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Effect of Sexually Transmitted Infections, Lifetime Sexual Partner Count, and Recreational Drug Use on Lower Urinary Tract Symptoms in Men Who Have Sex With Men

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OBJECTIVE To investigate the relationship of lower urinary tract symptoms (LUTS) to urinary tract infection, prostatitis, sexually transmitted infection, lifetime sexual partner count, and recreational drug use in a population of men who have sex with men. LUTS in men are a source of considerable morbidity, distress, and medical expense.

METHODS We conducted a cross-sectional, Internet-based survey of urinary quality-of-life outcomes in men who have sex with men. The main outcome was the International Prostate Symptom Score (IPSS), classified as none/mild (IPSS 0-7), moderate/severe (IPSS 8-35), or severe (IPSS 20-35). The participants were also asked whether they ever sought medical attention for urinary problems.

RESULTS The survey web site was accessed by 2783 men, of whom 2348 (84.3%) completed the questionnaire. The median age was 39 years (range 18-81). Age, depression, human immunodeficiency virus infection, gonorrhea, syphilis, prostatitis, and prescription drug abuse were all associated with LUTS. Men who sought medical attention for LUTS were more likely to report older age, diabetes, depression, gonorrhea, urinary tract infection history, and prostatitis.

CONCLUSION Specific infectious conditions of the urinary tract and depressive symptoms are independent predictors of LUTS in men who have sex with men. Although LUTS are often multifactorial, a common unifying explanation for our finding could be the effects of local and systemic inflammation on the lower urinary tract. UROLOGY 79: 188–193, 2012. © 2012 Elsevier Inc.

Lower urinary tract symptoms (LUTS) in men are a source of considerable morbidity and distress. Billions of dollars are spent annually to treat this condition.[1] LUTS can be caused by bladder outlet obstruction secondary to benign prostatic hyperplasia. However, it is increasingly recognized that conditions affecting the urethra and bladder are also significant contributors to LUTS in men.[2]

Both LUTS and benign prostatic hyperplasia have been associated with local and systemic inflammation. The inflammatory marker C-reactive protein has been shown to be elevated in men with LUTS,[3] inflammatory tissue is common in benign prostatic hyperplasia prostatic nodules,[4] and inflammation has been shown to induce prostatic epithelial cell growth and proliferation by way of cytokine modulation in animal models.[5] A history of urinary tract infection (UTI) with either sexually or nonsexually transmitted pathogens has been linked to LUTS.[6-8] There is also evidence that recreational drugs, such as ketamine, elicit bladder inflammation and dysfunction.[9]

In the present study, we investigated the relationship of LUTS to UTI, prostatitis, sexually transmitted infection (STI), lifetime sexual partner count, and recreational drug use in a population of men who have sex with men (MSM). MSM constitute 4%-5% of the male

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population of the United States.[10] MSM are of particular interest, because this population has been reported to have elevated STI rates and have sexual practices that generally differ from the rest of the male population.[11] We hypothesized that MSM would have similar risk factors for LUTS as the general male population and that a history of urinary tract inflammation and drug use would be associated with a greater burden of urinary symptoms.

MATERIAL AND METHODS

Study Design and Cohort Description

The institutional review board approved the study before initiation. We conducted a cross-sectional, Internet-based survey of urinary quality-of-life outcomes in MSM. The cohort was restricted to literate, Internet-using MSM who were >17 years of age. International sampling was achieved by distribution of a survey invitation to local, national, and international lesbian, gay, bisexual, and transgender community centers, organizations catering to MSM, and advertisements on Facebook (available from www.facebook.com, Palo Alto, CA) aimed at self-identified MSM. The potential respondents were given the option of clicking on a link to the survey, which was posted on the Internet-based survey site "Survey Monkey" (available from www.surveymonkey.com, Palo Alto, CA). The respondents were informed that they would be asked questions regarding their sexual and urinary wellness and given the option to decline participation or to stop the survey at any point. To maintain privacy, no personal identifying information was collected. The responses were collected from January 19, 2010 to May 19, 2010.

