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*Sex Transm Infect* 2010 86: 21-24 originally published online October 19, 2009
doi: 10.1136/sti.2009.038190

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The prevalence of urethral and rectal Mycoplasma genitalium and its associations in men who have sex with men attending a genitourinary medicine clinic

S Soni,1 S Alexander,2 N Verlander,2 P Saunders,2 D Richardson,1 M Fisher,1 C Ison2

ABSTRACT

Objectives To determine the prevalence of rectal and urethral Mycoplasma genitalium (MG) in men who have sex with men (MSM) attending a genitourinary medicine clinic and to measure its associations with symptoms, clinical signs, sexual behaviour and concomitant sexually transmitted infections (STI).

Methods MSM attending for STI screening were tested for MG using a real-time PCR assay that targets the MgPa gene. Data were collected on demographics, sexual behaviour, past STI history and clinical symptoms and signs.

Results 849 first-void urine and rectal specimens were collected from 438 MSM. The overall prevalence of MG in MSM was 6.6% with first-void urine positivity of 2.7% and rectal positivity of 4.4%. MG was significantly associated with HIV positivity (OR 7.6, 95% CI 3.2 to 18.7, p < 0.001) in contrast to Chlamydia trachomatis (OR 1.5, 95% CI 0.5 to 4.1, p = 0.4) and Neisseria gonorrhoeae (OR 1.7, 95% CI 0.7 to 3.8, p = 0.194). MG was more prevalent than C. trachomatis (p = 0.15) and N. gonorrhoeae (p = 0.02) in this subgroup of HIV-positive MSM. Urethral infection was associated with dysuria (p < 0.001) but there was no association between rectal infection and anorectal symptoms or signs.

Conclusion Rates of MG are much higher in HIV-positive MSM than HIV-negative MSM at both urethral and rectal sites, and MG is more prevalent in HIV-positive MSM than other bacterial STI. Although the subclinical nature of MG in the rectum questions its significance, the high prevalence seen at this site could be a potential source of onward urethral transmission. Future work should assess the need for appropriate screening and treatment of MG in MSM, particularly those with HIV infection and high-risk sexual behaviour.

This study aimed to determine the prevalence of urethral and rectal MG in MSM attending a genitourinary medicine (GUM) clinic in Brighton, UK, and to measure its associations with symptoms, clinical signs, sexual behaviour and concomitant STI.

METHODS

Participants Participants were HIV-negative and HIV-positive men, self-identifying as gay or bisexual, who attended the GUM clinic in Brighton for STI screening between February and July 2008. The clinic operates an open access system that sees symptomatic and asymptomatic patients, although some HIV-positive men were recruited through an appointment-only designated HIV—STI clinic at the same site. An information leaflet with study details was offered to all patients, and written informed consent was obtained from all participants. Data on the number of men not asked or who declined to participate and their reasons for declining were not captured.

Data collection Data were collected on demographics, sexual behaviour over the previous 3 months and clinical symptoms and signs, by retrospective case-note review. Urethral symptoms and signs included: dysuria, urethral discomfort and visible discharge. Rectal symptoms and signs included: discharge, pain, tenesmus, change in bowel habit, bleeding, mucosal erythema and ulceration. Urethral and rectal smear microscopy was performed only in those subjects reporting urethral and rectal symptoms, respectively, reflecting the clinic policy. NGU was defined as polymorphonuclear leucocyte (PMNL) counts of 5 cells/hpf or more on urethral smear. As rectal smears were not obtained from asymptomatic men, the dataset for rectal PMNL counts was incomplete and therefore was not analysed. Data regarding past history of STI and concurrent STI were retrieved from the clinic’s computerised results reporting system and case notes. For those participants who attended the clinic for screening more than once during the study period, only their first visit was included for analysis.

Specimen collection All nurses and doctors who consulted with patients in clinic were involved in recruitment, clinical examination and the obtaining and labelling of specimens. Proctoscopy was performed on all patients to obtain rectal swab specimens unless the patient declined, and in those cases (<1% of participants) a blind swab was taken. In those
patients who declined to give either a urine or rectal specimen, the unpaired specimen was processed as usual and included for analysis. MG detection was performed on the routine clinical specimens and no additional specimens were required from participants.

