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BRIEF REPORT

Enhanced Sexually Transmitted Infection Screening for *Mycoplasma genitalium* in Human Immunodeficiency Virus -Infected US Air Force Personnel

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Three-site genital and extragenital screening for *Mycoplasma genitalium* in 102 asymptomatic Air Force members with human immunodeficiency virus (HIV) infection revealed 19 (18.6%) cases of *M. genitalium*, commonly (58%) in rectal samples. Because *M. genitalium* is associated with both HIV acquisition and transmission, these findings suggest that it should be included in routine screening of HIV-infected individuals for sexually transmitted infections.

Keywords. *Mycoplasma genitalium* HIV Air Force.

The rates of curable sexually transmitted infections (STIs)—chlamydia, gonorrhea, and syphilis—have been rising in the United States, especially among individuals aged 15–24 years and men who have sex with men (MSM), with highest reported rates in the southern and northeastern United States [1]. Among MSM, the prevalence of STIs was higher among men with human immunodeficiency virus (HIV) infection than among those who were uninfected [1]. STIs are risk factors for HIV acquisition and transmission. *Neisseria gonorrhoeae* infection, *Trichomonas vaginalis* infection, urethritis, and other STIs have been associated with increased HIV viral load levels in semen, thereby increasing its infectious potential and HIV disease progression [2, 3]. National STI treatment guidelines recommend screening for *Chlamydia trachomatis, N. gonorrhoeae,* and syphilis at the first HIV-related visit and at subsequent annual visits [4].

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Mycoplasma genitalium has been recognized as an etiologic agent of urethritis in men, and data suggest an association with symptomatic proctitis, with patients exihibiting symptoms having a 26% higher load of *M. genitalium* than asymptomatic patients [5]. In an effort to inform and enhance STI screening among HIV-infected US Air Force (USAF) members, screening for *M. genitalium* and *T. vaginalis* was added to the existing STI panel among patients with new or chronic HIV infection.

METHODS

Patient Population

By Air Force regulation, active duty personnel with a diagnosis of HIV infection undergo mandatory medical evaluations every 6–12 months at the USAF HIV Medical Evaluation Unit (MEU; Joint Base San Antonio, Texas) [6]. All HIV-infected service members with a clinical visit from May 16 through 30 September 2016 were included in this analysis.

Urine and extragenital samples from patients were tested for *M. genitalium* and *T. vaginalis*. A nurse practitioner collected an extra rectal and oropharyngeal sample from all patients routinely tested for extragenital *C. trachomatis* and *N. gonorrhoeae* and conducted a brief risk assessment using a standardized 1-page instrument that solicited patient demographics, history of STI diagnosis and symptoms, and sexual contact and condom use since the last visit or in the past year. In addition, an aliquot of urine, provided by patients for urinalysis and *C. trachomatis* and *N. gonorrhoeae* testing, was acquired for *M. genitalium* and *T. vaginalis* screening. Patient testing and data collection were undertaken as a part of an HIV/blood-borne pathogen threat reduction project that was approved by the Army Public Health Center's Public Health Research Board (No. 14–311) as a public health programmatic activity, and by the Walter Reed Army Institute of Research's Institutional Review Board (No. 1861E) as a public health activity/clinical initiative and did not require informed consent.

Laboratory Procedures

All extragenital and urine samples for *M. genitalium* and *T. vaginalis* screening were collected in a urine transport tube, or a unisex swab collection kit (Aptima; Hologic) and shipped to the HIV Diagnostics and Reference Laboratory for analysis. Two nucleic acid amplification test assays conducted on the Panther platform (Hologic) were used for qualitative detection of ribosomal *M. genitalium* and *T. vaginalis* RNA (Aptima *M. genitalium* research-use-only analyte-specific reagents and Aptima *T. vaginalis*, Hologic). Validations of *M. genitalium* and *T. vaginalis* assays for extragenital samples were performed at the HIV Diagnostics and Reference Laboratory by calculating

the percentage of agreement in a comparison study with reference specimens obtained from College of American Pathology–accredited laboratories performing the same assays on the Panther platform. A specimen was considered positive for *M. genitalium* if the assay result was ≥50 000 relative light units (RLU) [7, 8]. Testing for *C. trachomatis* and *N. gonorrhoeae* were conducted at MEU clinical laboratories at routine visits for HIV care.

