

## HIV Status is An Independent Risk Factor for Reporting Lower Urinary Tract Symptoms

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### Abbreviations and Acronyms

HAART = highly active antiretroviral therapy

I-PSS = International Prostate Symptom Score

LUTS = lower urinary tract symptoms

MSM = men who have sex with men

UTI = urinary tract infection

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**Purpose:** HIV/AIDS is a worldwide epidemic. Limited evidence suggests that men infected with HIV/AIDS are at increased risk for lower urinary tract symptoms. We determined whether HIV/AIDS status is an independent risk factor for self-reported bothersome lower urinary tract symptoms in a large contemporary cohort.

**Materials and Methods:** We performed a cross-sectional, Internet based survey of urinary quality of life outcomes in adult HIV infected and HIV uninfected men who have sex with men. The main outcome measure was International Prostate Symptom Score.

**Results:** Of respondents with complete data 1,507 were HIV uninfected (median age 42 years, mean 43) and 323 HIV infected (median age 45 years, mean 45.1). Of the HIV infected respondents 148 were nonAIDS defining HIV infected and 175 were AIDS defining HIV infected. After adjusting for age and other comorbid conditions, nonAIDS defining HIV infected and AIDS defining HIV infected status increased the odds of severe lower urinary tract symptoms by 2.07 (95% CI 1.04–3.79) and 2.49 (95% CI 1.43–4.33), respectively. HIV infected men had a worse total International Prostate Symptom Score for all domains including quality of life compared to HIV uninfected men. Within the population of men with HIV, those with AIDS had worse mean total International Prostate Symptom Score and all individual International Prostate Symptom Score components relative to nonAIDS defining HIV infected men.

**Conclusions:** HIV status is an independent risk factor for bothersome lower urinary tract symptoms. The odds of severe lower urinary tract symptoms are greater in HIV infected men with a history of AIDS.

**Key Words:** urinary tract, signs and symptoms, HIV

HUMAN immunodeficiency virus and AIDS are major public health concerns worldwide. In the United States recent estimates indicate the prevalence of HIV infection is at more than 1.1 million cases with 55,400 new infections annually.<sup>1,2</sup> It is predicted that the prevalence of HIV/AIDS will continue to increase as new cases continue to be diagnosed

and patients with HIV live progressively longer.<sup>2</sup>

With the development of HAART, HIV infection has evolved from a terminal diagnosis to a chronic disease in patients with access to treatment.<sup>3</sup> As HIV infected individuals live longer lives, age associated illnesses are becoming more common sources of morbidity.<sup>3</sup> Indeed there is evidence

that HIV infected individuals are at greater risk for nonAIDS related complications such as heart, renal and bone disease compared with age matched HIV uninfected subjects.<sup>4-6</sup> These data indicate that age related conditions tend to appear earlier in people infected with HIV.

Urinary problems may pose a major detriment to quality of life and have been associated with significant patient morbidity.<sup>7</sup> Urinary problems are common in aging men and are also likely to affect aging men with HIV/AIDS. However, it is unclear whether HIV/AIDS imposes an additional risk of urinary conditions beyond the normal risk associated with age. Evidence exists that HIV infection is associated with LUTS and abnormalities of bladder function as demonstrated by urodynamics.<sup>8,9</sup> However, existing case series are hampered by small numbers of subjects, lack of an HIV uninfected control group and potential lack of applicability to patients in the modern era of HAART.

There is a clear need for data on the prevalence of bothersome urinary tract symptoms in HIV positive individuals in the modern era. In a contemporary cohort of MSM we determined whether HIV infected status is associated with greater odds of self-reported LUTS. We hypothesized that HIV infection is an independent risk factor for the presence and severity of LUTS.

## METHODS

### Study Design and Cohort Description

Institutional review board approval was obtained before initiating the study. We performed a cross-sectional, Internet based survey of urinary quality of life outcomes in MSM. The cohort was restricted to literate, Internet using MSM 30 years old or older. 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 ([www.facebook.com](http://www.facebook.com), Palo Alto, California) aimed at self-identified MSM. Potential subjects were given the option of clicking on a link to the survey which was posted on an Internet based survey site SurveyMonkey® ([www.surveymonkey.com](http://www.surveymonkey.com)). Respondents were informed that they would be asked questions regarding their sexual and urinary wellness, and given the option to decline participation or stop the survey at any time. To maintain privacy no personally identifying information was collected. Responses were collected from January 19 to May 19, 2010.

### Description of Variables

**Outcome variables.** The main outcome variable was the I-PSS, an internationally validated metric of bothersome LUTS.<sup>10,11</sup> The I-PSS is graded on a scale of 0 to 35, and based on 7 questions pertaining to the urinary symptoms of frequency, urgency, nocturia, intermittency, weak stream, straining and incomplete emptying. Validated

categorical severity scales exist which divide LUTS into none/mild (I-PSS 0 to 7), moderate (8 to 19) or severe (20 to 35). An additional eighth I-PSS question regarding quality of life is scored separately (0 to 5). Each component of the I-PSS was examined and compared by self-reported HIV/AIDS status. In addition, components of the I-PSS were grouped to summarize voiding symptoms (intermittency, weak stream, straining, incomplete emptying) and storage symptoms (frequency, urgency, nocturia).<sup>12,13</sup> For multiple logistic regression I-PSS was made binary as (none/mild—0 to 7 vs moderate/severe—8 to 35) or (none/mild/moderate—0 to 19 vs severe—20 to 35). Respondents with missing data were excluded from all subsequent analyses.<sup>11</sup>

**HIV specific questions.** Respondents were asked if they were HIV infected (yes/no/uncertain), if they ever had a CD4 count less than 200 cells per  $\mu\text{l}$  (yes/no/uncertain) and if they ever had an AIDS defining illness (yes/no/uncertain).<sup>14</sup> HIV infected individuals who responded yes to having had an AIDS defining illness or a CD4 count less than 200 cells per  $\mu\text{l}$  met AIDS defining criteria.<sup>14</sup> Individuals who were uncertain regarding their HIV disease specific characteristics were not included in subsequent analyses.

**Exposure variables.** Respondents reported their age, geographic location, size of city and race/ethnicity (African-American, Asian-American, Caucasian, Latin American, Native American, other). Respondents were asked if they had ever been diagnosed or treated for the medical conditions diabetes (yes/no), coronary artery disease (yes/no), hyperlipidemia (yes/no), high blood pressure (yes/no) and depression (yes/no). We determined the history of previous UTI (yes/no), previous prostatitis (yes/no) and sexual transmitted infection status (chlamydia [yes/no], gonorrhea [yes/no]).

### Statistical Analysis

**Descriptive statistics.** Descriptive statistics were used to characterize the study population. Mean I-PSS was compared among HIV uninfected, nonAIDS defining HIV infected and AIDS defining HIV infected groups using the Cuzick nonparametric test for trend across ordered groups.<sup>15</sup> This test is essentially an extension of the Wilcoxon rank sum/Mann-Whitney test to the ordered category case. Groups were stratified by HIV/AIDS status. The distribution of none/mild, moderate and severe I-PSS scores were compared across HIV/AIDS status using a chi-square test of independence.

**Statistical modeling.** Odds ratios with 95% confidence intervals were reported to estimate the association between HIV/AIDS status and demographic factors with I-PSS as a binary generated threshold version of the continuous I-PSS. Multiple logistic regression models were fitted with a priori selected predictor variables based on variables known to influence the prevalence/severity of LUTS. These variables included age in 10-year increments, the presence of comorbidities (diabetes, coronary artery disease, hyperlipidemia, depression), sexually transmitted infection status (gonorrhea, chlamydia), previous UTI and history of prostatitis. Only variables associated with  $p \leq 0.20$  in the initial model were included in the final

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