**Laboratory testing**

Following routine CT nucleic acid amplification testing in the local laboratory by strand displacement amplification using the BD ProbeTec assay (Becton-Dickinson Diagnostic Systems, Sparks, Maryland, USA) residual first-void urine (FVU) and rectal swab specimens were sent to the Sexually Transmitted Bacteria Reference Laboratory of the Health Protection Agency, Colindale, UK, for MG testing. Samples were stored at 4°C before testing and all specimens were processed within 6 weeks of collection. MG DNA was detected using a previously published real-time PCR method that targets the \( MgpA \) adhesin gene, with a minor modification to the forward primer. \(^7\) \(^8\) All MG-positive specimens were also examined using a confirmatory real-time PCR that targets the \( Mgp219 \) gene. \(^8\) Culture methods were used for the detection of urethral and rectal GC.

**Follow-up**

Patients were not informed if they tested positive for MG unless they had attended or re-presented with symptoms of recurrent urethritis, and in these cases they were treated with 500 mg azithromycin start followed by 250 mg once a day for 4 days.

**Statistical analysis**

Statistical analyses were performed using EpiData Analysis and STATA (V. 10). To investigate significant associations between risk factors and MG-positivity, those factors with \( p \) values of 0.2 or less and elevated odds ratios (OR) from a single variable analysis were considered for inclusion in a multivariable logistic regression model. The multivariable modelling procedure consisted of a backwards stepwise approach, whereby at each step the least significant value with a \( p \) value greater than 0.05 was removed unless it was a substantial confounder (ie, a variable, whose omission leads to a change of 10% or more in the OR of the variables remaining in the model). \( p \) Values for comparing the proportion positive between tests were obtained using the McNemar’s test for paired observations.

**RESULTS**

**Demographics**

Four hundred and thirty-eight MSM were recruited to the study between February and July 2008. Mean age was 36 years (range 16–81 years) and 94.4% of men were of white ethnicity. Ninety out of 438 men (20.5%) were known to be HIV positive. HIV status was recorded for all men, although not all men underwent HIV testing at this visit. The clinic serves a local MSM population of approximately 15,000, and diagnoses between 90 and 110 cases of HIV in MSM annually.

**Clinical specimens**

Four hundred and twelve paired sets of rectal and FVU specimens were obtained and 26 men gave FVU specimens alone. Of the total 412 rectal and 438 urine samples processed, 20 rectal and 11 FVU specimens were \( MgpA \) real-time PCR positive, respectively. When examining these specimens using the confirmatory \( Mgp219 \) PCR assay, 26 (84%) specimens were confirmed as positive; however, due to the reproducibility of the \( MgpA \)-positive results and the extensive validation of the \( MgpA \) gene as an appropriate target for the laboratory detection of MG, all 31 \( MgpA \)-positive results were regarded as true positives.

**Overall prevalence and symptom/sign associations**

The overall prevalence of MG at either site in this patient group was 6.6% (95% CI 4.5% to 9.4%) compared with CT 7.8% (95% CI 5.4% to 10.7%) and GC 5.0% (95% CI 3.2% to 7.5%). The prevalence of urethral MG infection was 2.7% (12/438) and rectal MG infection was 4.4% (19/438) (see table 1).

At the urethral site, urethral symptoms (11/12), particularly dysuria (8/12), were significantly associated with MG positivity (\( p<0.001 \)), and all smears for urethral microscopy in asymptomatic men showed PMNL counts greater than 20 cells/hpf. There was no association between rectal symptoms and rectal MG (\( p=0.5 \)). The dataset for rectal smear microscopy was incomplete and therefore was not analysed. MG was isolated simultaneously at both urethral and rectal sites in two subjects, both of whom were HIV positive but had no other concurrent STI. Urethral and rectal MG were significantly associated with the presence of non-chlamydial NGU (\( p<0.001 \)), but were not associated with concurrent CT or GC infection (\( p>0.999 \) for both pathogens). There was some evidence of an increasing risk of MG positivity with increasing numbers of sexual partners (see table 2).