Data Analysis

Demographic, laboratory, behavioral risk, and clinical characteristics for the patient population were assessed using data collected from risk assessment interview, local and send-out laboratory results, and past STI history extracted from electronic medical records available for service members since their entry into military service or since 2004 when the electronic medical record system was implemented. The risk assessment form solicited information about patient symptoms such as discharge or discharge or itching or burning in the penis, vagina, or anus; pain during sexual intercourse or in the lower abdominal area or the rectum/during bowel movements; or bleeding from the rectum/anus, or ulcers/sores in the genital area. The overall frequency (prevalence) of *M. genitalium*, *T. vaginalis, C. trachomatis,* and *N. gonorrhoeae* was examined, as well as the frequency of *M. genitalium* by demographic and clinical characteristics and 2-tailed confidence intervals at 0.95 probability (95% CIs), obtained using the Clopper-Pearson (exact) method. To compare proportions, prevalence odds ratios (ORs) and tests of significance were estimated using logistic regression. Data were managed and analyzed using Statistical Analysis Software (SAS; version 9.3).

RESULTS

Patient Population

A total of 102 patients received HIV care at the MEU from May 16 through 30 September 2016 and provided 298 urine, rectal, or oropharyngeal samples (Table 1). Almost all patients (99%) were male, with a median age of 31.0 years (interquartile range [IQR], 26.0–36.0 years) and an HIV diagnosis for a median of 3 years (IQR, 1–6 years); a majority (74%) had an undetectable or unquantifiable viral load (<20 copies/mL), and the median CD4 cell count was 748.0 cells/μL (IQR, 573.5–976.5 cells/μL).

Frequency of Sexually Transmitted Infection

Nineteen patients (18.6%; 95% CI, 11.6%–27.6%) tested positive for *M. genitalium* in 21 specimens (11 of 21 positive specimens [52.3%] were rectal specimens, 9 [42.9%] were urine specimens, and 1 [4.8%] was an oropharyngeal specimen); all 19 patients were male. Two patients (2%; 95% CI, 0.2%–6.9%) tested positive for *T. vaginalis,* exclusively in oropharyngeal samples. No one was coinfected with *M. genitalium* and *T. vaginalis*. The prevalence of other STIs was as follows: *C. trachomatis,* 9.8% (95% CI, 5.1%–18.3%; 10 of 96); *N. gonorrhoeae,* 6.9% (3.0%–14.7%; 7 of 94), and *C. trachomatis*/*N. gonorrhoeae,* 15% (8.6%–23.3%; 15 of 101); only 2 patients were coinfected with *M. genitalium* and *C. trachomatis,* and none with *M. genitalium* and *N. gonorrhoeae*.

A higher prevalence of *M. genitalium* was detected among patients who were not coinfected with *C. trachomatis*/*N. gonorrhoeae* (19% vs 13%; OR, 1.48; 95% CI, 0.30–7.24); no patient with *M. genitalium* was coinfected with *N. gonorrhoeae*. Only 2 patients with *M. genitalium* had a history of *C. trachomatis*/*N. gonorrhoeae* infection and azithromycin/ceftriaxone treatment in the prior 3 months. Although no one reported symptoms of an STI at their screening visit, 31% reported a STI symptom during the interval between their last and current screening visit (median, 356.0 days; IQR, 236.0–365.0 days); a greater proportion of *M. genitalium*–positive patients reported a symptom compared with patients positive for *C. trachomatis*/*N. gonorrhoeae* (32% [6 of 19] vs 13% [2 of 15], respectively).

A majority of *M. genitalium*–positive patients (n = 15) had negative urine leukocyte esterase levels; of 3 patients with trace leukocyte esterase levels, only 1 had a total of 5 urinary white blood cells per high-power field. The prevalence of *M. genitalium* was higher among patients with HIV infection diagnosed within the past year than among those whose HIV infection was diagnosed >1 year before *M. genitalium* positivity (25% vs 14%). A majority (95%) of *M. genitalium*–positive patients reported having had sexual contact in the past year with male partners and had higher odds of infection than patients with no partners or female partners in the past year (OR, 8.21; 95% CI 1.04–64.81, $P = .046$) and 58% reported having new partners and had higher odds of infection than those who did not report new partners (OR, 2.43; 95% CI, 0.88–6.70; $P = .09$).

DISCUSSION

This is the first report in the United States to describe the results of incorporating *M. genitalium* as part of standard STI screening for HIV-infected patients. The prevalence of *M. genitalium* was high and substantially higher than the prevalences of *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis* among USAF patients with newly diagnosed or chronic HIV infection who were stationed throughout the United States and receiving HIV specialty care at a central medical facility. *M. genitalium* was detected most commonly in rectal samples, among patients with recently diagnosed HIV infection, as well as patients who reported having male sex partners in the past year.

In men, *M. genitalium* has been associated consistently with both nongonococcal urethritis (NGU) and nonchlamydial NGU, with nonchlamydial NGU prevalence ranging from 10% to 35% and with a higher prevalence among those reporting symptoms [9, 10]. Comparatively, the prevalence among men and women in the general population has ranged from 1% to 3.3% [10]. Similarly, and unlike the findings for *C. trachomatis*

Table 1. Prevalence of *Mycoplasma genitalium* by Patient Characteristics

Characteristic	Patients Positive for *M. genitalium*, No./ Patients Tested No. (Prevalence %; 95% CI)	Prevalence OR (95% CI)	*P* Value
Age, y			
20–29	8/46 (17.4; 7.8–31.4)	1.00	…
30–60	11/56 (19.6; 10.2–32.4)	1.16 (.42–3.18)	.77
Race			
White	10/40 (25.0; 12.7–41.2)	1.96 (.72–5.37)	.19
Black	9/50 (18.0; 8.6–31.4)	1.00	…
Other	0/12 (0.0; 0.0–26.5)		
Education, highest level			
High school	2/12 (16.7; 2.1–48.4)	1.00	…
Some college or more	17/90 (18.9; 11.4–28.5)	1.16 (.23–5.81	.85
Marital status			
Ever married	5/31 (16.1; 5.5–33.7)	1.00	…
Never married	14/71 (19.7; 11.2–30.9)	1.28 (.42–3.92)	.67
Pay grade			
E1–E5	12/62 (19.4; 10.4–31.4)	1.20 (.35–4.17)	.77
E6–E9	4/24 (16.7; 4.7–37.4)	1.00	…
Officer	3/16 (18.7; 4.0–45.6)	1.15 (.22–6.02)	.87
Ethnicity			
Missing	8/59 (13.5; 6.0–25.0)	…	…
Hispanic	5/13 (38.5; 13.9–68.4)	2.50 (.60–10.46	.21
Non-Hispanic	6/30 (20.0; 7.7–38.6)	1.00	…
Sample type[a]			
Urine	9/97 (9.3; 4.3–16.9)	…	…
Rectal swab	11/99 (11.1; 5.7–19.0)	…	…
Pharyngeal swab	1/102 (0.98; 0.0–5.3)	…	…
Coinfection with *Chlamydia trachomatis/Neisseria gonorrhoeae*			
Yes	2/15 (13.3; 1.7–40.5)	1.00	…
No	16/86 (18.6; 11.0–28.4)	1.48 (.30–7.24)	.62
Coinfection with *C. trachomatis*			
Yes	2/10 (20.0; 1.7–40.5)	1.09 (.21–5.65)	.91
No	16/86 (18.6; 10.2–25.8)	1.00	…
Coinfection with *N. gonorrhoeae*			
Yes	0/7 (0.0; 0.0–41.0)	…	
No	17/87 (19.5; 11.8–29.4)	…	
History of past STI			
Yes	12/54 (22.2; 12.0–35.6)	1.67 (.60–4.67)	.32
No	7/48 (14.6; 6.1–27.8)	1.00	…
History by type			
C. trachomatis	6/24 (25.0; 9.8–46.7)	1.67 (.56–5.00)	.36
N. gonorrhoeae	7/27 (25.9; 11.1–46.3)	1.84 (.64–5.30)	.26
Syphilis	1/4 (25.0; 0.6–80.6)	1.48 (.15–15.08)	.74
Other STI	5/16 (31.2; 11.0–58.7)	2.34 (.70–7.78)	.17
Treatment history			
Azithromycin (1 g; oral)/ rocephin (250 mg)/ doxycycline (100 mg)/ cefixime (400 mg)	9/38 (23.7; 11.4–40.2)	1.68 (.61–4.59)	.31
None	10/64 (15.6; 7.8–26.9)	1.00	…
Symptoms[b] of STI before visit			
Yes	6/22 (27.3; 10.7–50.2)	1.93 (.64–5.87)	.24
No	13/80 (16.3; 8.9–26.2)	1.00	…
Urine leukocyte esterase			
Positive	3/7 (42.8; 10.7–26.8)	3.90 (.79–19.23)	.09
Negative	15/93 (16.1; 9.7–24.7)	1.00	…
Time since HIV diagnosis, y			
0–1	11/44 (25.0; 13.2–40.3)	2.08 (.76–5.73)	.15
2–16	8/58 (13.8; 6.1–25.4)	1.00	…
Type of sexual partners in past year			
Men, men and women	18/75 (24.0; 14.9–35.3)	8.21 (1.04–64.81)	.046
None/women only	1/27 (3.7; 0.1–19.0)	1.00	…
New same-sex/male partner in past year			
Yes	11/41 (26.8; 14.2–42.9)	2.43 (.88–6.70)	.09
No	8/61 (13.1; 5.8–24.2)	1.00	…

… denotes that the logistic regression model could not be fit to the data.

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; STI, sexually transmitted infection.

[a]Two patients had positive results in both urine and rectal samples.

[b]Patients were asked if they had had discharge or itching or burning in the penis, vagina, or anus; pain during sexual intercourse or in the lower abdominal area or the rectum/during bowel movements; or bleeding from the rectum/anus, or ulcers/sores in the genital area.

or *N. gonorrhoeae*, HIV-infected men bear a higher burden of *M. genitalium* than uninfected men, which reportedly has been at least 8 times higher in 1 study [11].

Our preliminary findings of an overall *M. genitalium* prevalence of 18.6%, and 24.0% among patients reporting MSM risk in the past year, are consistent with the findings of a study among asymptomatic HIV-infected men in China in which *M. genitalium* prevalence was 25.5% among men reporting same-sex acquisition of HIV and 28.8% among those who acquired HIV heterosexually; in that study only urine specimens were tested for *M. genitalium* [12]. Comparatively, in Guangdong province, China, *M. genitalium* prevalence in urine specimens from largely asymptomatic HIV-uninfected MSM was 7.6% [13]. Various reasons have been cited for the disproportionate burden and include (1) the association of more sexual partners among HIV-infected men with *M. genitalium* infection, (2) a hypothesis that T-cell deficiency in rectal mucosa may contribute to susceptibility to *M. genitalium*, and (3) the association of *M. genitalium* with HIV infection [11, 14].

Among HIV-infected patients, *M. genitalium* was more commonly detected among those whose HIV infection was recently diagnosed. This may be related to the immune status of these patients compared with chronically infected patients receiving antiretroviral therapy, with associated viral load suppression and immune reconstitution. Median CD4 cell counts were slightly lower among patients with HIV infection diagnosed ≤2 years ago than among those with a diagnosis for >2 year (671.5 cells/μL vs 830.5 cells/μL, respectively; $P > .05$).

Alternatively, *M. genitalium* infection may have played a role in acquisition of HIV. In a meta-analysis of cross-sectional studies that examined the association of *M. genitalium* and HIV infection, individuals with *M. genitalium* were found to have an overall 2-fold higher odds of HIV infection, with a stronger association among those in sub-Saharan Africa [15]. This effect also was seen in a longitudinal study of women, recruited from family planning and STI clinics, and sex worker networks; this study found an overall *M. genitalium* prevalence ranging from 6.5% to 14.9%, and women with *M. genitalium* had a ≥2-fold higher risk of HIV acquisition than those without *M. genitalium* [14].

Routine extragenital screening and treatment of identified *C. trachomatis* and *N. gonorrhoeae* infections was initiated in February 2013 as part of routine HIV care among USAF HIV-infected patients. Although this therapeutic practice may have cleared prevalent *M. genitalium* infection in patients with chronic HIV infection and may account for a higher prevalence of *M. genitalium* among patients with recently diagnosed HIV infection who were not routinely screened for *C. trachomatis* and *N. gonorrhoeae*, the low prevalence of *M. genitalium* and *C. trachomatis*/*N. gonorrhoeae* coinfection suggests otherwise. Whether there is a significant relationship between *M. genitalium* infection and factors such as duration of HIV infection and history of *C. trachomatis*/*N. gonorrhoeae* remains to be determined with a larger cohort of patients. In conclusion, preliminary findings from enhanced STI screening of HIV-infected individuals revealed a high prevalence of *M. genitalium* and low prevalence of *T. vaginalis*. Screening for and treatment of *M. genitalium* should therefore be considered in routine HIV care.

Notes

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