

Clinical characteristics and symptoms associated with *Mycoplasma genitalium* infections among heterosexual men in Hanoi, Vietnam

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ABSTRACT

Background *Mycoplasma genitalium* (MG) is a critical pathogen of sexually transmitted infections (STIs) in men, associated with high antibiotic resistance. Understanding the clinical characteristics of MG infections can improve testing and treatment guidelines.

Aims To investigate the clinical features and characteristics of asymptomatic, acute and chronic MG infections in heterosexual males.

Methods From January 2018 to September 2023, men diagnosed with urethral STIs using multiplex real-time PCR were enrolled into this cross-sectional study. Testing indications included males with urethritis, suspected STIs and asymptomatic screening. Based on clinical symptoms, participants were classified as acute, chronic or asymptomatic groups. An electronic-based survey was administered to assess demographic, behavioural and clinical information. Univariate and multivariate logistic regression were performed to assess for factors associated with the presence of symptoms.

Result Among the 2102 men who have sex with women and were tested for STI, 879 records met the eligibility criteria for further analysis; MG was detected in 14.6% of the 2102 cases. Most patients presented with acute urethral symptoms (75.6%). Among men infected with MG, mono-infection accounted for 52.8%, while *Chlamydia trachomatis* and *Neisseria gonorrhoeae* co-infections occurred in 39.3% and 21.3%, respectively. Co-infections were more prevalent among acute urethritis compared with chronic urethritis or asymptomatic groups. Multivariable analysis revealed associations between chronic symptoms with absence of urethral discharge (aOR 0.31; 95% CI 0.2 to 0.47), previous antibiotic use (aOR 6.83; 95% CI 4.47 to 10.4), marriage (aOR 1.66; 95% CI 1.09 to 2.51) and history of STIs (aOR 2.08; 95% CI 1.24 to 3.49).

Conclusion Our study revealed a 14.6% prevalence of MG among individuals tested for STIs. Most patients presented with acute urethral symptoms, while chronic symptoms were associated with marriage, antibiotic use history and previous STIs. Routine MG screening of asymptomatic patients is not recommended, but improved access to diagnostics and further research is needed for clinical practice in low-resource settings.

INTRODUCTION

Mycoplasma genitalium (MG) is a bacterial sexually transmitted infection (STI) and a major cause of non-gonococcal urethritis (NGU).^{1–7} MG is found in the lower urogenital tract of about 1% to

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ *Mycoplasma genitalium* (MG) is a significant cause of non-gonococcal urethritis (NGU), often overlooked due to its mild or asymptomatic presentation.
- ⇒ While MG can lead to chronic infections, its diagnosis and treatment are challenging due to antibiotic resistance and limited availability of sensitive diagnostic tests, particularly in developing countries like Vietnam.

WHAT THIS STUDY ADDS

- ⇒ This study demonstrates that the prevalence of MG among heterosexual men visiting an andrology clinic in Vietnam is 14.6%, with MG mono-infection accounting for over half of the cases.
- ⇒ Chronic symptoms were linked to MG mono-infections, while co-infections were more prevalent in acute cases.
- ⇒ This highlights the role of undiagnosed MG in chronic urethritis and its association with sexual behaviours.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ The findings emphasise the need for routine MG screening in sexually transmitted infection (STI) management, particularly in chronic NGU cases, and suggest a broader implementation of diagnostic tests for MG in Vietnam.
- ⇒ This study could influence future research on MG's role in undiagnosed urethritis and shape public health strategies and policies to improve STI screening and antibiotic stewardship.

6.4% of individuals in the general population and accounts for 20–30% of male urethritis cases.^{4 5 8} While many individuals with MG infections experience acute urethral symptoms, some are asymptomatic, or develop chronic urethritis with vague and persistent symptoms.^{2 6 9} The mild and non-specific nature of MG symptoms often leads to misdiagnosis.^{6–8 10} Therefore, individuals with undiagnosed and untreated MG infections are at risk for transmitting the infection to their sex partners.¹⁰ Compounding this issue, antimicrobial resistance (AMR) in MG is an emerging issue, as the prevalence of resistance to first-line antibiotics, such as quinolones and macrolides, is on the rise. AMR

poses a significant challenge in some low- and middle-income countries (LMICs), including Vietnam, where diagnostic testing capacity, including antibiotic susceptibility testing, is limited.^{11–14}

Nucleic-acid amplification tests (NAATs) are the preferred method for diagnosing MG, and several tests are available that have a high sensitivity and specificity.¹⁵ However, access to these tests are limited in many LMICs. In Vietnam, they are only available in some tertiary hospitals, leaving most healthcare facilities with tests that can only detect *Neisseria gonorrhoeae* (NG) or *Chlamydia trachomatis* (CT) infections. A prior study in Vietnam found a high prevalence (19.5%) of MG among men with acute urethritis, the majority of whom were not co-infected with NG or CT.¹⁶ This raises concerns about the frequency of misdiagnosis of MG infections, which could lead to inappropriate treatment, and could also limit the detection of treatment failures, as MG infections are often misdiagnosed.¹⁷ Understanding the clinical characteristics of MG infections in settings where diagnostic testing is limited can help improve our understanding of the epidemiology and burden of these infections.

STIs constitute a significant global health challenge and countries with lower Human Development Index scores, including Vietnam, have a higher prevalence of MG infections.¹¹ Additionally, the scope of sex education and STI prevention efforts in Vietnam remains limited, contributing to a rising incidence of STIs.¹⁸ Yet few studies have examined the prevalence of MG, especially in the context of co-infections, the clinical characteristics of asymptomatic and chronic infections, and the risk factors for infections. Our study aimed to characterise the prevalence of MG infections among men in Hanoi, Vietnam, and to investigate the factors associated with infections, including coinfections with other STIs.

MATERIALS AND METHODS

Study design and population

This study presents a cross-sectional analysis of STI cases in men who have sex with women (MSW) attending the Andrology and Sexual Medicine Clinic at Hanoi Medical University from January 2018 to September 2023. All clinic patients were interviewed for a detailed medical and sexual history, including antibiotic use prior to consultation. According to clinical protocol, STI tests are indicated for those presenting with symptoms of urethritis, including urethral discharge, irritation, dysuria, burning, pain or discomfort. We also provide STI tests with transparent consultations for men with vague urethral signs with sexual behaviours that increase the risk for infections, such as having multiple sex partners, condomless intercourse with new partners or sex workers; or those seeking screening for STIs. For STI screening purposes, clients are prescribed blood tests for HIV, HBV, HCV, syphilis and a urethral swab for other pathogens. Eligible participants were males with confirmed MG infection via PCR testing from a urethral swab. Men who reported having sex with men were excluded in this study.

At the end of the consultation session, written informed consent was obtained from each patient, specifically agreeing to the future use of their clinical data for scientific purposes.

Data collection

Demographic data, including age, marital status, STI history and antibiotic treatment prior to consultation, were extracted from medical records. Sexual behaviours, including condomless sex, new sex partners, engagement in exchange sex or contact with STI-positive partners, were also collected from medical records. Sexual partners were categorised into four types based on sexual

behaviours in the past 3 months, as outlined in our previous article.¹⁹ Briefly, having one regular sexual partner refers to engaging in frequent sexual activity with a stable partner in a relationship lasting more than 3 months. Having a casual/new sexual partner involves sexual activity with one casual or new partner in a relationship lasting less than 3 months. Additionally, having multiple sex partners was defined as engaging in sexual activity with more than two partners who are not sex workers within the prior 3 months. Finally, having condomless sex with female sex workers within the past 3 months is categorised as the fourth group. Symptoms lasting less than 30 days were classified as acute urethritis; symptoms persisting ≥ 30 days were considered chronic.⁶ Antibiotics used for urethral symptoms before attending the clinic were recorded.

Specimen collection and testing

Clinical examination data included foreskin characteristics and the presence of urethral discharge on urethral massage. Urethral swabs were collected using sterile swabs for multiplex PCR testing. DNA from urethral swabs was extracted using the QIAcube system with the QIAamp DNA Mini QIAcube Kit (Qiagen, Germany), following the manufacturer's instructions. The extracted DNA was then analysed for 12 STI pathogens using the careGENETM STD-12 detection kit (WELLS BIO, South Korea). In addition to MG, the pathogen panel included *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), *Treponema pallidum* (TP), *Mycoplasma hominis* (MH), *Ureaplasma parvum* (UP), *Ureaplasma urealyticum* (UU), *Gardnerella vaginalis* (GV), *Trichomonas vaginalis* (TV), *Candida albicans* (CA), herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2).

Data analysis

Data collection and storage were conducted with Microsoft Excel V.365. Data were analysed using STATA V.15 for Windows. Categorical variables were described as frequencies and percentages, while continuous variables were summarised using mean, SD and ranges. Comparison of categorical variables between groups of co-infection statuses employed the χ^2 , while continuous data between groups of presence symptoms were compared using the Kruskal-Wallis test. The associations between co-infections and sexual behaviours (type of partner, marital status and history of STIs) with the presence of symptoms (acute/chronic/asymptomatic) were assessed with univariate logistic regression and all variables were included in the multivariate analysis. Statistical significance was determined at a p value ≤ 0.05 .

RESULTS

Among the 2102 patients seeking STI-related consultations, records of all MG-infected men and 572 non-MG individuals met the eligible criteria for further analysis, resulting in a total of 879 records. The prevalence of MG infection was 14.6% (307/2102) of all cases during the study period. Overall, the median age was 30 (IQR 26–36). One regular sexual partner was reported by 45.9% (403/879) and 13.3% (117/879) reported having a prior diagnosis of an STI. The majority of patients (91.3%) had an uncircumcised foreskin (803/879) and 69.3% (609/879) had urethral discharge on examination (Table 1).

Acute urethritis was the main complaint in 69.7% (214/307) of MG infected men and 78.8% (451/572) of non-MG infected men. In contrast, only a small proportion of patients were asymptomatic, with 13 (4.2%) in the MG-positive groups and 7 (1.2%) in the MG-negative group, who underwent STI screening

Table 1 Demographic, behavioural and clinical data of 307 men diagnosed with *Mycoplasma genitalium* (MG) infections in Hanoi, Vietnam

	Total (n=879)	MG positive (n=307)			MG negative (n=572)		
		Acute urethritis (n=214)	Chronic urethritis (n=80)	Asymptomatic (n=13)	Acute urethritis (n=451)	Chronic urethritis (n=114)	Asymptomatic (n=7)
Age (mean±SD, median, IQR)	32.12±8.95 (30, 26–36)	30.42±6.99* [#] (29, 25–35)	33.38±8.80* (32, 27–38)	33.62±9.49* (31, 28–40)	31.74±8.82* [#] (29, 26–36)	35.82±11.53* (31, 27–44)	31.71±7.02* (31, 26–36)
Marital status (N, %)							
Yes	442 (50.3)	77 (36.0)* [#]	52 (65.0)*	8 (61.5)*	231 (51.2) [#]	71 (62.3)	3 (42.9)
No	437 (49.7)	137 (64.0)* [#]	28 (35.0)*	5 (38.5)*	220 (48.8) [#]	43 (37.7)	4 (57.1)
History of STIs (N, %)							
Yes	117 (13.3)	22 (10.3)*	21 (26.3)*	1 (7.7)*	38 (8.4)*	34 (29.8)*	1 (14.3)*
No	762 (86.7)	192 (89.7)*	59 (73.8)*	12 (92.3)*	413 (91.6)*	80 (70.2)*	6 (85.7)*
Previous treatment (N, %)							
Yes	195 (22.2)	34 (15.9)*	45 (56.2)*	2 (15.4)*	51 (11.3)*	62 (54.4)*	1 (14.3)*
No	684 (77.8)	180 (84.1)*	35 (43.8)*	11 (84.6)*	400 (88.7)*	52 (45.6)*	6 (85.7)*
Type of sexual partner (N, %)							
One regular sexual partner	403 (45.9)	106 (49.5)* [#]	26 (32.5)* [‡]	3 (23.1)* [†]	186 (41.2)* [#]	75 (65.8)* [‡]	7 (100.0)* [†]
One casual/new sexual partner	184 (20.9)	55 (25.7)* [#]	41 (51.3)* [‡]	6 (46.1)* [†]	74 (16.4)* [#]	8 (7.0)* [‡]	0 (0.0)* [†]
Multiple partners	90 (10.2)	18 (8.4)* [#]	6 (7.50)* [‡]	1 (7.7)* [†]	53 (11.8)* [#]	12 (10.5)* [‡]	0 (0.0)* [†]
Female sex workers	202 (23.0)	35 (16.4)* [#]	7 (8.7)* [‡]	3 (23.1)* [†]	138 (30.6)* [#]	19 (16.7)* [‡]	0 (0.0)* [†]
Urethral discharge (N, %)							
Yes	609 (69.3)	165 (77.1)*	36 (45.0)*	3 (23.1)*	361 (80.0)*	44 (38.6)*	0 (0.0)*
No	270 (30.7)	49 (22.9)*	44 (55.0)*	10 (76.9)*	90 (20.0)*	70 (61.4)*	7 (100.0)*
Urethral irritation (N, %)							
Yes	662 (75.3)	165 (77.1)*	56 (70.0)*	0 (0.0)*	365 (80.9)*	76 (66.7)*	0 (0.0)*
No	217 (24.7)	49 (22.9)*	24 (30.0)*	13 (100.0)*	86 (19.1)*	38 (33.3)*	7 (100.0)*
Circumcision (N, %)							
Yes	76 (8.7)	24 (11.2) [#]	9 (11.2)	2 (15.4)	29 (6.4) [#]	12 (10.5)	0 (0.0)
No	803 (91.3)	190 (88.8) [#]	71 (88.8)	11 (84.6)	422 (93.6) [#]	102 (89.5)	7 (100.0)

*p<0.05 when separately comparing subgroups of MG positive and negative groups using analysis of variance for continuous variables and χ^2 or Fisher's exact tests for categorised variables. #p<0.05 when comparing acute urethritis men between MG positive and negative groups using t-test for continuous variables and χ^2 or Fisher's exact tests for categorised variables. ‡p<0.05 when comparing chronic urethritis men between MG positive and negative groups using t-test for continuous variables and χ^2 or Fisher's exact tests for categorised variables. †p<0.05 when comparing asymptomatic men between MG positive and negative groups using t-test for continuous variables and χ^2 or Fisher's exact tests for categorised variables.

STI, sexually transmitted infection.

after having condomless sex with new partners or female sex workers. A similar pattern was observed regarding the relationship between the main complaint and history of STIs, previous antibiotic treatment and the presence of urethral symptoms in both groups. Specifically, people with acute symptoms were less likely to have a history of STIs and experience previous antibiotic treatment, compared with those with chronic symptoms. In addition, patients with chronic (36/80, 45%) and asymptomatic symptoms (3/13, 23.1%), regardless of MG status, were less likely to report urethral discharge on examination. Notably, among men with chronic symptoms, those in the MG-positive group were significantly more likely to report having casual or new sexual partners (51.3%) compared with only 7% in the MG-negative group (table 1).

Among men with MG infections, 47.2% (145/307) had a co-infections. Of the co-infections, the most common were CT (39.3%), followed by NG (21.3%) and *Ureaplasma parvum* (20%). None tested positive for syphilis in urethral swab specimens (figure 1). One co-infection occurred in 39.2% (101/307) of MG infections, while 12.1% had two, and 2.3% had three co-infections. Gonococcal urethritis and non-gonococcal urethritis with CT accounted for 10.2% and 18.4% of cases,

respectively. The correlation between the type of pathogens and the duration of symptoms is shown in table 2. Men with chronic presentation were more likely to be infected with MG compared with co-infection with NG and CT.

Using multivariable logistic regression, we found that the presence of urethral discharge during the examination was significantly less likely in the asymptomatic group (aOR=0.04, 95% CI 0.01 to 0.17) and the chronic group (aOR=0.31, 95% CI 0.2 to 0.47) compared with the acute group (table 3). Conversely, a history of antibiotic treatment prior to consultation (aOR=6.83, 95% CI 4.47 to 10.4), being married (aOR=1.66, 95% CI 1.09 to 2.51) and history of previous STIs (aOR=2.08, 95% CI 1.24 to 3.49) were predictors of chronic symptoms. In terms of sexual partners, patients in the chronic group were more likely to have just one regular sexual partner (aOR=1.68, 95% CI 1.0 to 2.84).

DISCUSSION

In this retrospective study of men visiting an andrology clinic in Hanoi, Vietnam, for more than a 5-year period, we found that the prevalence of urethral MG was 14.6%, with mono-infection accounting for approximately half of all cases. Those

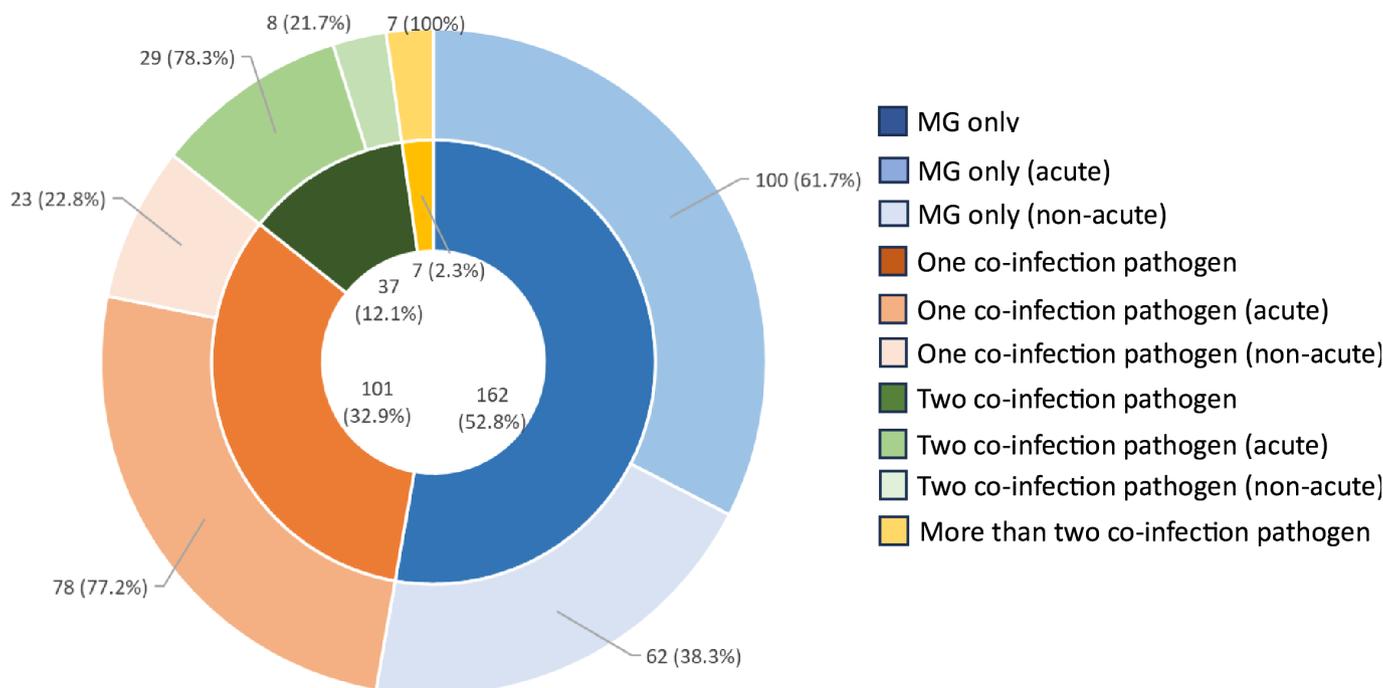


Figure 1 Distribution by number of co-infection pathogens in *Mycoplasma genitalium* (MG)-positive males (N=307).

who presented with acute urethritis were more likely to have a co-infection with NG/CT, whereas MG mono-infections were more common in chronic cases. Additionally, a history of previous STIs or antibiotic treatment prior to consultation were associated with chronic urethritis. These findings highlight the prevalence of MG in Vietnam and emphasise the importance of testing for MG in patients with chronic urethritis.

Few studies have reported the prevalence of MG in Vietnam.¹⁹ Our findings on MSW with urethritis revealed a significant prevalence of MG infection. This result is consistent with prior studies, with prevalences of 19.7% and 13.8%.^{20 21} Among attendees of STI clinics, prevalence rates ranged from 4% to 38%.^{1 11 12 22} Among MG infections, the most common co-infection was CT (39.3%), followed by NG (21.3%), which is also similar to prior reports.^{23 24} CT and NG are among the most prevalent STIs, thus leading to a higher rate of co-infections with MG. However, this result can also indicate that routine testing for only urethral NG and CT might overlook many MG infections.²⁵ Therefore, our large sample size may provide valuable insights to elucidate the prevalence of MG in men with urethritis, further informing clinical management and public health strategies for STI prevention and treatment.

We also found that among those with MG infections and chronic urethritis, infections were more likely to be a mono-infection than those with acute urethritis. This observation can be explained by several factors. First, MG is a less well-known compared with CT and NG, even among healthcare providers, who are more familiar with testing and treating CT and NG.²⁴ Consequently, MG often goes undiagnosed and untreated, particularly in chronic cases with milder symptoms.²⁶ Additionally, conventional STI testing methods usually exclude MG and other *Mycoplasma* and *Ureaplasma* species, as standard panels in Vietnam focus on more common pathogens like CT and NG,^{16 19} contributing to MG's persistence in the population.^{23 24} Furthermore, MG exhibits higher antibiotic resistance compared with CT and NG, making it more challenging to treat effectively.²⁷ The resistance of MG to commonly used antibiotics means that standard treatments for STIs may not be sufficient to eradicate the infection and can lead to symptoms of chronic urethritis. Consequently, patients previously treated for CT or NG may still harbour MG, resulting in a higher prevalence of MG mono-infections in chronic cases.^{26 27}

In our study, several factors were more likely to be associated with acute urethritis compared with chronic or asymptomatic

Table 2 Correlation between symptoms at presentation and co-infection status of those being positive and negative with *Mycoplasma genitalium* (N=879)

	MG mono-infection (n=162)	MG+NG (n=31)	MG+CT (n=57)	MG+other pathogens (n=57)	No MG+NG (n=187)	No MG+CT (n=224)	No MG+other pathogens (n=161)
	N (%)						
Acute urethritis (n=665)	100 (61.7)	28 (90.3)**	44 (77.2)*	42 (73.7)	178 (95.2)**	197 (87.9)**	76 (47.2)*
Chronic urethritis (n=194)	55 (34.0)	2 (6.5)**	10 (17.5)*	13 (22.8)	8 (4.3)**	25 (11.2)**	81 (50.3)*
Asymptomatic (n=20)	7 (4.3)	1 (3.2)**	3 (5.3)*	2 (3.5)	1 (0.5)**	2 (0.9)**	4 (2.5)*

*p < 0.05 when comparing with MG mono-infection group **p < 0.01 when comparing with MG mono-infection group
MG, *Mycoplasma genitalium*.

Table 3 Multivariable logistic regression analysis of the correlation between clinical characteristics and symptom status (acute symptoms used as reference)

	Chronic symptoms		Asymptomatic	
	Adjusted pOR	95% CI	Adjusted pOR	95% CI
Type of sexual partners				
One regular sexual partner	–	–	–	–
One casual/new sexual partner	1.68*	1.00 to 2.84	1.93	0.58 to 6.46
Multiple partners	1.13	0.56 to 2.29	0.90	0.10 to 7.78
Female sex workers	0.51*	0.29 to 0.90	0.74	0.19 to 2.91
Previous antibiotic treatment				
No	–	–	–	–
Yes	6.83**	4.47 to 10.4	1.00	0.26 to 3.92
Marital status				
Single	–	–	–	–
Married	1.66*	1.09 to 2.51	1.17	0.43 to 3.21
Discharge during examination				
No	–	–	–	–
Yes	0.31**	0.20 to 0.47	0.04**	0.01 to 0.17
History of STIs				
No	–	–	–	–
Yes	2.08**	1.24 to 3.49	0.67	0.13 to 3.47
MG positive				
No	–	–	–	–
Yes	0.64	0.40 to 1.03	2.82	0.84 to 9.45
NG positive				
No	–	–	–	–
Yes	0.18**	0.08 to 0.39	1.29	0.22 to 7.48
CT positive				
No	–	–	–	–
Yes	0.30**	0.18 to 0.49	0.74	0.21 to 2.62
Co-infection				
No	–	–	–	–
Yes	1.11	0.72 to 1.71	1.29	0.47 to 3.53
Pseudo R squared	0.3190		0.2545	

*p<0.05; **p<0.01.

adjusted pOR, adjusted prevalence odd ratio; CT, *Chlamydia trachomatis*; MG, *Mycoplasma genitalium*; STI, sexually transmitted infection.

status among men with MG infections. Those with MG co-infections were more likely to have acute symptoms than those with MG mono-infections, suggesting co-infections with CT or NG are more likely the driver of acute symptoms. While urethral discharge typically presents in men with acute symptoms, chronic symptoms are associated with an STI history due to the exposure to high-risk sexual behaviours, making these individuals more susceptible to persisting MG, even after treatment. Additionally, individuals with co-infections may already have compromised mucosal barriers or immune responses, which can allow MG to persist undetected.²⁸ Our report also found that patients with chronic symptoms were more likely to have to be married or having a casual/new sexual partner. One potential explanation of this is that individuals in romantic relationships might have a lower perception of risk for STIs compared with female sex workers who are often perceived as having higher occupational risk for STIs.²⁹ As a result, the mild symptoms of MG could be

less likely to prompt them to seek medical attention after sex with a familiar partner compared with a female sex worker, leading to chronic infection.

This study has several limitations. First, the medical history of STIs and antibiotic use did not specify the specific pathogen or the antibiotics the patient has previously taken, which might be useful in determining impact on MG. Second, we did not assess extragenital sites of infections or sexual behaviours associated with those sites; extragenital sites can be infected with MG, usually reported among men who have sex with men, although the clinical impact of infections at those sites is not clear.³⁰ The limited data from the control group and the small number of asymptomatic patients restricted the ability to accurately detect risk factors for MG infection, potentially contributing to the wide confidence intervals observed in the multivariate analysis. Lastly, the use of medical records and self-reported behaviours could potentially lead to recall or social desirability biases.

In conclusion, our study found the prevalence of MG in a urology clinic-based population in Hanoi, Vietnam, undergoing NAATs for STIs was 14.6%. The majority of patients presented with acute urethral symptoms; however, about a quarter experienced chronic symptoms, and a small proportion were asymptomatic. Patients with chronic or no symptoms did not typically present with urethral discharge. Additionally, those with chronic symptoms were more likely to be married or have an unstable partner, have a history of previous STI and antibiotic treatment before consultation. While MG mono-infections accounted for most cases, NGU was most common among co-infection group, with urethral discharge during examination serving as a key predictor. Currently, routine MG screening for STI testing has not been established. However, improving access to diagnostic testing is needed in LMICs and future research is needed to understand the impact of MG infections among those with co-infections to improve testing and treatment guidelines.

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Ethics approval This study uses retrospective data from medical records stored in Hanoi Medical University Hospital's system. The study was approved by the Institutional Review Board of Hanoi Medical University (HMU#IRB1775). At the end of the consultation session, written informed consent was obtained from each patient, specifically agreeing to the future use of their clinical data for scientific purposes.

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