Original research

The clinical indications for testing women for *Mycoplasma genitalium*

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ABSTRACT

Background While the contribution of *Mycoplasma genitalium* (MG) to symptoms in men is well described, less is known about its association with common genital symptoms in women. We aimed to determine the prevalence of MG and macrolide resistance, and its association with common genital symptoms in women attending a sexual health service, to inform indications for testing and clinical practice.

Methods We undertook a cross-sectional study of symptomatic and asymptomatic women attending Melbourne Sexual Health Centre (MSHC), between April 2017 and April 2019. Women were tested for MG and macrolide resistance, *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, bacterial vaginosis and vulvovaginal candidiasis. Women completed a questionnaire on symptoms, and symptomatic women underwent examination. The prevalence of MG (and macrolide resistance) and other genital infections was calculated with 95% CIs, and associations between these outcomes and specific genital symptoms were examined using logistic regression.

Results Of 1318 women, 83 (6%, 95% CI: 5% to 8%) had MG, of which 39 (48%, 95% CI: 36% to 59%) had macrolide-resistant MG; 103 (8%, 95% CI: 6% to 9%) women had CT. MG prevalence was similar in asymptomatic (10 of 195; 5%) and symptomatic (73 of 1108; 7%) women, p=0.506. MG was associated with mucopurulent cervicitis on examination (adjusted OR=4.38, 95% CI: 1.69 to 11.33, p=0.002), but was not associated with other specific genital symptoms or signs.

Conclusions MG was as common as CT among women attending MSHC. MG was not associated with genital symptoms, but like CT, was significantly associated with cervicitis. These data provide evidence that routine testing for MG in women with common genital symptoms is not indicated. The presence of macrolide resistance in 48% of women supports use of resistance-guided therapy.

INTRODUCTION

Mycoplasma genitalium (MG) is a recognised cause of urethritis in men,[1] but in women an association with syndromes and sequelae has been less consistently observed. However, a large cross-sectional study of 5000 women attending an emergency gynaecological hospital by Bjartling *et al* found MG was significantly associated with both cervicitis (OR 3.8, 95% CI: 2.1 to 7.0) and pelvic inflammatory disease (PID, OR 9.0, 95% CI: 1.6 to 49.9),[2] and a meta-analysis in 2015 by Lis *et al* reported MG to be associated with an increased odds of both cervicitis and PID in women.[3] A recent synthesis of cohort study data indicated 5% of MG infections progress to PID.[4] Based on these findings, UK and Australian guidelines recommend testing for MG in women with cervicitis and PID.[5 6]

While there is a substantial body of evidence supporting the association between MG and STI syndromes, less data exist to inform MG testing practices in women presenting with common genitourinary symptoms. While Bjartling *et al* assessed a range of symptoms, they found MG to be associated with the symptom of post-coital bleeding only (OR 2.1, 95% CI: 1.2 to 3.7).[2] Other research has reported associations between MG and abnormal vaginal discharge[7 8] and dysuria,[7] but some studies conducted among STI clinic attendees in Sweden and America found no association between MG and genital symptoms in women.[9 10]

Women are disproportionately affected by the adverse consequences of STIs,[11 12] however STI testing is associated with significant costs to services, and so it is important to have robust evidence that underpins recommendations for MG testing in women. We undertook a cross-sectional study of symptomatic and asymptomatic women attending Melbourne Sexual Health Centre (MSHC) to determine the prevalence of MG and macrolide-resistant MG in women, the prevalence of coinfections, and the association of MG with common genital symptoms and signs, to inform indications for testing and clinical practice.

METHODS

This cross-sectional study was conducted among women attending MSHC, the largest public sexual health service in Victoria, Australia, between April 2017 and April 2019, with >50 000 consults per annum. MSHC provides a walk-in service, where on arrival clients are triaged as asymptomatic or symptomatic; if triaged as asymptomatic they are screened for STIs by a nurse, and if symptomatic they are seen by a clinician. In this study, women