**Prevalence in HIV-positive men**

When analysed according to HIV status, stark differences in the prevalence of MG were noted between HIV-positive and HIV-negative MSM. MG positivity rates in HIV-positive MSM in FVU and rectal specimens were 7/90 (7.8%) and 12/83 (14.1%), respectively, compared with 5/348 (1.4%) and 6/329 (1.8%) in HIV-negative MSM (see table 3). MG was significantly associated with HIV positivity; a finding not observed with either CT or GC (see table 4). Furthermore, MG was more prevalent than CT (\( p=0.15 \)) and GC (\( p=0.02 \)) in this group but not in MSM overall. The symptom association of dysuria with the presence of urethral MG was significant in this group of MSM (\( p=0.04 \)) although no association between rectal MG and anorectal symptoms was observed.

**DISCUSSION**

**Urethral MG in MSM**

The observed prevalence of urethral MG was low but similar to that of CT and GC. Nearly all men with urethral MG had symptomatic urethritis and smears for urethral microscopy indicated evidence of marked inflammation, supporting findings from previous work. \(^9\) \(^10\)

Interestingly, only nine of 57 (15.8%) non-chlamydial NGU diagnoses were attributable to MG, leaving other sexually transmitted pathogens such as *Ureaplasma urealyticum*, *Trichomonas vaginalis* and herpes simplex virus as possible causes. More commonly in MSM, organisms including coliforms and oropharyngeal flora as well as trauma may account for other cases, although in clinical practice, these would all have been assumed to be bacterial infections and treated with 1 g oral azithromycin in this clinic.
prevalence have detected the organism in healthy individuals, although those studies have had small participant numbers or used culture rather than molecular techniques for detection.5 12 We were unable to compare rectal mucosal inflammation between MG-negative and MG-positive participants, as routine rectal microscopy is not undertaken in asymptomatic individuals at our clinic. Previous work has found no association of PMNL counts with rectal MG infection (D Taylor-Robinson, unpublished data) but further research is warranted to investigate this association. Following rectal inoculation with MG it is possible that MG persists and colonises the rectum, although this may still provide a reservoir for onward urethral infection in those MSM practising insertive anal intercourse.

MG in HIV-positive MSM

HIV-positive MSM are disproportionately affected by STI compared with their HIV-negative counterparts,13 and the difference in prevalences of MG observed between these two groups in our study reflects this. Francis et al10 reported similar observations between HIV-positive and HIV-negative MSM in 2005 with respect to rectal MG, and Martinelli et al14 detected MG in urethral specimens from 52 out of 187 (27.8%) HIV-infected heterosexual male injecting drug users compared with only eight out of 114 healthy volunteers. On the other hand, Hartmann et al15 found no association with HIV status in a study in which only three out of 61 (5%) male and female HIV-infected patients tested positive for MG, although that study did not specify the gender or sexuality of the participants.

Sexual behaviour could account for our findings; HIV-positive men may be more likely to change sexual partners more frequently and may have more unprotected sex with other HIV-infected men. Nevertheless, our study shows that despite a correlation of higher numbers of partners with MG infection, unprotected anal sex (self-reported) was not associated. Alternatively, mucosal T-cell immunodeficiency in the rectum may make HIV-positive men more susceptible to persistent infection with MG.

The interplay between STI and rising incident HIV infection has gained much attention over recent years, with several studies linking the acquisition of HIV to co-infection with bacterial STI and genital ulcer disease.16-18 It follows that an organism such as MG, with the potential to cause mucosal inflammation, may also facilitate HIV transmission. Interestingly, an increased risk of HIV transmission was suggested in one study comparing HIV-concordant and HIV-discordant couples19; HIV-positive concordance was associated with the presence of antibodies to MG but not to syphilis, CT or hepatitis B. Although no studies so far have looked specifically at HIV shedding in seminal fluid in the presence of MG infection, a recent study showed increased HIV-DNA shedding from the cervixes of women infected with MG who had high mycoplasmal DNA loads.20 Sadiq et al21 showed increased HIV-RNA shedding in semen samples from men with gonococcal or chlamydial

