinal or urologic tract that would affect their ability to achieve continence; if they had an acute urinary tract infection; or if they or their caregiver(s) were not literate in English.

Informed consent was implied upon completion of the questionnaire (Appendix 1). A waiver of formal written consent was approved by our institutional review board, as the study involved no more than minimal risk to participants. Completion was voluntary, and no compensation was provided to participants. Children were asked to complete the questionnaire independently, with the help of their caregiver(s) only as needed. All questionnaires were collected during the same visit at which they were completed.

### Survey Instrument

The prevalence of LUTS was assessed using the validated 13-item Vancouver NLUTS/DES questionnaire, which has a sensitivity of 80% and specificity of 91% (AUC 0.9) for the presence of LUTS defined by a score of 11 or higher.[25] This same cut-off value to define

LUTS was used in the current study. The questionnaire has good content and construct validity, as well as test-retest reliability and internal consistency (Cronbach's alpha 0.45) when completed by children older than 9 years of age. The 14th item in the original questionnaire assessed difficulty completing the survey, and this item was excluded as it was not part of the psychometric testing completed by the original authors and was included for author feedback alone. [25]

In addition to the Vancouver Symptom Score for assessing LUTS, a single question to assess the degree of bother which respondents attributed to their LUTS was included using a 4-point Likert scale (never a bother [0], rarely a bother [1], sometimes a bother [3] and always a bother [4]). Demographic information was also collected from the medical record, including DM status (no DM, Type 1 DM, Type 2 DM); demographic information (age, sex, ethnicity); and body mass index-for age and sex (BMI). Obesity was defined using the Centers for Disease Control and Prevention definition of a BMI at or above 95the percentile for children of the same age and sex.

### Statistical Analysis and Sample Size Estimates

This was an exploratory study so a power calculation was not carried out. We sought to enroll 90 older children without DM and 30 with DM to develop an understanding of the prevalence.

Demographic characteristics of children with and without DM and children with and without LUTS were compared descriptively. Group comparisons were made using the two-sample Wilcoxon test for continuous variables and the Chi-square test for categorical variables. Logistic regression analysis was conducted to examine whether patient factors (age, sex, race/ethnicity, BMI and DM) were associated with LUTS. All statistical analyses were completed in R version 3.4.1.

## Results

Families of 123 eligible patients were approached; 120 patients completed the questionnaire. The three patients who declined to participate were female patients who stated they were uncomfortable with the topic of voiding symptoms.

The average age of children completing the questionnaire was 13 years, with an average BMI of 21.7 (Table 1). Most (56%) were female; most (55%) were non-Hispanic whites; and 25% had DM. There were no statistically significant differences between the patients with DM and those without DM except for age; patients with DM were significantly older (median 14 vs 12.5 years, p=0.015).

The unadjusted prevalence of LUTS was 20.8% in the overall cohort, and LUTS was much more prevalent (33.3% vs. 16.7%, p=0.092) in patients with DM than in those without DM Table 1).

When the cohort was stratified by self-reported LUTS, there were no significant differences in age, sex, BMI, obesity or DM status (Table 2). Respondents who reported any degree of

bother (a score of 1 or above) of their urinary symptoms were significantly more likely to have LUTS.

Using logistic regression (Table 3), children were more likely to self-report LUTS if they were of Hispanic/Latino ethnicity (odds ratio (OR) 8.45, p =0.011). For each increased degree of reported bother the odds of LUTS increased by a factor of 3.9 (p<0.001) (Table 3). Despite a 2.5-fold increase in the odds of self-reported LUTS in children with DM, this association approached but did not achieve statistical significance (p = 0.056).

## Discussion

In this study, we found that the prevalence of LUTS in older children to be 20.8%. There is no commonly accepted rate of LUTS in the pediatric population in the United States. Prior studies have found rates of daytime urinary incontinence to be 18% in healthy Turkish school children. [22] A large population study in Finland found rates of LUTS to be 45% in 4–7 year olds and 10% in 13–17 year olds.[17]

In logistic regression, we found that Hispanic/Latino ethnicity was strongly associated with self-reported prevalence of LUTS. The association of Hispanic/Latino descent with increased LUTS rates has previously been noted in the adult population. Prior studies have found significantly increased risks for LUTS in Hispanic/Latino and African American descent adults regardless of gender or comorbidities.[26–29] This association has not been previously noted in pediatric children.

This study also found that the unadjusted prevalence of LUTS was much more common in older children with DM than those without DM. This prevalence of LUTS in these children approached that noted in adult studies (37–70%) [1,2,6–9]. This is interesting since children with DM should have had a shorter duration of disease than the adult cohorts, yet this study identifies rates of LUTS nearing those of adults. This supports the hypothesis that LUTS occurs early in DM disease progression. Castro et al. examined bladder capacity and post void residuals in adolescent patients with and without DM and found increased bladder capacities and post void residuals in patients who had DM for as few as 5 years[30]. These bladder characteristics are accepted to be early signs of DBD.

LUTS have been shown to severely reduce the quality of life; thus, providers should screen for LUTS along with other diabetic sequelae in affected children and adults. With the increasing number of pediatric patients developing DM and the known associated complications of the disease, healthcare providers should improve our assessment and understanding of these DM-related complications in children. LUTS in DM can contribute to severe renal complications including end stage renal failure. Healthcare providers caring for children with DM should consider inquiring about LUTS in an effort to identify patients early. The timing of symptoms onset and optimal treatment for these symptoms needs to be explored in future studies.

This pilot study had several limitations, most notably limited statistical power. To understand whether the large effect size associated with diabetes in a more powered cohort, we are currently carrying out a multi-site follow-up study with a large cohort of children to further

explore this subject. We did not power this study to identify differences in LUTS rates between Type 1 and Type 2 DM. All of the Type 2 patients (n=5) were also obese which may be a confounder. Stratification by Type 1 versus Type 2 DM patients may be important to determine the role of DM in causing LUTS and is actively being addressed in the design of our follow-up studies. Further, increasing the population sample, including Spanish literate only patients/families would be important in future studies to understand the larger population presence of LUTS in those with and without DM. It is unknown if our questionnaire had language issues to account for the association of LUTS with Hispanic/Latino ethnicity for those that were literate in English.

In summary, there may be an increased risk of developing LUTS in pediatric patients with DM over their peers. While this finding will need to be confirmed in larger, multi-center studies, providers should consider screening for LUTS in children with DM using the validated 13-item Vancouver survey, especially in their Hispanic/Latinos.

## Conclusion

Over one-fifth of older children reported LUTS, and the prevalence was doubled in those with DM. Hispanic/Latino ethnicity was associated with increased rates of LUTS in the pediatric population, regardless of DM status.

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## Appendix 1.: Instructions: Please circle the best answer for each question or statement. We prefer if the child completes the questionnaire herself/himself with parental help as needed.

| **Does child have a diagnosis of Diabetes?** | **Type 1** | **Type 2** | **Unknown type** | **Does not have diabetes** | |
|---|---|---|---|---|---|
| I pee in my underwear during the day | Never | 1 day a week | 2–3 days a week | 4–5 days a week | Everyday |
| When I pee in my underwear, they are | I don't pee in my underwear | Almost dry | Damp | Wet | Soaked |
| In a normal day, I go to the bathroom to pee | 1–2 times | 3–4 times | 5–6 times | 7–8 times | More than 8 times |
| I feel that I have to rush to the bathroom to pee | Never | Less than half of the time | Half of the time | More than half of the time | Everyday |
| I hold my pee by crossing my legs or sitting down | Never | Less than half of the time | Half of the time | More than half of the time | Everyday |
| It hurts when I pee | Never | Less than half of the time | Half of the time | More than half of the time | Everyday |
| I wet my bed at night | Never | 3–4 nights per month | 1–2 nights per week | 4–5 nights per week | Every night |
| I wake up to pee at night | Never | 3–4 nights per month | 1–2 nights per week | 4–5 nights per week | Every night |
| When I pee, it stops and starts | Never | Less than half of the time | Half of the time | More than half of the time | Everyday |
| I have to push or wait for my pee to start | Never | Less than half of the time | Half of the time | More than half of the time | Everyday |
| I have bowel movements (poop) | More than once per day | Everyday | Every other day | Every 3 days | More than every 3 days |
| My stool (poop) is hard | Never | Less than half of the time | Half of the time | More than half of the time | Everyday |
| I have bowel (poop) accidents in my underwear | Never | 1–2 times per week | 3 times per week | 4–5 times a week | Everyday |
| These symptoms are: | Never a bother | Rarely a bother | Sometimes a bother | Always a bother | |
| BMI or Height & Weight: | Age (years): | Gender: | Ethnicity: | | |

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**Table 1.**

Patient characteristics for those with and without DM.

| Patient Characteristics | Without DM | With DM | P-value |
|---|---|---|---|
| | n=90 | n=30 | |
| Female, n (%) | 48 (53.3) | 19 (63.3) | 0.458 |
| Male, n (%) | 42 (46.7) | 11(36.7) | |
| Age, median [IQR] | 12.50 [11.00, 15.00] | 14.00 [12.00, 16.00] | **0.015** |
| Non-Hispanic White, n (%) | 47 (52.2) | 19 (63.3) | 0.563 |
| Non-Hispanic Black, n (%) | 33 (36.7) | 9 (30.0) | |
| Hispanic/Latino, n (%) | 5 (5.6) | 2 (6.7) | |
| Other, n(%) | 5 (5.6) | 0 (0.0) | |
| BMI, median [IQR] | 21.59 [18.81, 27.47] | 21.55 [19.09, 24.47] | 0.694 |
| Non-obese, n(%) | 60 (66.7) | 25 (83.3) | 0.106 |
| Obese, n(%) | 30 (33.3) | 5 (16.7) | |
| Without LUTS, n(%) | 75 (83.3) | 20 (66.7) | 0.092 |
| With LUTS, n(%) | 15 (16.7) | 10 (33.3) | |
| Vancouver score, median [IQR] | 6.00 [4.00, 9.75] | 7.50 [5.25, 11.00] | 0.092 |
| Bother score, n (%) | | | 0.008 * |
| 0 | 74 (82.22) | 18 (60.00) | |
| 1 | 14 (15.56) | 8 (26.67) | |
| 2 | 2 (2.22) | 3 (10.00) | |
| 3 | 0 (0.00) | 1 (3.33) | |

* P-value from Wilcoxon rank sum test comparing the two distributions

**Table 2.**

Patient characteristics for those with and without LUTS.

| Patient Characteristics | Without LUTS | With LUTS | P-value |
|---|---|---|---|
| | **N = 95** | **N = 25** | |
| Female, n (%) | 52 (54.7) | 15 (60.0) | 0.806 |
| Male, n (%) | 43 (45.3) | 10 (40.0) | |
| Age, median [IQR] | 13.00 [11.50, 15.00] | 12.00 [12.00, 15.00] | 0.602 |
| Non-Hispanic White, n (%) | 57 (60.0) | 9 (36.0) | **0.023** |
| Non-Hispanic Black, n (%) | 32 (33.7) | 10 (40.0) | |
| Hispanic/Latino, n (%) | 3 (3.2) | 4 (16.0) | |
| Other, n (%) | 3 (3.2) | 2 (8.0) | |
| BMI, median [IQR] | 21.92 [19.23, 27.27] | 19.76 [17.74, 23.49] | 0.068 |
| Non-obese, n(%) | 64 (67.4) | 21 (84.0) | 0.139 |
| Obese, n(%) | 31 (32.6) | 4 (16.0) | |
| Without DM, n(%) | 75 (78.9) | 15 (60.0) | 0.092 |
| With DM, n(%) | 20 (21.1) | 10 (40.0) | |
| Bother score, median [IQR] | 0 [0,0] | 1 [0,1] | <**0.001** |

**Table 3.**

Logistic regression of patient factors associated with LUTS.

| Candidate Predictor for +LUTS | OR | 95% CIs | P-value |
|---|---|---|---|
| Sex (Male) | 0.81 | (0.32, 1.96) | 0.638 |
| Age | 0.94 | (0.75, 1.16) | 0.575 |
| Ethnicity | | | |
| Non-Hispanic White | ref | | |
| Non-Hispanic Black | 1.98 | (0.73,_5.48) | 0.181 |
| Hispanic/Latino | 8.45 | (1.62,_49.35) | **0.011** |
| Other | 4.22 | (0.50,_29.14) | 0.142 |
| BMI | 0.93 | (0.85,_1.01) | 0.104 |
| Obesity | 0.39 | (0.11, 1.14) | 0.112 |
| DM | 2.50 | (0.96,_6.39) | 0.056 |
| Bother Score | 3.90 | (1.91,_8.70) | **<0.001** |
| Sample size = 120 | | | |