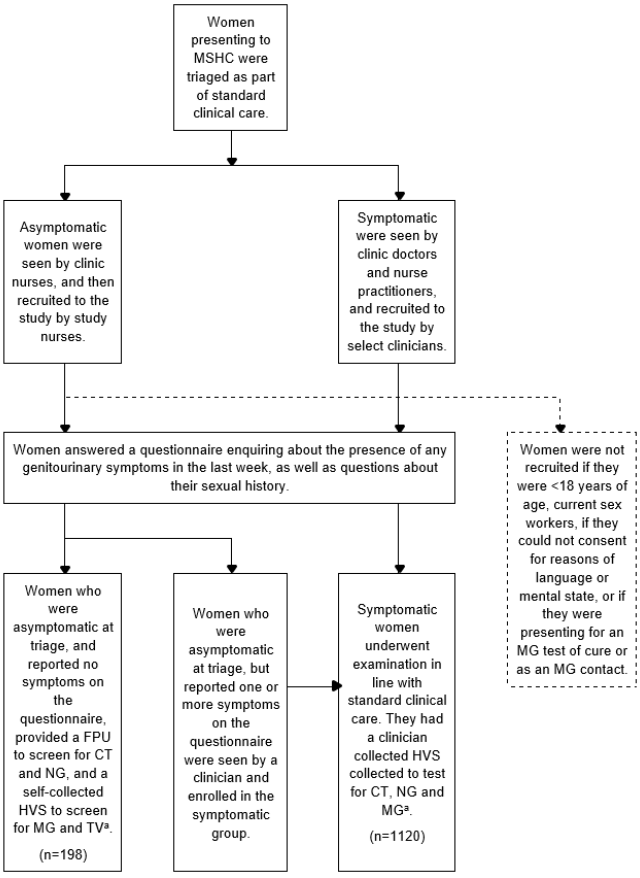

Figure 1 Flow diagram detailing the enrolment of participants in the study. [a]Bacterial vaginosis and vulvovaginal candidiasis were also investigated. Vaginal smears for Gram stain and wet preparation were prepared for all participants, and vaginal pH was recorded for all participants. CT, *Chlamydia trachomatis*; FPU, first pass urine; HVS, high vaginal swab; MG, *Mycoplasma genitalium*; MSHC, Melbourne Sexual Health Centre; NG, *Neisseria gonorrhoeae*; TV, *Trichomonas vaginalis.*

identified as asymptomatic at triage were screened for eligibility and recruited by a research nurse, and women triaged as symptomatic were screened for eligibility and recruited by select clinicians who were experienced in study recruitment. Women were eligible if they were sexually active, aged ≥18 years and were presenting with common genitourinary symptoms or presenting for routine STI screening. Women were ineligible if they were unable to consent to the study for reasons of language or mental state; if they were current sex workers; if they were presenting for MG test of cure or as an MG contact; or if they were aged under 18 years (figure 1). Women with moderate or severe PID were not recruited in order to expedite their clinical care.

All participants completed a questionnaire which captured whether they had experienced any of the following genital symptoms in the week prior to presentation: abdominal or pelvic pain, dyspareunia, abnormal vaginal discharge, vaginal odour, postcoital bleeding, intermenstrual bleeding, vaginal itch, dysuria, urinary frequency or urgency, and/or fevers or sweats. Participants also answered questions about prior sexual practices.

Asymptomatic participants were not examined but provided a first pass urine (FPU) for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) screening (in keeping with standard clinical practice), and were given instructions to self-collect a vaginal swab for MG screening (figure 1). Symptomatic participants had a clinician collected cervicovaginal swab for MG, and a clinician collected cervicovaginal swab for CT and NG testing (figure 1). Clinicians completed a standardised checklist recording the presence or absence of each of the following clinical signs: abnormal vaginal discharge, abnormal vaginal odour, vulval redness or vulvitis, cervicitis (defined as mucopurulent cervicitis and/or cervical friability), cervical contact bleeding, and cervical or adnexal motion tenderness. Speculum and bimanual examination was performed in keeping with clinical practice at MSHC. Speculum examination is undertaken in women with vaginal discharge, abdominal and/or pelvic pain, whereas bimanual examination is generally restricted to women with abdominal or pelvic pain and those found to have cervicitis on examination (n=754). Asymptomatic women were not examined, also in keeping with clinic protocol.

All participants had vaginal pH recorded, and vaginal smear prepared for Gram stain to assess for bacterial vaginosis (BV) and vulvovaginal candidiasis (VVC). Wet preparation and culture for *Trichomonas vaginalis* (TV) was performed in women with vaginal discharge and/or itch only, as TV is extremely uncommon at MSHC and present in <1% of attendees.[13]

Detection of MG and macrolide-resistance mutations was performed using the ResistancePlus MG test (SpeeDx, Sydney, Australia).[14 15] Samples were tested for CT and NG by transcription-mediated amplification (Aptima Combo 2, Hologic, Massachusetts, USA). TV was detected using a wet preparation that was examined within 5 min of collection at the onsite MSHC laboratory, and culture. BV was diagnosed using both Amsel criteria and Nugent score (NS; BV defined as ≥3 Amsel criteria and NS=4–10). VVC was diagnosed based on the presence of typical clinical features (thick white or curdy candidal discharge and/or vulvovaginal erythema) and/or presence of visible pseudohyphae and/or budding yeasts on microscopy. Vaginal polymorphonuclear cell counts (PMNL) on Gram stain were recorded as either <5 or ≥5 vaginal PMNL/high power field (hpf).

Sample size and statistical methods

Sample size calculations were based on a study population of 1350 women, in which we assumed MG positivity would be 8% among 250 women with a specific symptom, and 4% among 1100 women without that specific symptom (estimates based on a prior Australian study[8]); this would yield 80% power (α=0.05) to detect an OR of ≥2.3 for the symptom of interest. The proportion of women with each infection (MG, CT, NG, TV, BV and VVC) and with genital coinfections was determined with 95% binomial CIs. First, we compared demographic and behavioural characteristics between asymptomatic and symptomatic women using logistic regression. Next, we compared the proportion of women with each individual infection by asymptomatic or symptomatic status using logistic regression, adjusting for number of male sexual partners (MSPs) in the prior 12 months, as a significant risk factor for STI acquisition. Logistic regression was then used to investigate the association between MG and other genital infections, adjusting for MSPs in the prior 12 months.

Using logistic regression, we determined the association between demographic and behavioural factors, and clinical symptoms and signs and (1) MG and (2) CT, compared with women without MG or CT. As MG and CT have overlapping genital symptoms and signs, and can be associated with cervicitis and/or PID, women with CT were excluded from analyses of MG, and women with MG were excluded from analyses of CT. All analyses were then adjusted for number of MSPs, VVC, NG and BV

so that we could determine the independent association of MG (or CT) with each characteristic. Analyses were not adjusted for TV, as TV was not assessed in all women. Additionally, we did not adjust for BV in associations between MG/CT and individual Amsel criteria (ie, vaginal discharge, abnormal vaginal odour and vaginal pH) as these are used in the diagnosis of BV (ie, correlated with BV). We also tested for interaction terms between MG (and CT) and genital infections, and conducted stratified analyses where appropriate. Variables were considered significant if the p value was <0.05. Statistical analyses were performed using Stata/IC (V.14, StataCorp, College Station, USA).

RESULTS

From April 2017 to April 2019, 16 956 individual women attended MSHC with a total of 36 891 consultations. Of these, 16.3% were sex workers and ineligible. As a public sexual health clinic, MSHC has a high proportion of non-English-speaking clients who were not approached for the study, with the exact number unknown. A total of 1355 women were recruited to the study by select clinicians and a research nurse. Thirty-seven women were excluded, 25 women disclosed post-recruitment that they were sex workers and 12 women were inadvertently recruited twice; 1318 women were included in final analyses.

Of the 1318 women analysed, 1120 were symptomatic (reported at least one genital symptom in the week prior to presentation) and 198 were asymptomatic (reported no genital symptoms in the prior week). The most frequently reported symptoms were abnormal vaginal discharge (34%), abnormal vaginal odour (24%) and vulvovaginal itch (21%). Dyspareunia (10%), post-coital bleeding (8%) and fever (3%) were less frequently reported. Compared with asymptomatic women, symptomatic women were more likely to report inconsistent condom use in the prior 12 months (OR=1.79, 95% CI: 1.07 to 3.00, p=0.026) and an STI in the past 6 months (OR=2.42, 95% CI: 1.35 to 4.36, p=0.003; table 1).

Prevalence of MG and other genital infections

Of the 1318 women, 15 (1%) had an invalid test for MG. Of 1303 remaining women, 83 (6%, 95% CI: 5% to 8%) had MG detected, with no significant difference in the proportion with MG between completely asymptomatic women (5%, 95% CI: 2% to 9%) and women with one or more recent symptoms (7%, 95% CI: 5% to 8%, table 1). Macrolide resistance was detected in 39 of 82 MG-positive samples (48%, 95% CI: 36% to 59%), and was not assessable in one sample. There was no difference in the proportion with macrolide resistance between asymptomatic women and symptomatic women (40% vs 49%, p=0.741). One hundred women had CT (8%, 95% CI: 6% to 9%), 12 had NG (1%, 95% CI: 0% to 2%), 379 had BV (30%, 95% CI: 28% to 33%) and 314 had VVC (24%, 95% CI: 22% to 27%). Only 6 of 684 participants tested by culture and wet preparation were positive for TV. BV and VVC were the only infections detected more frequently in symptomatic women compared with asymptomatic women (33% vs 17%, p<0.001, and 26% vs 15%, p=0.001, respectively), which is a reflection of how common the symptoms of vaginal discharge, odour and itch were in female STI clinic attendees. All women with NG were symptomatic.

MG and genital coinfections

Of the 83 women with MG, 8 (10%, 95% CI: 4% to 18%) were coinfected with CT, 1 (1%, 95% CI: 0% to 7%) with NG, 29 (36%, 95% CI: 26% to 48%) had concurrent BV, 21 (26%, 95% CI: 17% to 36%) had concurrent VVC,and 1 (1.2%, 95% CI: 0% to 7%) was coinfected with TV. MG was not significantly associated with presence or absence of any genital infection (online supplemental file 1online supplemental table 1).

Associations between demographic and behavioural characteristics and MG

We investigated the association between demographic and behavioural characteristics and MG infection compared with women without MG. MG was not associated with specific demographic or behavioural characteristics following adjustment for number of MSPs and genital coinfections (table 2). Similarly, CT positivity was not associated with any demographic or behavioural characteristics in adjusted analyses (online supplemental file 1online supplemental table 2).

Association between self-reported symptoms and MG

We investigated the association between self-reported symptoms in the week prior to recruitment and MG. MG was negatively associated with self-reported vaginal odour (adjusted OR (AOR)=0.48, 95% CI: 0.24 to 0.96, p=0.037), but was not associated with any other symptoms (table 2). In contrast, CT was associated with self-reported vaginal discharge (AOR=2.12, 95% CI: 1.32 to 3.42, p=0.002; online supplemental file 1). Additionally, in stratified analyses, CT was associated with dyspareunia in women with VVC (AOR=8.66, 95% CI: 1.90 to 39.54, p=0.005), but this association was not found in women without VVC. Importantly, very few women were coinfected with CT and VVC (n=11), which may have influenced this finding. There were no significant differences in symptoms between women with MG and CT, although the small number of women with each infection is likely to have impacted this comparison (online supplemental file 1).

Association between signs on examination and MG

We next investigated the association between clinical signs and MG. We tested for interaction terms between MG and genital infections, and the only significant interaction was between MG and BV for cervicitis (p=0.020, table 3). To account for potential confounding by BV on the relationship between MG and cervicitis, data were then stratified by BV status, and the association between MG and cervicitis was investigated within each stratum. In women without BV, MG was strongly associated with cervicitis (AOR=4.38, 95% CI: 1.69 to 11.33, p=0.002, table 3), but this association was not found in women with BV. MG was not associated with any other clinical signs, including vaginal PMNL count; although all women with MG cervicitis had ≥5 PMNL/hpf detected.

In order to determine if there were key differences in the clinical presentation between CT and MG in our clinic population, we then assessed the association between clinical signs and CT. CT was associated with vaginal discharge (AOR=2.13, 95% CI: 1.19 to 3.82, p=0.011), mucopurulent cervicitis (AOR=2.85, 95% CI: 1.49 to 5.44, p=0.002) and ≥5 PMNL/hpf on microscopy of vaginal secretions (AOR=2.50, 95% CI: 1.49 to 4.20, p=0.001; online supplemental file 1). There were no significant differences in clinical signs between women with MG and CT (online supplemental file 1).

DISCUSSION

MG was detected in 6% of women attending a large public sexual health centre in Melbourne, Australia. MG was not associated with common genital symptoms, but was significantly associated with cervicitis.[5 6] Specific symptoms were not helpful

Table 1 Demographic and epidemiological characteristics and prevalence of common genital infections in asymptomatic and symptomatic women*

	Asymptomatic women n=198 median (IQR) or n (%, 95% CI)	Symptomatic women† n=1120 median (IQR) or n (%, 95% CI)	OR (95% CI)	P value‡
Median age	25 (22–29)	26 (23–29)	1.01 (0.98 to 1.04)	0.389
Median number of male partners in the past 12 months	4 (2–6)	4 (2–6)	1.01 (0.97 to 1.04)	0.638
Condom use in the past 12 months				
Always	21 (11, 7 to 16)	69 (6, 5 to 8)	1	
Not always	175 (89, 84 to 93)	1032 (94, 92 to 95)	1.79 (1.07 to 3.00)	**0.026**
STI in the past 6 months§				
No	184 (93, 89 to 96)	934 (85, 83 to 87)	1	
Yes	13 (7, 4 to 11)	160 (15, 13 to 17)	2.42 (1.35 to 4.36)	**0.003**
	Asymptomatic women N=198 n (%, 95% CI)	**Symptomatic women† N=1120 n (%, 95% CI)**	**Adjusted OR¶ (95% CI)**	**P value‡**
Mycoplasma genitalium				
Negative	185 (95, 91 to 98)	1035 (93, 92 to 95)	1	
Positive	10 (5, 2 to 9)	73 (7, 5 to 8)	1.26 (0.64 to 2.49)	0.506
Unassessable	3	12		
Chlamydia trachomatis				
Negative	183 (92, 88 to 96)	1025 (92, 91 to 94)	1	
Positive	15 (8, 4 to 12)	85 (8, 6 to 9)	0.99 (0.56 to 1.76)	0.977
Unassessable/not tested	0	10		
Neisseria gonorrhoeae				
Negative	198 (100, 98 to 100)**	1098 (99, 99 to 100)		
Positive	0 (0, 0 to 2)**	12 (1, 1 to 2)	Omitted	0.232††
Unassessable/not tested	0	10		
Bacterial vaginosis‡‡				
Negative	165 (83, 77 to 88)	713 (67, 64 to 70)	1	
Positive	33 (17, 12 to 23)	346 (33, 30 to 36)	2.4 (1.61 to 3.57)	**<0.001**
Not assessed	0	61		
Vulvovaginal candidiasis§§				
Negative	164 (85, 80 to 90)	818 (74, 71 to 77)	1	
Positive	28 (15, 10 to 20)	286 (26, 23 to 29)	2.04 (1.34 to 3.12)	**0.001**
Not assessed	6	16		

Continued

Table 1 Continued

	Asymptomatic women n=198 median (IQR) or n (%, 95% CI)	Symptomatic women† n=1120 median (IQR) or n (%, 95% CI)	OR (95% CI)	P value‡

Bold values are statistically significant.
*_Trichomonas vaginalis_ is extremely uncommon at MSHC and present in <1% of attendees. Of the 684 participants who were tested by culture and wet prep, only 6 were positive for _T. vaginalis_.
†Women were classified as 'symptomatic' if they reported the presence of one or more of the following genital symptoms: abdominal pain, dyspareunia, vaginal discharge, abnormal odour, post-coital bleeding, intermenstrual spotting, vaginal itch, dysuria, urinary frequency, fevers.
‡P value calculated using logistic regression and bold indicates significant findings.
§STI in the past 6 months referred to bacterial STI only, however some women may have misinterpreted this question and answered with regard to warts or other non-bacterial STIs.
¶Adjusted for number of male sexual partners in the past 12 months (continuous variable).
**One-sided, 97.5% CI.
††P value calculated using Fisher's exact test, not adjusted for partner number.
‡‡Bacterial vaginosis diagnosis was defined as Nugent score=4–10 and 3–4 Amsel criteria OR Nugent score=4–10 and presence of clue cells if client was either asymptomatic (ie, Amsel criteria not assessed) or other factors (ie, blood/menses) prevented clinical examination of Amsel criteria.
§§Vulvovaginal candidiasis was diagnosed microscopically or clinically by a doctor.
MSHC, Melbourne Sexual Health Centre; n, number.

in informing additional indications for MG testing at our service. Importantly, one in two MG infections in women was macrolide resistant, highlighting the value of resistance testing and individualising therapy where possible.

MG was common in women attending our STI service (6%; 95% CI: 5% to 8%) compared with a previous study of 1116 women attending Australian primary healthcare services (2%; 95% CI: 1% to 3%),[8] which aligns with a recent meta-analysis reporting MG prevalence in the general population to be 1.3% (95% CI: 1.0% to 1.8%) in developed nations.[16] In our study, CT was detected in 8% (95% CI: 6% to 9%) of women, compared with 5% (95% CI: 3% to 7%) of women attending primary care facilities in the previous Australian study.[8] The high prevalence of MG and CT in our study compared with the general population highlights the high-risk nature of our clinic population.[17]

Our study aligns with that of Bjartling *et al* in that women with MG had fourfold increased odds of cervicitis after adjusting for genital coinfections.[2] Both estimates are higher, but in the range of two prior meta-analyses, which found that women with MG had twofold increased odds of cervicitis (OR=1.7; 95% CI: 1.35 to 2.04[3] and OR=2.2; 95% CI: 1.6 to 2.9[18]). This association was only found in women without BV, potentially because the pathogenesis of cervicitis in women coinfected with BV and MG may be influenced/confounded by the presence of BV-associated organisms; an association that has previously been observed.[19] However, lack of consistency in the criteria used for the diagnosis of cervicitis internationally is likely to have impacted on the comparability of estimates between countries.[20 21] The Centers for Disease Control and Prevention uses two major diagnostic signs to diagnose cervicitis: (1) mucopurulent endocervical exudate on examination, and/or (2) inducible endocervical bleeding when swabbing the cervical os.[22] While studies of asymptomatic cervicitis often rely on the presence of high vaginal or cervical PMNLs only, yet the criteria of increased PMNLs have not been standardised and are known to be less reliable.[21 22] Our study did not find MG to be associated with elevated vaginal PMNL count, although all women with MG cervicitis had an elevated PMNL count in vaginal secretions. A review of MG and cervicitis determined that a high vaginal PMNL count (>30 PMNL/hpf) was not a specific sign of MG cervicitis and may fail to detect less severe inflammation.[20]

Our study did not find MG to be positively associated with any symptoms in women which was similar to Bjartling *et al* who only found MG to be associated with post-coital bleeding.[2] In both studies, chlamydia was commonly associated with genital symptoms and signs in women including vaginal discharge, mucopurulent cervicitis and elevated vaginal PMNL count, in line with other research.[2 23 24] Although associated with symptoms and signs in our study, like MG, CT was as common in women and without genital symptoms. CT is known to be predominately asymptomatic in women, despite its established association with a range of symptoms and clinical syndromes.[24] We did not find significant differences in symptoms or signs between women with MG or CT, although this is likely to have been due to limited numbers for comparison. Interestingly, Falk *et al* also found no difference in presentation between women with MG and CT among 461 women attending an STI clinic.[25] In contrast, Bjartling *et al* reported that vaginal discharge, abdominal pain and dysuria were significantly more common among women with CT compared with MG.[2] These differences may have been due to the fact that our and Falk *et al*'s studies involved STI clinic attendees, whereas Bjartling *et al* included women presenting to an emergency service who are likely to have more acute symptoms. Overall, these data suggest that CT

Table 2 Associations between *Mycoplasma genitalium* (MG) and demographics, past sexual practices and self-reported symptoms in the prior week*

	MG negative n=1128 median (IQR) or n (%, 95% CI)	MG positive n=75 median (IQR) or n (%, 95% CI)	Adjusted OR (95% CI)†	P value‡
Median age	26 (23–29)	26 (23–29)	0.96 (0.92 to 1.01)	0.136
Median number of male partners in the past 12 months	4 (2–6)	4 (3–7)	1.03 (1.00 to 1.07)	0.053
Condom use in the past 12 months§				
Always	82 (7, 6 to 9)	4 (5, 1 to 13)	1	
Not always	1027 (93, 91 to 94)	70 (95, 87 to 99)	1.17 (0.41 to 3.31)	0.772
STI in the past 6 months§¶				
No	959 (87, 85 to 89)	62 (85, 75 to 92)	1	
Yes	147 (13, 11 to 15)	11 (15, 8 to 25)	1.1 (0.55 to 2.22)	0.78
Self-reported symptoms (in the prior week to recruitment)				
Abdominal pain				
No	962 (86, 83 to 88)	64 (86, 77 to 93)	1	
Yes	161 (14, 12 to 17)	10 (14, 7 to 23)	1.08 (0.54 to 2.17)	0.827
Missing	5	1		
Dyspareunia				
No	1010 (90, 89 to 92)	66 (90, 81 to 96)	1	
Yes	107 (10, 8 to 11)	7 (10, 4 to 19)	1.16 (0.51 to 2.61)	0.724
Missing	11	2		
Vaginal discharge				
No	752 (67, 64 to 70)	48 (65, 53 to 76)	1	
Yes	367 (33, 30 to 36)	26 (35, 24 to 47)	0.9 (0.53 to 1.54)	0.703
Missing	9	1		
Abnormal vaginal odour**				
No	850 (76, 73 to 79)	60 (81, 70 to 89)	1	
Yes	268 (24, 21 to 27)	14 (19, 11 to 30)	0.48 (0.24 to 0.96)	**0.037**
Missing	10	1		
Vaginal itch				
No	888 (79, 77 to 81)	55 (74, 63 to 84)	1	
Yes	234 (21, 19 to 23)	19 (26, 16 to 37)	1.16 (0.62 to 2.14)	0.644
Missing	6	1		
Post-coital bleeding				
No	1025 (92, 90 to 93)	64 (89, 79 to 95)	1	
Yes	92 (8, 7 to 10)	8 (11, 5 to 21)	1.32 (0.58 to 2.99)	0.511
Missing	11	3		
Intermenstrual bleeding				
No	1009 (90, 88 to 92)	65 (88, 78 to 94)	1	
Yes	110 (10, 8 to 12)	9 (12, 6 to 22)	1.28 (0.61 to 2.68)	0.512
Missing	9	1		
Dysuria				
No	973 (87, 85 to 89)	64 (85, 75 to 92)	1	
Yes	148 (13, 11 to 15)	11 (15, 8 to 25)	1.12 (0.56 to 2.25)	0.745
Missing	7	0		
Urinary frequency				
No	930 (83, 81 to 85)	62 (83, 72 to 90)	1	
Yes	191 (17, 15 to 19)	13 (17, 10 to 28)	0.85 (0.43 to 1.71)	0.654
Missing	7	0		

Bold values are statistically significant.
*Women with an unassessable MG result (n=15) and/or *Chlamydia trachomatis* were excluded from the analysis (n=100; includes eight women coinfected with MG and *C. trachomatis*).
†All analyses were adjusted for number of male sexual partners, vulvovaginal candidiasis, *Neisseria gonorrhoeae* and concurrent BV.
‡P value calculated using logistic regression.
§Data missing for up to 3% of participants.
¶STI in the past 6 months referred to bacterial STI only, however some women may have misinterpreted this question and answered with regard to warts or other non-bacterial STIs, and therefore this should be interpreted with caution.
**Abnormal vaginal odour refers to any self-reported odour, not specifically a fishy odour.
BV, bacterial vaginosis; n, number.

Table 3 Associations between *Mycoplasma genitalium* (MG) and clinical signs among symptomatic women*†

	Total women n=1023	MG negative n=956 (%, 95% CI)	MG positive n=67 (%, 95% CI)	Adjusted OR (95% CI)‡	P value§
Vaginal discharge					
No	322	307 (35, 32 to 38)	15 (25, 14 to 37)	1	
Yes	611	565 (65, 62 to 68)	46 (75, 63 to 86)	1.56 (0.84 to 2.87)	0.158
Not assessed/missing	90	84	6		
Abnormal odour¶					
No	707	663 (76, 73 to 79)	44 (72, 59 to 83)	1	
Yes	228	211 (24, 21 to 27)	17 (28, 17 to 41)	1.22 (0.67 to 2.22)	0.517
Not assessed/missing	88	82	6		
Vulval redness					
No	679	633 (73, 70 to 76)	46 (75, 63 to 86)	1	
Yes	248	233 (27, 24 to 30)	15 (25, 14 to 37)	0.83 (0.41 to 1.66)	0.591
Not assessed/missing	96	90	6		
Mucopurulent cervicitis**					
Women with BV					
No	208	188 (86, 81 to 90)	20 (95, 76 to 100)	1	
Yes	32	31 (14, 10 to 19)	1 (5, 0 to 24)	0.36 (0.05 to 2.85)	0.336
Women without BV					
No	405	389 (91, 88 to 93)	16 (70, 47 to 87)	1	
Yes	46	39 (9, 7 to 12)	7 (30, 13 to 53)	4.38 (1.69 to 11.33)	**0.002**
Cervical or adnexal motion tenderness					
No	476	445 (78, 75 to 82)	31 (86, 71 to 95)	1	
Yes	127	122 (22, 18 to 25)	5 (14, 5 to 29)	0.46 (0.16 to 1.34)	0.155
Not assessed/missing	420	389	31		
Cervical contact bleeding					
No	591	555 (86, 83 to 88)	36 (84, 69 to 93)	1	
Yes	101	94 (14, 12 to 17)	7 (16, 7 to 31)	1.29 (0.55 to 3.02)	0.563
Not assessed/missing	331	307	24		
Vaginal pH					
≤4.5	594	557 (61, 58 to 64)	37 (56, 43 to 68)	1	
>4.5	381	352 (39, 36 to 42)	29 (44, 32 to 57)	1.29 (0.77 to 2.17)	0.334
Not assessed/missing	48	47	1		
High vaginal polymorph count					
<5	589	554 (60, 57 to 63)	35 (54, 41 to 66)	1	
≥5	400	370 (40, 37 to 43)	30 (46, 34 to 59)	1.33 (0.77 to 2.29)	0.307
Not assessed/missing	34	34	2		

Bold values are statistically significant.
*Women with an unassessable MG result (n=15) or *Chlamydia trachomatis* were excluded from the analysis (n=100; includes eight coinfected women). In addition, asymptomatic women were not clinically assessed and have been excluded from the analysis (n=180).
†Clinical signs were elicited only in women with clinical indications for examination and in particular, cervical assessment and bimanual examination were undertaken in women with specific indications for a speculum and bimanual examination.
‡All analyses were adjusted for number of male partners, vulvovaginal candidiasis, *Neisseria gonorrhoeae* and concurrent BV, with the exception that we did not adjust for BV in models examining associations with individual Amsel criteria (ie, vaginal discharge, abnormal vaginal odour and vaginal pH).
§P value calculated using logistic regression and bold indicates significant findings p<0.05.
¶Abnormal vaginal odour refers to any odour, not specifically a fishy odour.
**We tested for interaction terms between MG and genital coinfections and the only significant interaction was between MG and BV for cervicitis (p=0.020). Therefore, the association between cervicitis and MG could not be adjusted for BV. To account for potential confounding by BV on the relationship between MG and cervicitis, data were then stratified by BV status, and the association between MG and cervicitis was investigated within each stratum.
BV, bacterial vaginosis; n, number.

seems to have capacity to cause more inflammation and symptoms of greater severity than MG.

Although perhaps more indolent than CT, MG is associated with the considerable challenge of increasing antimicrobial resistance, and more complex and costly treatment strategies. We found one in two MG infections in women was macrolide resistant, consistent with prior research at MSHC.[26] Recent Australian studies have reported that 50%–60% of MG infections in heterosexuals are macrolide resistant,[26] with resistance exceeding 80% in men who have sex with men.[27–29] Our data highlight the value of resistance testing and individualising therapy where possible, as up to 50% of women in our service can currently avoid quinolone use and achieve 95% first-line cure using a doxycycline-2.5 g azithromycin regimen.[30]

This was a large cross-sectional study, which captured detailed information on sexual practices, symptoms and signs in women tested for all common STIs and vaginal infections. However, as recruitment occurred at a single sexual health clinic and

non-English-speaking women were excluded, prevalence estimates are not generalisable to the community. We were unable to approach all women attending the clinic as only select doctors recruited symptomatic women, and women with marked PID were not recruited in order to expedite clinical care. This study therefore did not assess the association between MG and PID, and is likely to have biased recruitment towards women with milder symptoms. Examination was performed in keeping with clinical indications and practice at our service, resulting in one-third of the women having no information on cervicitis, which may have impacted on our findings. Doctors at our service systematically take patients in the order that they arrive to the walk-in service and therefore there was no other bias related to medical staff. Vaginal symptoms (eg, discharge and odour) were the most common symptoms reported in this study as they are the most likely reason for presentation to STI services. However, these symptoms are less likely to be associated with cervical STIs, which may have impacted on our ability to assess associations between other relevant symptoms and signs. As a consequence, our findings are most relevant to women with mild to moderate genitourinary symptoms attending outpatient STI services and general practices. Asymptomatic women were tested for CT and NG using FPU, compared with symptomatic women who received an endocervical swab, in accordance with standard clinical care at MSHC. While vaginal samples have generally been considered to be the optimal specimen for CT and NG, the Aptima Combo 2 assay used in our study is highly sensitive at detecting very low copy numbers of each organism. The Aptima Combo 2 assay has been shown to have near identical performance in urine compared with vaginal samples.[31 32] Lastly, the relatively small number of women with MG and CT meant we were underpowered to detect statistical differences between the two STIs on direct comparison.

Overall, MG was common in women attending a high output urban STI service, and half of MG infections were macrolide resistant. MG was not associated with specific genital symptoms, but was strongly associated with clinical signs of cervicitis. These data support an association between MG and cervicitis in women, particularly in the absence of other genital infections, and do not support routine testing for MG in women with common genital symptoms. These data are useful for clinicians in making decisions about indications for MG testing for women attending their services and help inform clinical practice and guidelines.

Key messages

- ⇒ *Mycoplasma genitalium* (MG) was as common as *Chlamydia trachomatis* (CT) but was not associated with genital symptoms.
- ⇒ Like CT, MG was significantly associated with mucopurulent cervicitis.
- ⇒ Routine testing for MG in women with common genital symptoms is not indicated.
- ⇒ Macrolide-resistant MG was detected in 48% of women.

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Contributors RLL wrote the ethics application, study protocol and study materials, assisted with data entry, performed data analysis and wrote the first draft of the manuscript, and assisted with reviewers' comments. LV provided extensive assistance with the data analysis and provided input into manuscript and reviewers' comments. ELP performed data analysis and extensive input into the manuscript, and assistance with reviewers' comments. MD put together study packs, completed data entry and maintained patient records, notified patients of test results, and provided input into the manuscript. GM provided input into the study protocol, coordinated testing of study samples and provided input into the manuscript. CKF provided input into the study protocol and manuscript. KB performed testing of study samples and provided input into the manuscript. TRHR assisted with the ethics application and study protocol, as well as design of the questionnaire and analysis. MK assisted with data entry and provided input into the manuscript. EM provided input into the study protocol and manuscript. RG provided input into the study protocol and manuscript. EPFC provided input into the study protocol and manuscript. CB formulated the study concept, assisted with study protocol and data analysis, and provided input into the manuscript and reviewers' comments.

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