Table 2 Non-symptom associations with urethral and/or rectal MG in MSM

<table>
<thead>
<tr>
<th>Variable</th>
<th>Positive</th>
<th>Negative</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>2</td>
<td>27</td>
<td>1.1 (0.4 to 3.4)</td>
<td></td>
</tr>
<tr>
<td>21–30</td>
<td>8</td>
<td>119</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>31–40</td>
<td>9</td>
<td>129</td>
<td>1.04 (0.5 to 2.1)</td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>10</td>
<td>134</td>
<td>1.1 (0.6 to 2.2)</td>
<td></td>
</tr>
<tr>
<td>Total no of sexual partners</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 or 1</td>
<td>6</td>
<td>115</td>
<td>0.8 (0.4 to 1.6)</td>
<td>0.9 (0.4 to 1.7)</td>
</tr>
<tr>
<td>2–5</td>
<td>2</td>
<td>132</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>6–10</td>
<td>6</td>
<td>50</td>
<td>1.7 (0.8 to 3.9)</td>
<td>1.9 (0.8 to 4.2)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>6</td>
<td>50</td>
<td>1.9 (0.9 to 3.8)</td>
<td>2.1 (1.0 to 4.2)</td>
</tr>
<tr>
<td>Previous STI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27</td>
<td>312</td>
<td>3.9 (0.96 to 34.7)</td>
<td>3.9</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>91</td>
<td>p = 0.06</td>
<td></td>
</tr>
<tr>
<td>UAI in past 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>18</td>
<td>192</td>
<td>1.8 (0.8 to 4.3)</td>
<td>1.8</td>
</tr>
<tr>
<td>No</td>
<td>11</td>
<td>210</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>GC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>21</td>
<td>28</td>
<td>0.7 (0.02 to 4.4)</td>
<td>0.7</td>
</tr>
<tr>
<td>Negative</td>
<td>28</td>
<td>387</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>2</td>
<td>32</td>
<td>0.9 (0.1 to 3.8)</td>
<td>0.9</td>
</tr>
<tr>
<td>Negative</td>
<td>27</td>
<td>377</td>
<td>p = 1.00*</td>
<td></td>
</tr>
<tr>
<td>HIV status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>18</td>
<td>72</td>
<td>7.6 (3.2 to 18.7)</td>
<td>8.6 (5.1 to 14.6)</td>
</tr>
<tr>
<td>Negative</td>
<td>11</td>
<td>337</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Non-chlamydial, NGU</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>11</td>
<td>46</td>
<td>4.8 (1.9 to 11.5)</td>
<td>4.3 (2.5 to 7.6)</td>
</tr>
<tr>
<td>Negative</td>
<td>18</td>
<td>362</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s exact test.
† Wald test p value.
‡ Obtained from model selection procedure described in the text.
CT, C trachomatis; GC, N gonorrhoeae; MG, M genitalium; MSM, men who have sex with men; NGU, non-gonococcal urethritis; OR, odds ratio; STI, sexually transmitted infection; UAI, unprotected anal intercourse.

Table 3 Prevalence estimates and 95% CI for MG infection

<table>
<thead>
<tr>
<th>HIV status</th>
<th>Urethral</th>
<th>Rectal</th>
<th>Urethral and/or rectal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>95% CI</td>
<td>Estimate</td>
</tr>
<tr>
<td>HIV-positive</td>
<td>7.8%</td>
<td>3.2 to</td>
<td>14.1%</td>
</tr>
<tr>
<td>(7/90)</td>
<td>(12/83)</td>
<td>23.4</td>
<td>(19/173)</td>
</tr>
<tr>
<td>HIV-negative</td>
<td>1.4%</td>
<td>0.5 to</td>
<td>2.1%</td>
</tr>
<tr>
<td>(5/348)</td>
<td>(7/329)</td>
<td>4.0</td>
<td>(12/667)</td>
</tr>
</tbody>
</table>

MG, M genitalium.

