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Relationship of Lifestyle and Clinical Factors with Lower Urinary Tract Symptoms (LUTS): Results from the Boston Area Community Health (BACH) Survey

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Abstract

Objectives—Since lifestyle factors and comorbidities may influence lower urinary tract symptoms (LUTS) by gender and race/ethnicity differently, we investigated these associations in the Boston Area Community Health (BACH) Survey.

Methods—Using a multi-stage stratified cluster random sample, 5506 adults aged 30–79 were enrolled; 2301 men, 3205 women, 1770 Black, 1877 Hispanic, 1859 White. Adiposity, lifestyle factors, comorbidities (cardiovascular diseases, diabetes, high blood pressure, high cholesterol, depressive symptoms, prior urinary tract infections) were considered in predicting the odds of LUTS (American Urological Association Symptom Index 8+) by gender and race/ethnicity.

Results—The prevalence of LUTS was 18.7% with similar rates by gender (men 18.7%, women 18.6%) and race/ethnicity (Black 19.3%, Hispanic 16.2%, White 18.9%); however, prevalence did increase substantially with age. Depressive symptoms were associated with increased odds of LUTS across all gender and racial/ethnic groups; overall odds ratio (95% confidence interval): 2.4 (1.9, 3.2), $p < 0.001$. Age increased the odds of LUTS among all groups. Physical activity decreased the odds of LUTS, particularly among women: 0.4 (0.2, 0.7), $p = 0.003$ comparing high to low activity. Cardiovascular diseases and prior urinary tract infections increased the odds of LUTS overall: 1.6 (1.2, 2.1), $p = 0.004$; 1.9 (1.4, 2.4), $p < 0.001$, respectively, and for most groups.

Conclusions—Lifestyle and clinical factors associated with LUTS are similar by gender and race/ethnicity.

Keywords

AUA-SI; comorbid conditions; depressive symptoms; urinary tract infections; physical activity; cardiovascular diseases

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INTRODUCTION

While lower urinary tract symptoms (LUTS) are common in both aging men and women, previous studies have focused on benign prostatic hyperplasia (BPH) in men of particular ages and racial/ethnic groups. The Olmsted County study[1] was conducted in White men aged 40–79 years and the Flint study[2] included Black men aged 40–79 years. A study using NHANES data[3] included significant numbers of non-Hispanic White, non-Hispanic Black and Mexican Americans, but involved only men aged 60 or older and considered only four of the seven symptoms (nocturia, incomplete emptying, hesitancy, weak stream) from the American Urological Association Symptom Index (AUA-SI). Of population based surveys conducted in Europe[4–7], only the UrEpik study[4] included women, albeit in a non-random sample by recruiting female partners of the randomly selected men. In contrast, the Boston Area Community Health (BACH) Survey is a population-based, cross-sectional, random sample of both men and women spanning a broad age range (30–79 years) and three racial/ethnic groups (Black, Hispanic, White). In addition, all seven symptoms from the AUA-SI are considered.

Previous studies have investigated the relationships between lifestyle and clinical factors with LUTS; however, the BACH data provide an opportunity to study these in a diverse sample. Multiple studies[2,5,8,9] have documented associations between LUTS and physical activity, body mass index (BMI), waist-to-hip ratio (WHR), diabetes and heart disease. A study using NHANES data[9] found an inverse relationship between physical activity and LUTS. Other studies[2,5,6] have failed to find significant relationships between BMI and LUTS. Among Black men[2], a history of diabetes as well as heart disease were found to be associated with LUTS. One study[10] found that LUTS were associated with depressive symptoms in men.

We consider BACH Survey data to investigate the association of LUTS with lifestyle and clinical factors. Specifically, our aims are to investigate 1) the relationships of lifestyle and clinical factors with LUTS in our diverse sample and 2) whether there are differences in these relationships by gender and racial/ethnic group.

METHODS

Design, sampling and data collection

The BACH Survey was a population-based, random sample epidemiologic survey of a broad range of urologic symptoms. The study design was a multi-stage, stratified cluster sample with 24 design cells defined by age categories (30–39, 40–49, 50–59, 60–79 years), gender, and race/ethnicity (Black, Hispanic, White). From April 2002 through June 2005, 5506 people were recruited. All participants provided written, informed consent. Respondents provided a venous blood sample, anthropometric measurements, information on medical history, comorbidities, lifestyle and psychosocial factors and detailed self-reported symptoms of urologic and urogynecologic conditions. Additional details are provided elsewhere[11].

Definition of LUTS

LUTS were assessed using the AUA-SI[12], a clinically validated multi-dimensional measure of urological symptoms [12,13]. The scale has a validated Spanish version and has been widely used in epidemiologic studies of LUTS [1,2,4,5,10]. Although there are no studies of the validation of the AUA-SI in women, it has been used in epidemiologic studies of women[4, 14]. Studies of both patients with voiding difficulties and healthy individuals have shown that women often report LUTS and have AUA-SI scores similar to those of age-matched men[15–18]. These results demonstrate that LUTS are not BPH- or gender-specific. LUTS is defined as an AUA-SI score of 8 or above (moderate or severe symptoms).

Covariates

The following categorical covariates were considered: age, 30–39 (reference), 40–49, 50–59, 60–79 years; race/ethnicity (Black, Hispanic, White (reference)), body mass index (BMI): <25 (reference), 25–29, 30+ kg/m^2; self report of smoking status: current, previous, never (reference); physical activity as measured by the Physical Activity Scale for the Elderly (PASE) [19]: <100 (reference),100–249, 250+ with increasing values indicating increasing activity; alcoholic drinks including beer, wine and hard liquor consumed per day: 0 (reference), <1, 1–2, 3+ alcoholic drinks/day; self reports of comorbidities including heart conditions (coronary artery bypass or angioplasty, myocardial infarction, angina pectoris, congestive heart failure), vascular conditions (carotid artery surgery, intermittent claudication, surgery or angioplasty for arterial disease of the leg, aortic aneurysm, Raynauds disease, peripheral vascular disease), stroke or transient ischemic attack (TIA), diabetes, cancer, depressive symptoms (5+ symptoms on the abbreviated CES-D scale[20]), high blood pressure, high cholesterol and prior urinary tract infections (UTIs). A combined measure of cardiovascular diseases including heart conditions, vascular conditions and strokes/TIAs was also considered. An indicator variable for LUTS medications including non-specific alpha blockers (Doxazosin, Terazosin, Prazosin), selective alpha blockers (Tamsulosin, Alfuzosin), anticholinergics (Tolterodine, Oxybutinin, Imipramine) and Finasteride as well as a variable for genitourinary cancers (testicular, uterine, kidney, cervical, prostate, ovarian, bladder and/or vulva sites) were also considered.

Statistical Analysis

Bivariate logistic regression models to predict the odds of LUTS based on each covariate separately were fit (not presented). A manual forward selection-type procedure was used to find parsimonious models predicting the odds of LUTS overall, by gender and by racial/ethnic group. Variables statistically significant according to $p < 0.05$ from Wald F tests of each covariate (not accounting for multiple comparisons) remained in the models. Final models included all covariates that were statistically significant in at least one of the groups (overall, by gender or by race/ethnicity). Age, race/ethnicity, genitourinary cancers and medications for LUTS were adjusted for in all models regardless of significance level. Estimates of odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were reported. While all covariates had 5% or fewer missing observations, multiple imputation was used to impute missing values. All analyses were weighted to the Boston population and were conducted in SUDAAN Version 9.0 (Research Triangle Park, NC).

RESULTS

We considered 5506 adults (2301 men, 3205 women); the distribution by racial/ethnic group was 1770 Black, 1877 Hispanic and 1859 White (Table 1). As in Kupelian *et al.*[21], the prevalence rate of LUTS was 18.7%; this did not vary significantly by gender (men 18.7%, women 18.6%), nor by racial/ethnic group (Black 19.3%, Hispanic 16.2%, White18.9%). Prevalence increased with age ($p < 0.001$); those aged 30–39 years having LUTS prevalence of 10.5%, 40–49 years 18.3%, 50–59 years 26.1% and 60–79 years 26.2%.

In a model with lifestyle and clinical covariates predicting the odds of LUTS overall (Table 2), as age increased, the odds of LUTS increased ($p < 0.001$) with the highest odds for those aged 50–59. The odds of LUTS did not vary by racial/ethnic group. Increased BMI was not significantly associated with the odds of LUTS although the ORs indicate an increase in the odds of LUTS with increasing BMI. Increased physical activity was associated with a decrease in the odds of LUTS ($p = 0.003$); people scoring 250+ on the PASE scale had nearly half the odds of LUTS compared with those scoring <100: OR (95% CI); 0.6 (0.4, 0.8). Cardiovascular diseases were associated with a significant increase in the odds of LUTS ($p = 0.004$): 1.6 (1.2, 2.1). Diabetes was not associated with the odds of LUTS although the OR indicates a small

increase in the odds. A large increase in the odds of LUTS was due to those reporting depressive symptoms: 2.4 (1.9, 3.2) ($p < 0.001$). Having prior UTIs also significantly increased the odds of LUTS: 1.9 (1.4, 2.4) with $p < 0.001$.

Most relationships between covariates and odds of LUTS remained similar or were more pronounced when considered by gender. A significant increase in the odds of LUTS was seen in those with BMI 30+ compared to <25 among women: 1.6 (1.1, 2.3), $p = 0.009$ but BMI was not associated with the odds of LUTS among men. Increased physical activity in women was associated with a decrease in the odds of LUTS; comparing activity scores 250+ with <100: 0.4 (0.2, 0.7), $p = 0.003$; the relationship was not statistically significant in men but the ORs decreased with increasing exercise. The relationship between cardiovascular diseases and the odds of LUTS reached statistical significance in males: 1.7 (1.1, 2.7), $p = 0.024$, but not in females: 1.4 (1.0, 1.9), $p = 0.078$, although the odds of LUTS increased in both cases. The relationship of depressive symptoms with the odds of LUTS was statistically significant for both genders ($p < 0.001$ for both); however, it may be stronger in men: 3.4 (2.2, 5.4) compared with 2.1 (1.5, 2.9) in women. Prior UTIs also were associated with a significant increase in the odds of LUTS for both genders ($p < 0.001$ for both) with males 3.0 (1.8, 4.9) and females 2.0 (1.5, 2.8).

The odds of LUTS was associated with an increase with age for all racial/ethnic groups although among Blacks, the effect was only marginally significant ($p = 0.056$). The effect of BMI did not reach statistical significance among any of the racial/ethnic groups. Among Blacks ($p = 0.025$) and Whites ($p = 0.048$), the odds of LUTS was associated with a statistically significant decrease with physical activity; the effect was similar but not statistically significant among Hispanics. Cardiovascular disease was associated with a statistically significant increase in the odds of LUTS among Blacks: 1.6 (1.0, 2.6), $p = 0.046$ and Hispanics: 2.5 (1.5, 4.0), $p < 0.001$ and marginally among Whites: 1.4 (0.9, 2.1), $p = 0.12$. Diabetes was associated with a marginally statistically significant increase in the odds of LUTS among Blacks: 1.5 (1.0, 2.4), $p = 0.053$, a statistically significant increase among Hispanics: 1.6 (1.0, 2.5), $p = 0.034$, and a non-significant increase among Whites: 1.2 (0.6, 2.4). Depressive symptoms were found to be significantly associated with LUTS across all three racial/ethnic groups ($p < 0.001$ for all) with odds ratios ranging from 2.3 (1.5, 3.6) in Whites to 2.8 (1.6, 5.0) in Hispanics. Prior UTIs were associated with a statistically significant increase in the odds of LUTS among Blacks: 2.8 (1.8, 4.2), $p < 0.001$ and Whites: 1.7 (1.2, 2.4), $p = 0.002$ but not significantly among Hispanics: 1.0 (0.6, 1.7). People on medications for LUTS had statistically significantly higher odds of LUTS overall: 4.3 (2.7, 6.9), $p < 0.001$ and for all groups except Hispanics: 2.3 (0.7, 7.1) where there were too few Hispanic people on medications for LUTS to detect an increase (not presented).

Depressive symptoms was the only factor that remained statistically significantly associated in multivariate models with an increase in the odds of LUTS across all gender and racial/ethnic groups. The magnitude of the relationship between the odds of LUTS and depressive symptoms was similar to that of the effect of age; that is, overall, the odds of LUTS was 2.4 (1.7, 3.3) for those 50–59 years compared with 30–39 years and the odds of LUTS was 2.4 (1.9, 3.2) for those with depressive symptoms compared to those without. Investigating both the effect of age and depressive symptoms among each age group, there is a statistically significant increase in the prevalence of LUTS among those with depressive symptoms compared to those without. The prevalence of LUTS is the highest among those in the older age groups (50–59, 60–79 years) who also report depressive symptoms.

COMMENT

The analyses presented consider LUTS as the outcome variable; however, linear regression analyses with continuous AUA-SI score as the response revealed similar although slightly more

sensitive results. We also investigated the AUA-SI scale by symptom type: voiding (incomplete emptying, intermittency, weak stream, hesitancy) and storage (frequency, urgency, nocturia); results did not vary substantially by symptom type. We also considered analyses of the three racial/ethnic groups stratified by gender. Because of smaller sample sizes, relationships between LUTS and covariates were not as consistent but no major differences were found.

Although evidence for causality between depression and LUTS cannot be gained from this cross-sectional study, an intriguing possibility is that neurochemical changes in the central nervous system (CNS) that could predispose to depression also influence autonomic neural activity regulating the urinary tract. A subset of depressed patients is postulated to exhibit alterations in serotonergic function attributed to a range of defects including polymorphisms in genes for serotonin transporter or altered 5-HT1A function [22]. This central monoamine also profoundly influences pathways regulating micturition [23,24]. Reducing the amount of serotonin in the brains of experimental animals triggers urinary frequency and causes detrusor overactivity [23]. Similarly, mice with deletion of the gene for the serotonin reuptake transporter exhibit urinary frequency and detrusor overactivity [24]. Clinically, studies suggest that overactive bladder leading to urge urinary incontinence is associated with depression [25,26]. Indeed serotonin reuptake inhibitors or 5-HT1A agonists developed for depression are useful in treating LUTS [27]. Likewise, irritable bowel syndrome and pelvic pain disorders commonly occur with depression and are associated with derangements in serotonergic function [28]. Thus, it is tempting to speculate that altered serotonergic function could lead to a clustering of psychiatric (depression) and visceral (bladder, bowel) symptoms in some individuals.

Cardiovascular diseases were associated with significant increases in the odds of LUTS. There is accumulating experimental evidence that endothelial dysfunction or pelvic ischemia can lead to loss of bladder smooth muscle and partial denervation with subsequent detrusor overactivity [29]. This sequence of events would translate clinically into reduced force of urinary stream and urinary frequency. In animal models studying BPH, effects of ischemia are heightened and cause an overactive bladder that fails to empty completely [30]. The lack of statistical significance for cardiovascular disease and LUTS in women may reflect the relative protective effect of estrogen in younger women on the vasculature. If these hypotheses were true, it might be predicted increased physical activity would be associated with reduced odds of LUTS as found in the present study.

The BACH Survey was compared with three different government-sponsored national surveys (the National Health and Nutrition Examination Survey (NHANES), the National Health Interview Survey (NHIS) and the national Behavioral Risk Factor Surveillance System (BRFSS)) on different sociodemographic and health-related variables. While there are a few differences, most of the BACH health estimates are comparable, suggesting that the results are generalizable to the US as a whole.

CONCLUSIONS

The BACH Survey provides population-based data on the prevalence and correlates of LUTS by gender and racial/ethnic group; it is unique since it includes a sample of both genders across a wide age-range (30–79 years) with significant representation of Black and Hispanic people. Depressive symptoms is the only factor after multivariate analyses associated with statistically significant increases in the odds of LUTS consistently across gender and racial/ethnic groups. In addition to the odds of LUTS increasing among those with depressive symptoms, it is compounded by an increase with age. Cardiovascular diseases and prior UTIs were associated with increased odds of LUTS overall. The effects of BMI and physical activity on the odds of the LUTS were most pronounced in women. Although all covariates from the multivariate

models did not reach statistical significance in all gender and racial/ethnic groups, similar effects were found across the groups.

The implications of our most robust associations and the relatively high prevalence of LUTS, if confirmed in longitudinal studies, suggest that a biological basis for LUTS in some individuals may derive from complex changes in the vasculature or brain. If true, future epidemiological studies may lead to a better understanding of pathogenesis, preventive strategies (lipid control, avoidance of smoking) or therapies (serotonergic based drugs) in subsets of the population suffering from LUTS.

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Table 1

Design-adjusted* characteristics overall and by gender (n = 5506), Boston Area Community Health Survey (BACH), 2002–2005.

		Overall	Men	Women	*p*-value†
Age	30–39	35.2	37.2	33.5	0.026‡
	40–49	25.1	25.8	24.4	
	50–59	18.1	17.8	18.4	
	60–79	21.6	19.2	23.7	
Racial/ethnic group	Black	27.6	25.1	29.9	0.024‡
	Hispanic	13.2	13.0	13.3	
	White	59.2	61.9	56.8	
Body mass index	<25	30.1	26.6	33.3	<0.001
(kg/m^2)	25–29	34.4	40.7	28.6	
	30+	35.5	32.6	32.6	
Smoker	Never	47.8	45.2	50.1	0.092
	Previous	27.9	28.7	27.2	
	Current	24.3	26.2	22.6	
Physical activity	<100	27.4	26.8	27.9	<0.001
(higher value =	100–249	50.6	47.4	53.6	
higher activity)	250+	22.0	25.8	18.5	
Alcoholic drinks/day	0	34.9	27.5	41.6	<0.001
	<1	41.2	38.9	43.3	
	1–2	18.2	24.0	12.9	
	3+	5.7	9.6	2.2	
Heart conditions		9.0	10.2	7.9	0.055
Vascular conditions		6.2	6.2	6.2	0.981
Stroke or transient ischemic attack		3.5	4.2	2.8	0.059
Total Cardiovascular§		14.1	14.5	13.8	0.642
Diabetes		9.4	9.3	9.6	0.799
Cancer		7.9	6.8	9.0	0.039
Genitourinary cancers#		2.9	3.0	2.7	0.677
High blood pressure		27.3	26.1	28.3	0.221
High cholesterol		28.5	28.5	28.5	1.000
Depression		17.2	14.0	20.1	<0.001
Prior urinary tract infections		28.2	9.6	45.1	<0.001
Medication for LUTS**		2.7	3.5	2.0	0.016

*Adjusted inversely to the probability of selection.

†*p*-value from chi-square test of independence for the relationship between characteristic and gender.

‡These significant *p*-values are results of artifacts of the population because the sample was weighted to the population, e.g. there are more older women than men in the population.

§Cardiovascular diseases include heart conditions (coronary artery bypass or angioplasty, myocardial infarction, angina pectoris, congestive heart failure), vascular conditions (carotid artery surgery, intermittent claudication, surgery or angioplasty for arterial disease of the leg, aortic aneurysm, Raynauds disease, peripheral vascular disease) and stroke or transient ischemic attack.

#Genitourinary cancers include the following sites: testicular, uterine, kidney, cervical, prostate, ovarian, bladder and vulva.

**Medications for lower urinary tract symptoms (LUTS) include non-specific alpha blockers (Doxazosin, Terazosin, Prazosin), selective alpha blockers (Tamsulosin, Alfuzosin), anticholinergics (Tolterodine, Oxybutinin, Imipramine) and Finasteride

Table 2

Design-adjusted* odds ratios (95% confidence intervals) from multivariate † predicting LUTS overall, by gender and by race/ethnicity models

		Overall	Men	Women	Black	Hispanic	White
Age	30–39	**1.0**	**1.0**	**1.0**	1.0	**1.0**	**1.0**
	40–49	**1.7 (1.2,2.6)**	**2.5 (1.3,4.8)**	**1.3 (0.8,2.0)**	1.5 (0.8,2.8)	**2.2 (1.2,3.9)**	**1.7 (0.9,3.0)**
	50–59	**2.4 (1.7,3.3)**	**3.2 (1.7,5.7)**	**1.9 (1.3,2.7)**	2.1 (1.2,3.6)	**1.9 (1.1,3.3)**	**2.5 (1.6,4.1)**
	60–79	**2.0 (1.3,2.8)**	**3.6 (1.9,6.8)**	**1.3 (0.9,2.1)**	1.6 (0.8,2.9)	**1.2 (0.6,2.2)**	**2.2 (1.3,3.7)**
Race/ethnicity	Black	0.9 (0.7,1.2)	0.7 (0.5,1.0)	1.2 (0.9,1.7)			
	Hispanic	0.8 (0.6,1.1)	0.7 (0.4,1.1)	1.0 (0.7,1.5)			
	White	1.0	1.0	1.0			
Body Mass Index	<25	1.0	1.0	**1.0**	1.0	1.0	1.0
	25–29	1.0 (0.7, 1.4)	0.8 (0.5, 1.3)	**1.1 (0.7,1.6)**	1.0 (0.6,1.7)	0.7 (0.4,1.1)	1.0 (0.7,1.6)
	30+	1.3 (0.9, 1.7)	0.9 (0.5,1.4)	**1.6 (1.1,2.3)**	1.1 (0.7,1.9)	0.9 (0.5,1.6)	1.4 (0.9,2.2)
Physical Activity (higher value= higher activity)	<100	**1.0**	1.0	**1.0**	**1.0**	1.0	**1.0**
	100–249	**0.9 (0.7,1.2)**	1.0 (0.7, 1.6)	**0.8 (0.6,1.1)**	**0.8 (0.5,1.3)**	0.9 (0.5, 1.8)	**0.9 (0.6,1.3)**
	250+	**0.6 (0.4,0.8)**	0.8 (0.5,1.3)	**0.4 (0.2,0.7)**	**0.5 (0.3,0.8)**	0.8 (0.4, 1.7)	**0.6 (0.3,0.9)**
Cardiovascular Diseases‡		**1.6 (1.2,2.1)**	**1.7 (1.1,2.7)**	1.4 (1.0,1.9)	**1.6 (1.0,2.6)**	**2.5 (1.5,4.0)**	1.4 (0.9, 2.1)
Diabetes		1.3 (0.9,1.9)	1.5 (0.8, 3.0)	1.1 (0.7, 1.7)	1.5 (1.0, 2.4)	**1.6 (1.0,2.5)**	1.2 (0.6, 2.4)
Genitourinary cancers§		1.2 (0.7,1.9)	0.8 (0.4, 1.7)	1.4 (0.7, 2.7)	2.3 (0.9, 5.6)	2.3 (0.6,8.1)	0.8 (0.4, 1.6)
Depressive Symptoms		**2.4 (1.9,3.2)**	**3.4 (2.2,5.4)**	**2.1 (1.5,2.9)**	**2.5 (1.6,3.9)**	**2.8 (1.6,5.0)**	**2.3 (1.5,3.6)**
Prior Urinary Tract Infections		**1.9 (1.4,2.4)**	**3.0 (1.8,4.9)**	**2.0 (1.5,2.8)**	**2.8 (1.8,4.2)**	1.0 (0.6, 1.7)	**1.7 (1.2,2.4)**

*Adjusted inversely to the probability of selection.

†Values in bold indicate statistically significant relationships with the odds of LUTS ($p < 0.05$). Models also adjusted for medications for LUTS including non-specific alpha blockers (Doxazosin, Terazosin, Prazosin), selective alpha blockers (Tamsulosin, Alfuzosin), anticholinergics (Tolterodine, Oxybutinin, Imipramine) and Finasteride.

‡Cardiovascular diseases include heart conditions (coronary artery bypass or angioplasty, myocardial infarction, angina pectoris, congestive heart failure), vascular conditions (carotid artery surgery, intermittent claudication, surgery or angioplasty for arterial disease of the leg, aortic aneurysm, Raynauds disease, peripheral vascular disease) and stroke or transient ischemic attack.

§Genitourinary cancers include the following sites: testicular, uterine, kidney, cervical, prostate, ovarian, bladder and vulva.

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