Outcome Variables

The main outcome variable was the International Prostate Symptom Score (IPSS), an internationally validated metric of bothersome LUTS.[12,13] IPSS is graded on a scale of 0-35 and includes 7 Likert-style questions pertaining to urinary symptoms, including frequency, urgency, nocturia, intermittency, weak stream, straining, and incomplete emptying. Validated categorical severity scales distinguished LUTS into categories of none/mild (IPSS 0-7), moderate to severe (IPSS 8-35), and severe (IPSS 20-35).[14-16] The participants were also asked whether they had ever sought medical attention for problems related to urination (yes/no).

Exposure Variables

The respondents reported their age, geographic location and city size, and race/ethnicity (African-American, Asian-American, white, Latin-American, Native American, other). The respondents were asked whether they were receiving treatment, or had ever have been treated, for the following medical conditions: coronary artery disease, diabetes, hyperlipidemia, and depression, with a possible answer of yes or no. The respondents were asked whether they were human immunodeficiency virus (HIV)-positive (yes/no/uncertain). The men were also asked whether they had ever had Chlamydia (yes/no), gonorrhea (yes/no), syphilis (yes/no), and genital herpes (yes/no). We inquired whether the respondent had ever had a UTI that required antibiotic treatment (excluding sexually transmitted diseases) or if they had been diagnosed with prostatitis or chronic pelvic pain (yes/no). The participants were asked to report their number of lifetime sexual partners. They were also provided with an extensive list of sexual practices (eg, anal receptive and/or insertive intercourse, giving and receiving fellatio, sex with female partners) and asked whether they included these acts in their sexual repertoire (data not shown). Finally, the respondents were asked whether they used the following recreational drugs: methamphetamine, cocaine, ketamine, ecstasy, and/or prescription pills. For each drug, the participants were asked "how often do you use drugs to get high?" (never, rarely/about once per year, sometimes/several times a year, monthly, weekly, daily). For ease of interpretation, the variable was made binary by grouping several times a year, monthly, and daily as a positive response to drug use and never, and rarely/about once per year as a negative response.

Statistical Analysis

Descriptive statistics were used to characterize the study population. We then used age-adjusted odds ratios and 95% confidence intervals to identify the independent predictors of the presence of moderate to severe LUTS, the presence of severe LUTS, and whether the subjects had sought medical attention for urination problems. A so-called continuation ratio model was used to jointly compare moderate/severe to none/mild LUTS and severe to moderate LUTS. We tested the effects of each exposure overall and on each of the nested comparisons and finally assessed the equality of the 2 nested effects. The variables associated with the outcome with $P \leq .20$ after multiple adjustment were retained in the final multiple logistic model. Goodness of fit was checked using Hosmer-Lemeshow and le Cessie-van Houwelingen-Copas-Hosmer tests.[17] In the primary analysis, the respondents with missing data were excluded; however, a sensitivity analysis using multiple imputation of missing data was also conducted, without material changes to the results. Statistical significance was set at $P < .05$, and all tests were 2-sided. Stata, version 11 (StataCorp, College Station, TX), was used for all analyses.

RESULTS

The survey web site was accessed by 2783 men, of whom 2348 (84.3%) completed the questionnaire. The patient demographics, comorbidities and infectious disease history, lifetime sexual partner history, and recreational drug use history are listed in Table 1. The median age was 39 years (interquartile range 31-47; range 18-81). Most (~75%) of the cohort were from the United States, and 82% of the respondents were white. Having a history of treatment for, or currently being treated for, depression was common (39%). A history of gonorrhea and Chlamydia were reported by 19% and 12.6%, respectively.

The total IPSSs, stratified by age and categorized for the entire population, are listed in Table 2. Moderate to severe LUTS were reported by 33% of the population. Seeking medical attention for LUTS was endorsed by 18%, with a dramatic increase with increases in age.

In the continuation ratio model (Table 3), age, depression, HIV infection, gonorrhea, syphilis, prostatitis, and prescription drug abuse were all associated with LUTS, as determined by the overall P values. Age, diabetes, and depression were important in both nested comparisons.

Table 1. Descriptive statistics of respondent demographic, comorbid and infectious disease history, lifetime sexual partner estimate, and recreational drug use history

Variable	n (%)
Age (y)	
18-29	435 (18.5)
30-39	748 (31.9)
40-49	708 (30.2)
50-59	319 (13.6)
60-81	138 (5.9)
Geographic location	
Western United States	427 (18.3)
Midwest United States	331 (14.2)
Northeast United States	407 (17.4)
Southern United States	338 (14.5)
Southwest United States	146 (6.2)
Northwest United States	78 (3.3)
Canada	158 (6.8)
Europe	286 (12.2)
Australia	140 (6.0)
Other	27 (1.2)
City population	
<100 000	732 (31.3)
100 000-1 000 000	860 (36.8)
>1 000 000	746 (31.9)
Race/ethnicity	
African-American	68 (2.9)
Asian-American	66 (2.8)
White	1959 (83.4)
Latin-American	155 (6.6)
Native-American	31 (1.3)
Other	24 (1.0)
Comorbid conditions	
Coronary artery disease	121 (5.2)
Diabetes	163 (6.9)
Hyperlipidemia	441 (18.8)
Depression	916 (39.0)
Lifetime history of infectious condition	
HIV infection	331 (14.1)
Chlamydia	295 (12.6)
Gonorrhea	446 (19.0)
Syphilis	221 (9.4)
Genital herpes	190 (8.1)
UTI	531 (22.7)
Prostatitis	178 (7.6)
Estimated number of lifetime partners	
0-6	574 (25.9)
7-29	529 (23.9)
30-100	556 (25.1)
>100	554 (25)
Do you use the following drugs >1 time/y to get high?	
Methamphetamine	104 (4.98)
Cocaine	119 (5.72)
Ketamine	39 (1.88)
Ecstasy	117 (5.61)
Prescription pills	206 (9.94)

HIV, human immunodeficiency virus; UTI, urinary tract infection.

Table 2. Total IPSS stratified by age, distribution of categorized IPSS, and percentage of men who sought medical attention for LUTS by age

Variable	Value
Total IPSS	
Overall	6.6 ± 6
18-29	4.6 ± 4.4
30-39	5.9 ± 5.2
40-49	7.2 ± 6.3
50-59	8.3 ± 6.8
60-81	10.4 ± 7.7
Categorized IPSS	
None-mild	1570 (67)
Moderate	665 (28)
Severe	113 (5)
Those who sought medical attention for LUTS stratified by age	
Overall	422 (18)
18-29 y	23 (5)
30-39 y	93 (12)
40-49 y	130 (18)
50-59 y	103 (32)
60-81 y	73 (53)

IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms.

Data presented as mean ± standard deviation or numbers, with percentages in parentheses.

In the comparison of moderate/severe to none/mild LUTS, gonorrhea, UTI, prostatitis, lifetime number of partners, and prescription pill abuse were important; no other recreational drugs were important in either comparison. HIV infection was the only predictor that distinguished severe from moderate LUTS without also differentiating moderate/severe from none/mild. We were unable to detect any differences in the strength of the associations across the 2 nested comparisons.

In a separate analysis, we investigated the relationship between sexual activities and LUTS. None of the sexual activities about which we inquired were associated with a significantly different risk of LUTS (data not shown).

The variables associated with men seeking medical attention for their urinary symptoms are listed in Table 4. Increasing age, a history of diabetes, depression, gonorrhea, UTI history, and prostatitis all reached statistical significance in the multivariate model. Drug use, the number of sexual partners, HIV infection, Chlamydia, syphilis, and herpes were not associated with help-seeking behavior in the multivariate model.

COMMENT

In the present Internet survey of predominantly white, young and middle-aged MSM, we found that age, depression, HIV infection, gonorrhea, syphilis, prostatitis, and prescription drug were independently associated with LUTS by self-report. Help-seeking behaviors for LUTS were more common in older men and in those with diabetes, depression, a history of gonorrhea, UTI, or prostatitis.

Our results corroborate previous studies indicating that a history of urinary tract inflammation from infections, including HIV, gonorrhea, prostatitis, and nonsexually transmitted UTI increase the risk of subsequent moderate to severe LUTS.[7,18-21]

Despite their known inflammatory effects, Chlamydia and genital herpes infection were not independent predictors of LUTS in our sample. Chlamydia might have been

Table 3. Continuation ratio model comparing moderate/severe to none/mild LUTS and severe to moderate LUTS

	None/Mild vs Moderate/Severe			Moderate vs Severe			*P* Value	
Variable	OR	95% CI	*P* Value	OR	95% CI	*P* Value	Overall	For Equality
Age in 10-y increments	1.26	1.15-1.39	<.001	1.57	1.24-1.98	<.001	<.001	.091
Diabetes	1.57	1.07-2.29	.021	0.93	0.438-1.98	.859	.07	.231
Depression	1.57	1.29-1.93	<.001	1.51	0.92-2.46	.102	<.001	.869
Lifetime history of infectious condition								
HIV infection	1.21	0.89-1.64	.205	2.03	1.15-3.59	.015	.005	.867
Gonorrhea	1.43	1.08-1.88	.012	0.98	0.55-1.77	.958	.041	.262
Syphilis	1.4	0.97-2.01	.07	1.76	0.92-3.38	.087	.044	.542
UTI	1.3	1.3-1.65	.029	1.07	0.63-1.82	.789	.089	.516
Prostatitis	1.57	1.09-2.24	.014	0.88	0.43-1.80	0.735	.045	.159
Estimated number of lifetime partners								
0-6	Referent			Referent				
7-29	1.37	1.02-1.82	.033	0.76	0.36-1.58	.461	.16	.75
30-100	1.46	1.1-1.93	.009	0.85	0.44-1.67	.644		
>100	1.22	0.91-1.64	.185	0.67	0.34-1.3	.233		
Do you use the following drugs >1 time/y to get high?								
Prescription pills	1.69	1.21-2.36	.002	1.3	0.66-2.59	.451	.007	.507

OR, odds ratio; CI, confidence interval; other abbreviations as in Tables 1 and 2.

Table 4. Age-adjusted bivariate and multivariate predictors associated with seeking medical attention for urinary problems

	Age-Adjusted			Multiple Variable		
Variable	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age in 10-y increments*	1.95	1.76-2.14	<.001	1.74	1.56-1.96	<.001
Coronary artery disease	1.79	1.19-2.71	.006			
Diabetes	1.77	1.23-2.54	.002	1.91	1.27-2.88	.002
Hyperlipidemia	1.48	1.14-1.91	.003			
Depression	1.76	1.41-2.20	<.001	1.58	1.23-2.04	<.001
Lifetime history of infectious condition						
HIV infection	1.02	0.89-1.16	.758			
Chlamydia	1.23	0.89-1.69	.193			
Gonorrhea	1.53	1.19-1.98	.001	1.53	1.12-2.09	.007
Syphilis	0.81	0.56-1.16	.26	0.65	0.42-1.01	.059
Genital herpes	1.49	1.05-2.11	.023			
UTI	3.14	2.48-3.97	<.001	2.09	1.6-2.75	<.001
Prostatitis	6.03	4.29-8.46	<.001	4.59	3.16-6.69	<.001
Estimated number of lifetime partners						
0-6						
7-29	0.94	0.67-1.35	.743			
30-100	1.1	0.79-1.53	.543			
>100	1.15	0.84-1.58	.374			
Do you use the following drugs >1 time/y to get high?						
Methamphetamine	0.74	0.41-1.33	.322			
Cocaine	0.8	0.44-1.47	.5			
Ketamine	1.04	0.42-2.56	.09			
Ecstasy	0.34	0.15-0.75	.008	0.34	0.15-0.77	.009
Prescription pills	1.35	0.92-1.99	.115			

Abbreviations as in Tables 1 and 3.
* Not adjusted for age.

underreported, because it is often clinically silent and/or associated with gonorrhea in men. Additionally, herpes typically produces lesions on the external genitalia and might not involve the urinary tract. This could explain why urinary symptoms were not significantly associated with these entities after multivariate adjustment.

Others have demonstrated a link between infection and self-reported urinary bother.[7,18-21] Research from the Health Professionals Follow-up Study showed that self-report of a history of gonorrhea was associated with a 1.8-fold increased odds of moderate to severe LUTS.[18] In addition, self-report of prostatitis at a young age increased the odds of reporting moderate to severe LUTS by 1.6.

New evidence has suggested that systemic inflammation

could also be a risk factor for subsequent LUTS.[3,22,23] St Sauver et al[3] found that participants with greater levels of C-reactive protein were approximately 2 times more likely to have rapid progression of irritative LUTS and were almost 2.5 times more likely to have a rapid decrease in urinary flow rates.[3] However, men with elevated C-reactive protein levels were not more likely to experience increases in prostate volume independent of LUTS or prostate-specific antigen level.

Men reporting a history of >6 sexual partners might be at a slight increased risk of moderate to severe LUTS. In our study, the relationship was not strong. It was not present in the nested comparison of moderate to severe LUTS. In addition, the overall *P* value for the number of lifetime partners was not significant. A possible explanation for the positive findings includes an increased risk of contracting STIs associated with an increased partner count. Although we controlled for any history of each of the common STIs, the survey did not ascertain the frequency of these infections. Thus, the adjustment might not have fully captured these effects.

To our knowledge, this is the first large-scale examination of the association of recreational drug use with LUTS. Recreational drug use is associated with high-risk sexual behavior, including unprotected intercourse with multiple partners, and thus might also reflect more frequent STIs.[24] In addition, some recreational drugs might have direct effects on bladder function; in particular, ketamine is a known lower urinary tract irritant that has been associated with a painful bladder syndrome of unclear etiology.[9] However, with the exception of abuse of prescription medication, recreational drug use did not appear to increase the risk of LUTS in our sample.

Depression might, in part, explain the link between prescription drug abuse and LUTS. In our study, both were independently associated with LUTS. Individuals being treated for depression might have greater access to prescription medications and also might be more prone to using them as recreational drugs. However, we did not determine what type of prescription pills were used recreationally.

The relationship between depression and LUTS is of interest. Although self-reported LUTS is to some extent subjective and thus potentially influenced by depression, there could also be a physiologic link.[25] In particular, depression has been shown to elevate serum levels of the inflammatory cytokines, including tumor necrosis factor-α, C-reactive protein, and interleukin-6.[26] Inflammatory pathways have also been implicated in the relationships between depression and myocardial infarction, diabetes, and malignancy.[27] Whether inflammatory pathways and/or psychological factors mediate the relationship between LUTS and depression merits additional investigation. Because these conditions are frequently seen together, an improved understanding of this relationship might aid clinicians in the prevention and treatment of both disorders.

The likelihood of seeking medical attention for LUTS was, as might be expected, increased in men with conditions shown in our analysis to have independent associations with LUTS. It is noteworthy that 18% men reported having spoken to their healthcare provider about LUTS, and 33% reported significant LUTS (IPSS >8). Many men are embarrassed by urinary symptoms and/or believe that declines in urinary function are a necessary fact of aging; these men might be unlikely to report bothersome symptoms.[28] It is thus incumbent on providers to make efforts to screen patients with a history of these associated conditions for LUTS. Addressing these issues with patients could help to start a conversation that could lead to effective treatment and substantial enhancement of quality of life.

Several important limitations of the present study warrant mention. First, the cross-sectional nature of the data set makes causal inferences problematic. In addition, nonresponse bias and volunteer bias might diminish the generalizability of our results to the general MSM population. In particular, MSM who do not read or use computers were almost surely underrepresented. Also, the survey was available only in English. In addition, some researchers have raised the concern that Internet survey sampling might overestimate the disease prevalence in younger cohorts.[29] However, we did find positive associations with age and depression, both established risk factors for LUTS. We did not determine whether the reported gonorrhea infection arose from the urethra, rectum, or pharynx. This could have resulted in misclassification bias if a participant reported an affirmative response for gonorrhea exposure that did not involve the urethra.

Future investigations should explore the temporal relationship between infectious exposure and LUTS. The confirmation of associations in a prospective longitudinal data set would be informative.

CONCLUSIONS

Infectious conditions of the urinary tract and depressive symptoms are independent predictors of LUTS in men. Although LUTS are multifactorial, a common unifying explanation for our finding could be the effects of inflammation on the lower urinary tract.

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