Table 4 Association of GC, CT and MG infection with HIV status

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIV-positive</th>
<th>HIV-negative</th>
<th>OR 95% CI</th>
<th>χ² p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GC Positive</td>
<td>7</td>
<td>16</td>
<td>1.5 0.5 to 4.1</td>
<td>0.4*</td>
</tr>
<tr>
<td>Negative 83</td>
<td>332</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT Positive 12</td>
<td>27</td>
<td>1.7 0.7 to 3.8</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>Negative 78</td>
<td>321</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MG Positive 19</td>
<td>12</td>
<td>7.6 3.2 to 18.7</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Negative 71</td>
<td>336</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s exact test.
CT, C trachomatis; GC, N gonorrhoeae; MG, M genitalium; OR, odds ratio.
mg is highly prevalent in HIV-positive MSM and is more prevalent than other bacterial STI in this group.

- Although subclinical in the rectum, the high prevalence seen at this site provides a reservoir for onward urethral infection.
- MG causes an inflammatory urethritis and may be facilitating HIV transmission.
- Further work in more widespread MSM populations should help inform our MG testing policies of high-risk individuals.

urethritis, which fell following treatment of the urethritis. Further work is needed in this area, with specific regard to MG, to investigate its role in HIV transmission.

Treatment of MG urethritis with doxycycline has low clearance rates,22 and whereas earlier studies reported high success there is.

Men presenting with ongoing urethral symptoms. Clinicians should remain alert to the possibility of MG as a cause, potential for undiagnosed and persistent MG infection exists.24 Given that both these antibiotics are recommended for the treatment of NGU and non-specific proctitis in MSM, the potential for undiagnosed and persistent MG infection exists. Clinicians should remain alert to the possibility of MG as a cause of persistent urethritis and consider testing specifically for MG in men presenting with ongoing urethral symptoms.

There are some limitations of this study that should be considered. First, data were collected retrospectively, thereby relying on thorough history taking and careful case-note documentation. Self-reported sexual behaviour is subject to inaccuracies in recall and only behaviour in the preceding 3-month period was collected. Second, the actual numbers of men who declined to participate or were not offered the chance to participate in the study were not recorded. Although we acknowledge this as a potential source of bias, we observed that most men attending the clinic were offered the study and very few declined to participate. Third, the study was conducted from a single centre, limiting the sample population to Brighton; more studies are needed in other UK cities to determine whether or not this population is representative.

In this study, we have shown high rates of MG infection among HIV-positive MSM at both urethral and rectal sites, and that MG is more prevalent in HIV-positive MSM than other bacterial STI. While national guidelines advise screening for urethral and rectal GC and urethral CT in all MSM attending GUM clinics,23 there is currently insufficient evidence to support similar recommendations for MG in this group. The introduction of a commercial assay for MG detection should allow further work in large and more widespread MSM populations to clarify the role of MG in the rectum and to inform whether screening for and empirical treatment of MG should be considered in MSM, particularly in those who are HIV infected and report high-risk sexual behaviour.

Acknowledgements The authors would like to thank BASHH and the Health Protection Agency for providing the fellowship that has enabled this research. Dr John White and Professor David Taylor-Robinson are acknowledged for concept of idea and their helpful comments towards the manuscript. The authors also wish to acknowledge Nicky Perry, research manager and all clinic and laboratory staff at the Royal Sussex County Hospital and Sexually Transmitted Bacteria Reference Laboratory.

Contributors SS: principle investigator. Design of study, data collection, primary analysis, author of first and final draft of paper: SA: design of study, laboratory supervisor, amendments to paper: NV: statistical analysis, amendments to paper: PS: assistant laboratory supervisor: DR: design of study, amendments to paper: MF: design of study, amendments to paper: CI.

Epidemiology

Key messages

- MG is highly prevalent in HIV-positive MSM and is more prevalent than other bacterial STI in this group.
- Although subclinical in the rectum, the high prevalence seen at this site provides a reservoir for onward urethral infection.
- MG causes an inflammatory urethritis and may be facilitating HIV transmission.
- Further work in more widespread MSM populations should help inform our MG testing policies of high-risk individuals.

Funding This study was undertaken as a BASHH/HPA fellowship.

Competing interests None.

Ethics approval This study was approved by Brighton East Research Ethics Committee.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES