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RESEARCH ARTICLE

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Investigating the microbial pathogens of sexually transmitted infections among heterosexual Vietnamese men with symptomatic urethritis

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ABSTRACT

Objective: To explore the microbial etiology of urethritis in Vietnamese men and the association with patients' characteristics, especially their sexual behaviors.

Methods: This study was conducted on 349 men who presented with symptomatic urethritis and evidence of STIs (determined by multiplex PCR tests) at the Department of Andrology and Sexual Medicine—Hanoi Medical University Hospital. All information regarding medical history, sexual activities, and symptoms of urethritis was documented.

Results: *C. trachomatis* and *N. gonorrhoea* remained the two most common causative pathogens, followed by an unexpectedly high prevalence of *Mycoplasma* and *Ureaplasma* species. Coinfection was significant with a rate of 40.7%. Men who had sex with female sex workers (FSWs) were more likely to be positive with *N. gonorrhoea* but less likely to be positive with *C. trachomatis* and *M. genitalium* than those having sex with only one romantic partner.

Conclusions: Our findings suggested the important role of other microorganisms, especially *M. genitalium*, in the etiology of urethritis in men besides the previously well-known causes of STIs. Since the coinfection rate is quite high, targeted treatment with clear microbial evidence should be considered rather than empiric antimicrobial therapy.

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Introduction

Sexually transmitted infections (STIs) remain to be one of the most serious health problems in many third-world countries including Vietnam. In addition to the immediate effect of the infections, STIs may be associated with many consequences, such as physical disabilities, psychological and social insecurity, and impaired pregnancy outcomes. Several STIs also have negative effects on sexual function and sexual behaviors in men and women [1–3], making them highly relevant to the field of sexual medicine.

In men, urethritis is mostly caused by STIs, expressing a diversity of signs and symptoms ranging from urethral discharge, itching, tingling, dysuria, but it can be asymptomatic in some cases [4,5]. Besides the well-known pathogens, such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, other causative microorganisms have been studied but one-third of non-gonococcal urethritis is idiopathic [5,6]. Rather than empiric treatment, antibiotics use based on microbial evidence has been recommended to reduce the resistance phenomenon [4]. Since the etiology is different among countries and it is impossible to test all potential pathogens, studying microorganisms causing urethritis is required.

Previous studies in Vietnam only focused on the prevalence of *N. gonorrhoeae* and *C. trachomatis* in different subjects [7–12]. The roles and popularities of other microorganisms in urethritis are not well-documented. Thus, this study aims to investigate the microbial etiology of urethritis in Vietnamese men and the association between the possibilities of detecting specific microorganisms and patients' characteristics.

Materials and methods

For this present study, we retrieved data from medical records of patients diagnosed with symptomatic

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Table 1. Characteristics of the study population ($n = 349$).

	N	%	Mean ± *SD*	Min–Max
Age (year)			30.15 ± 8.12	15–65
<30	199	57.0%		
≥30	150	43.0%		
Marital status				
Married	163	46.7%		
Unmarried	186	53.3%		
History of previous STIs				
Yes	29	8.3%		
No	320	91.7%		
Having urethral discharge				
Yes	310	88.8%		
No	39	11.2%		
Be treated with antibiotics before attending a clinic				
Yes	39	11.2%		
No	310	88.8%		
Type of sexual partner				
One romantic partner	139	39.8%		
One unstable partner	65	18.6%		
Multiple sexual partners	57	16.3%		
Having sex with female sex workers	88	25.3%		

SD: standard deviation; STIs: sexually transmitted infections.

urethritis, presented at the Andrology and Sexual Medicine clinic of Hanoi Medical University's Hospital from 2018 to 2022. This clinic is specialized in treating and consulting men's problems including symptomatic urethritis related to sexually transmitted diseases. According to our protocol, suspected cases of sexually transmitted diseases with the complaint symptoms, including urethral discharge, dysuria, burning, pain, irritation, or discomfort feeling of the low urinary tract within one month would have their medical history carefully investigated, especially their sexual activities, partners, and orientations. The information related to antibiotics usage before attending was also noted. Subsequently, physical examination and laboratory tests were performed to confirm the diagnosis. Discharge (purulent or transparent) was inspected and urethral massage or milking was done if necessary. Urethral specimens were taken using plastic sterile swab sticks, one for multiplex polymerase chain reaction (PCR) and another for culture and antibiogram in gonococcal-suspected cases. Men with evidence of microorganisms in the above tests were defined as urethritis cases. All information was safely stored in the online system of the hospital to track progression and manage patients. Under the permission of the ethics committee of Hanoi Medical University's Hospital, we extracted data from symptomatic urethritis patients who had PCR results on the system. Patients' identifications were kept confidential.

According to the described protocol, data on urethritis were retrieved from 351 men ages ranging from 15 to 65 years). Eligible subjects were heterosexual men who were then divided into four groups based on the type of sexual partner. The three-month cutoff point was chosen based on the UK national guideline on taking a sexual history and a previous study by Shumin et al. [13,14].

- One romantic partner: having frequent sex with only one stable sexual partner for whom the relationship lasted for more than three months.
- One unstable partner: having sex with a casual partner or a new partner for whom the relationship lasted for <3 months.
- Multiple sex partners: having sex with more than two partners who were not sex workers within three months.
- Having unprotected sex with female sex workers (FSWs) within three months. In our study population, no men reported fully using a condom from the beginning to the end of the sex act with FSWs.

Among them, two men who declared to have had sex with only male partners, positive for *N. gonorrhoeae* and *C. trachomatis* coinfected with HSV type 1, were excluded.

DNA extraction and multiplex real-time polymerase chain reaction

DNA samples from urethral swabs were automatically extracted on the QIAcube system using the QIAamp DNA Mini QIAcube Kit (Qiagen cat#51326; Qiagen, Hilden, Germany) according to the manufacturer's instructions. Subsequently, the extracted DNA samples underwent analysis for 12 STD pathogens detection with the careGENE^{TM} STD-12 detection kit (WELLS BIO, Seoul, South Korea). The 15 µl master mix was prepared by mixing 10 µl of 2× reaction mixture and 5 µl of the set primer/probe mix. Each set primer/probe mix detected four types of STD-related pathogens and provided an internal control. The extracted DNA sample (5 µl) was added to each master mix tube. PCR was conducted using the CFX96 Real-Time PCR Detection System—IVD (Bio-Rad, Hercules, CA, USA). First, the predenaturation step was executed at 96 °C for 15 min; then, 40 cycles of amplification were repeated at 94 °C for 30 s and 60 °C for 1 min. A positive test result was defined as a cycle threshold (Ct) <39 for individual targets and those ≥39 or not available as negative results.

Data analysis

This study used STATA version 15.1 and R program version 3.6.3 for Windows. Differences between

Table 2. Results from multiplex polymerase chain reactions of urethral sample in symptomatic urethritis men.

NG	CT	MG	MH	TP	CA	UP	TV	UU	GV	HSV1	HSV2	Total $n = 349$	Non-treated $n = 310$	Treated $n = 39$
+	−	−	−	−	−	−	−	−	−	−	−	65	57	8
+	+	−	−	−	−	−	−	−	−	−	−	32	30	2
+	+	+	−	−	−	−	−	−	−	−	−	3	3	0
+	+	−	−	−	−	+	−	−	−	−	−	1	1	0
+	+	−	−	−	−	−	−	+	−	−	−	7	7	0
+	+	−	−	−	−	−	−	−	+	−	−	1	1	0
+	+	+	−	−	−	+	−	−	−	−	−	1	1	0
+	+	−	+	−	−	+	−	−	−	−	−	1	1	0
+	+	−	−	−	−	+	−	+	−	−	−	1	1	0
+	+	−	−	−	−	−	+	+	−	−	−	1	1	0
+	−	+	−	−	−	−	−	−	−	−	−	6	6	0
+	−	+	−	−	−	+	−	−	−	−	−	1	1	0
+	−	−	+	−	−	+	−	−	−	−	−	1	1	0
+	−	−	+	−	−	−	−	+	−	−	−	1	1	0
+	−	−	−	−	−	+	−	−	−	−	−	5	5	0
+	−	−	−	−	−	+	−	−	−	−	+	2	2	0
+	−	−	−	−	−	−	−	+	−	−	−	7	6	1
+	−	−	−	−	−	−	−	−	+	−	−	1	1	0
+	−	−	−	−	−	−	−	−	−	−	+	1	1	0
−	+	−	−	−	−	−	−	−	−	−	−	90	80	10
−	+	+	−	−	−	−	−	−	−	−	−	4	2	2
−	+	+	+	−	−	−	−	−	−	−	−	1	1	0
−	+	+	−	−	+	−	−	−	−	−	−	2	1	1
−	+	+	−	−	−	−	−	+	−	−	−	2	2	0
−	+	−	+	−	−	−	−	−	−	−	−	1	1	0
−	+	−	+	−	−	−	−	+	−	−	−	2	2	0
−	+	−	−	−	+	−	−	−	+	−	−	1	1	0
−	+	−	−	−	−	+	−	−	−	−	−	15	14	1
−	+	−	−	−	−	+	−	+	−	−	−	4	4	0
−	+	−	−	−	−	−	−	+	−	−	−	16	15	1
−	−	+	−	−	−	−	−	−	−	−	−	31	24	7
−	−	+	+	−	−	−	−	−	−	−	−	1	1	0
−	−	+	+	−	−	+	−	−	−	−	−	1	1	0
−	−	+	−	−	+	−	−	+	−	−	−	1	1	0
−	−	+	−	−	−	+	−	−	−	−	−	9	6	3
−	−	+	−	−	−	−	−	+	−	−	−	3	3	0
−	−	+	−	−	−	−	−	−	+	−	−	1	1	0
−	−	+	−	−	−	−	−	−	−	+	−	1	0	1
−	−	−	+	−	−	−	−	−	−	−	−	1	1	0
−	−	−	+	−	−	+	−	−	−	−	−	1	1	0
−	−	−	+	−	−	+	−	+	−	−	−	1	1	0
−	−	−	+	−	−	−	−	+	−	−	−	1	1	0
−	−	−	−	−	+	−	−	−	−	−	−	2	2	0
−	−	−	−	−	+	+	−	−	−	−	−	1	1	0
−	−	−	−	−	−	+	−	−	−	−	−	7	7	0
−	−	−	−	−	−	−	−	+	−	−	−	10	8	2
−	−	−	−	−	−	−	−	−	−	+	−	1	1	0

NG: *Neisseria gonorrhoeae*; CT: *Chlamydia trachomatis*; MG: *Mycoplasma genitalium*; MH: *Mycoplasma hominis*; TP: *Treponema pallidum*; CA: *Candida albicans*; UP: *Ureaplasma parvum*; TV: *Trichomonas vaginalis*; UU: *Ureaplasma urealyticum*; GV: *Gardnerella vaginalis*; HSV1: Herpes simplex virus type 1; HSV2: Herpes simplex virus type 2.

categorical variables were examed using the Chi-squared test. Multivariable logistic regressions were fitted to explore associations between the chance of detecting specific microorganisms (*C. trachomatis, N. gonorrhoeae,* or *M. genitalium*) or coinfections and other characteristics. The level of significance was set as $p = 0.05$.

Results

Characteristics of a study population was presented in Table 1. In the total of 349 heterosexual men diagnosed with symptomatic urethritis, we found that 11.2% reported using antibiotics before presenting at our clinic. Urethral discharge was the predominant symptom in most cases (88.8%). There were 53.3% unmarried men. The number of men who reported having sex with only one romantic partner, only one unstable partner, multiple sex partners, and a female sex worker was 139 (39.8%), 65 (18.6%), 57 (16.3%), and 88 (25.3%), respectively. There was a significant difference in the type of sexual partner regarding marital status, with $p < 0.01$. Married men were more likely to have sex with multiple sex partners (27.6 *vs.* 6.5%) or with a female sex worker (36.2 *vs.* 15.6%) than unmarried men, while the latter appeared to be

Table 3. Differences in positive rates of *N. gonorrhoeae*, *C. trachomatis*, *M. genitalium*, and coinfections between stratified groups.

	N	NG positive *n* (%)	CT positive *n* (%)	MG positive *n* (%)	Coinfection *n* (%) 2 microorganisms	Coinfection *n* (%) ≥3 microorganisms
Age						
<30	199	71 (35.7%)	125 (62.8%)**	37 (18.6%)	67 (33.7%)*	25 (12.6%)*
≥30	150	67 (44.7%)	61 (40.7%)**	31 (20.7%)	39 (26.0%)*	11 (7.3%)*
Marital status						
Unmarried	186	69 (37.1%)	119 (64.0%)**	36 (19.4%)	63 (33.9%)*	23 (12.4%)*
Married	163	69 (42.3%)	67 (41.1%)**	32 (19.6%)	43 (26.4%)*	13 (8.0%)*
Urethral discharge						
Yes	310	135 (43.6%)**	160 (51.6%)	65 (21.0%)*	101 (32.6%)*	33 (10.7%)*
No	39	3 (7.7%)**	26 (66.7%)	3 (7.7%)*	5 (20.4%)*	3 (7.7%)*
Treated/Non-treated						
Treated	39	11 (28.2%)	17 (43.6%)	14 (35.9%)**	11 (28.2%)	1 (2.6%)
Non-treated	310	127 (41.0%)	169 (54.5%)	54 (17.4%)**	95 (30.7%)	35 (11.3%)
Type of sexual partner						
One romantic partner	139	38 (27.3%)**	80 (57.6%)**	31 (22.3%)	42 (30.2%)	11 (7.9%)
One unstable partner	65	25 (38.5%)**	42 (64.6%)**	16 (24.6%)	19 (29.2%)	12 (18.5%)
Multiple sexual partners	57	29 (50.9%)**	32 (56.1%)**	11 (19.3%)	18 (31.6%)	7 (12.3%)
Having sex with female sex workers	88	46 (52.3%)**	32 (36.4%)**	10 (11.4%)	27 (30.7%)	6 (6.8%)

NG: *Neisseria gonorrhoeae*; CT: *Chlamydia trachomatis*; MG: *Mycoplasma genitalium*.
*$p < 0.05$.
**$p < 0.01$.

more faithful, with 47.3 *vs.* 31.3% reporting only one romantic partner in the last three months.

Table 2 showed results from urethral swabs of men with symptomatic urethritis involved in this study. *C. trachomatis* (CT) was the most common microorganism found in patients with a prevalence of 53.3% (186/349). Other pathogens detected by PCR of urethral discharge were *N. gonorrhoeae* (NG) (39.5%, 138/349), *M. genitalium* (MG) (19.5%, 68/349), *U. urealyticum* (UU) (16.3%, 57/349), *U. parvum* (UP) (14.9%, 52/349), *M. hominis* (MH) (3.7%, 13/349), *C. albicans* (CA) (2.0%, 7/349), *G. vaginalis* (GV) (1.2%, 4/349), HSV2 (0.9, 3/349), HSV1 (0.6%, 2/349), and *T. vaginalis* (TV) (0.3%, 1/349). There was no sample being positive with *T. pallidum* (TP).

Among 207 samples for which only one microorganism was found, CT was positive in 43.5% (20/207) followed by NG (31.4%, 65/207), MG (15.0%, 31/207), UU (4.8%, 10/207), UP (3.4%, 7/207), CA (1.0%, 2/207), MH (0.5%, 1/207), and HSV1 (0.5%, 1/207). In patients with monomicrobial infection, MH and HSV1 were only detected in cases with urethral discharge. TV, GV, and HSV2 did not occur as solitary infections.

Coinfections were found in 142 patients. The number of men who were positive with two, three, and four microorganisms were 106 (30.4%), 32 (9.2%), and 4 (1.2%), respectively. CT-NG, CT-UU, and CT-UP were the three most common coinfections with prevalences of 22.5% (32/142), 11.3% (16/142), and 10.6% (15/142).

Differences between stratified groups in terms of being positive with NG, CT, MG, or coinfection were illustrated in Table 3. Patients who were younger than 30 years old or unmarried men had significantly higher rates of being positive with CT or multiple microorganisms compared with men who were older than 30 years old or married. NG, MG, and coinfections of two or more than three microorganisms were scarcely detected in patients without urethral discharge. There were no differences in detecting NG, CT, or multiple microorganisms regardless of antibiotic usage before attending a clinic. However, the treated group had a higher percentage of MG positive than the untreated group (35.9 *vs.* 17.4%, $p < 0.01$). Men who had sex with female sex workers had the highest rate of NG positive (52.3%) but had the lowest rate of CT positive (36.4%).

Multivariate logistic regressions were fitted to investigate the associations between patients' characteristics and the chance of being infected with NG, CT, MG, or multiple microorganisms (Figures 1–4). Patients with urethral discharge were more likely to be positive with NG (adjusted odds ratio (aOR): 9.70, 95% confidence interval (95%CI): 2.81–3.55, $p < 0.01$) and multiple microorganisms (aOR: 3.02, 95%CI: 1.31–6.93, $p < 0.01$) but were less likely to be positive with CT (aOR: 0.35, 95%CI: 0.16–0.75, $p < 0.01$). MG was 3.16 times more prevalent among patients with previous antibiotics treatment compared with the untreated subjects (aOR: 3.16, 95%CI: 1.47–4.76, $p < 0.01$). In comparison with the presence of NG in men who had only one romantic partner, the prevalence of this pathogen was 2.60 times higher in those having multiple sex partners and 3.20 times higher in those having sex with female sex workers. However, patients reporting having sex with female sex workers were less likely to be positive with CT and MG than those who had one romantic partner. Being married was a protective factor with the CT infection since the

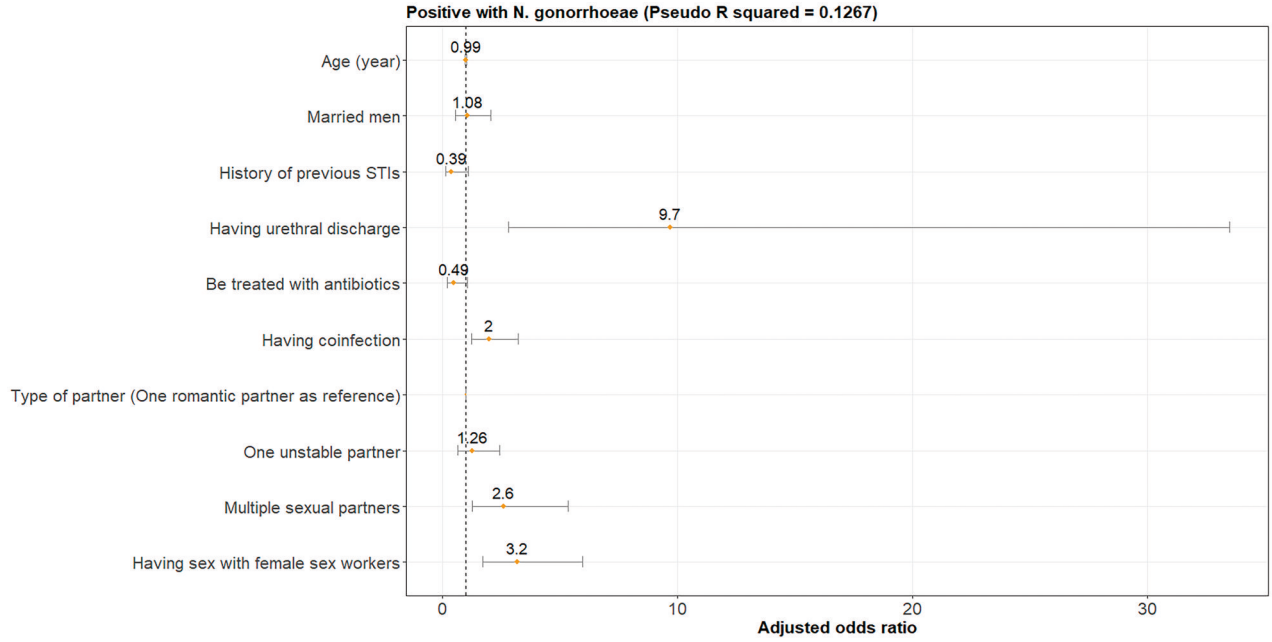

Figure 1. The multivariate logistic regression predicting the possibility of detecting *Neisseria gonorrhoeae* ($n = 349$).

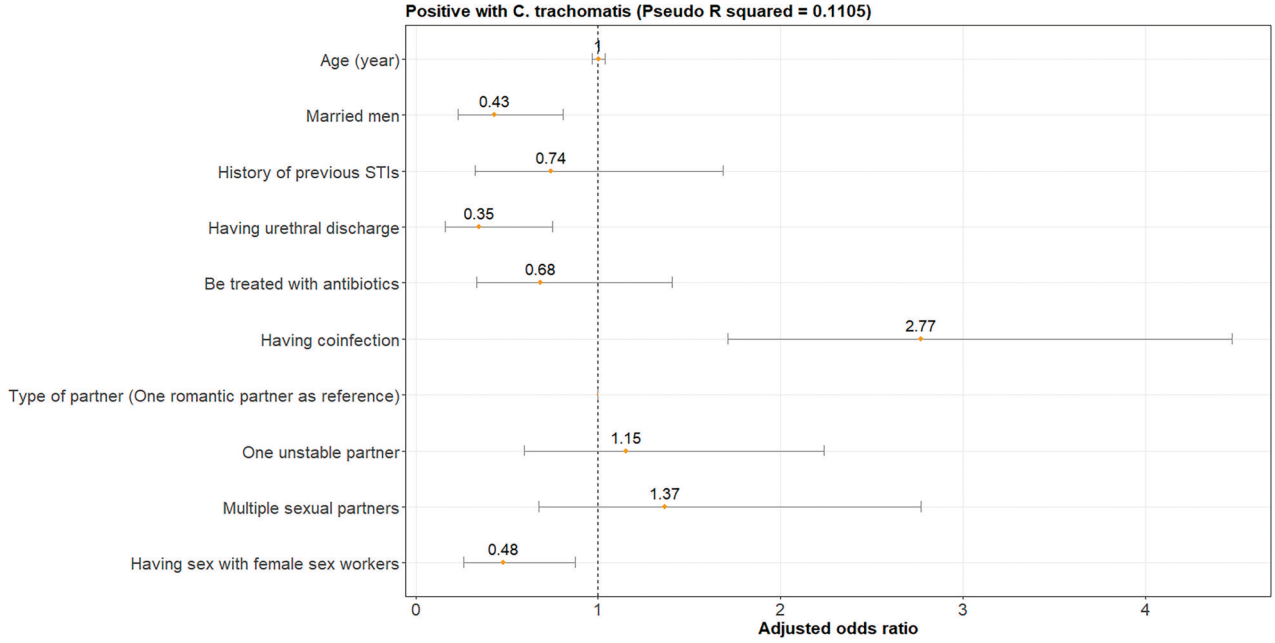

Figure 2. The multivariate logistic regression predicting the possibility of detecting *Chlamydia trachomatis* ($n = 349$).

adjusted OR of being positive with CT was 0.43 ($p < 0.01$). CT, NG, and MG were more likely to coinfect with others than presenting solitarily. There were no associations between a history of previous STIs and the chance of being positive with NG, CT, MG, or with more than two microorganisms.

Discussion

This is one of the very first studies investigating the microbial etiology of symptomatic urethritis in Vietnamese men. The present study shows the diversity of causative microorganisms detected by multiplex PCR of urethral swab samples. Similar to previous reports worldwide, *C. trachomatis, N. gonorrhoeae*, *M. genitalium*, *U. urealyticum*, *U. parvum*, and *M. hominis* were the most common pathogens of urethritis in men [5,15–19]. While *T. vaginalis* was a critical pathogen of STIs in several countries with high prevalences [16–18,20], it was only detected in one patient as a co-infected bacteria in this study. The presence of *G. vaginalis* in urethral samples has been reported at

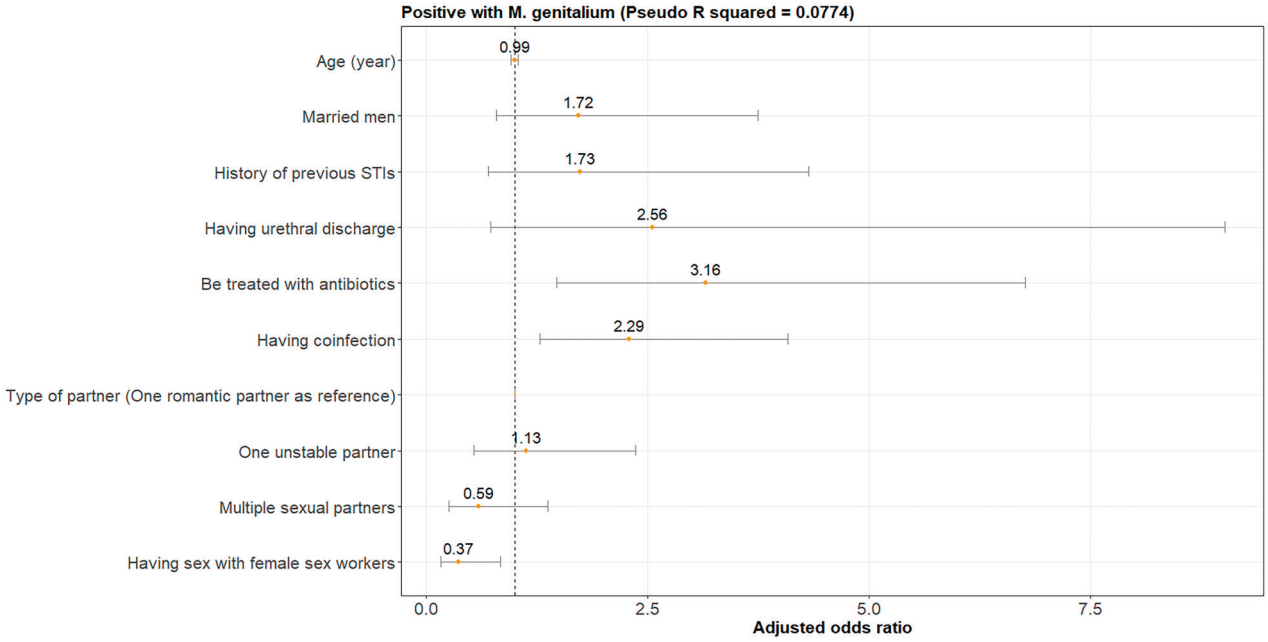

Figure 3. The multivariate logistic regression predicting the possibility of detecting *Mycoplasma genitalium* ($n = 349$).

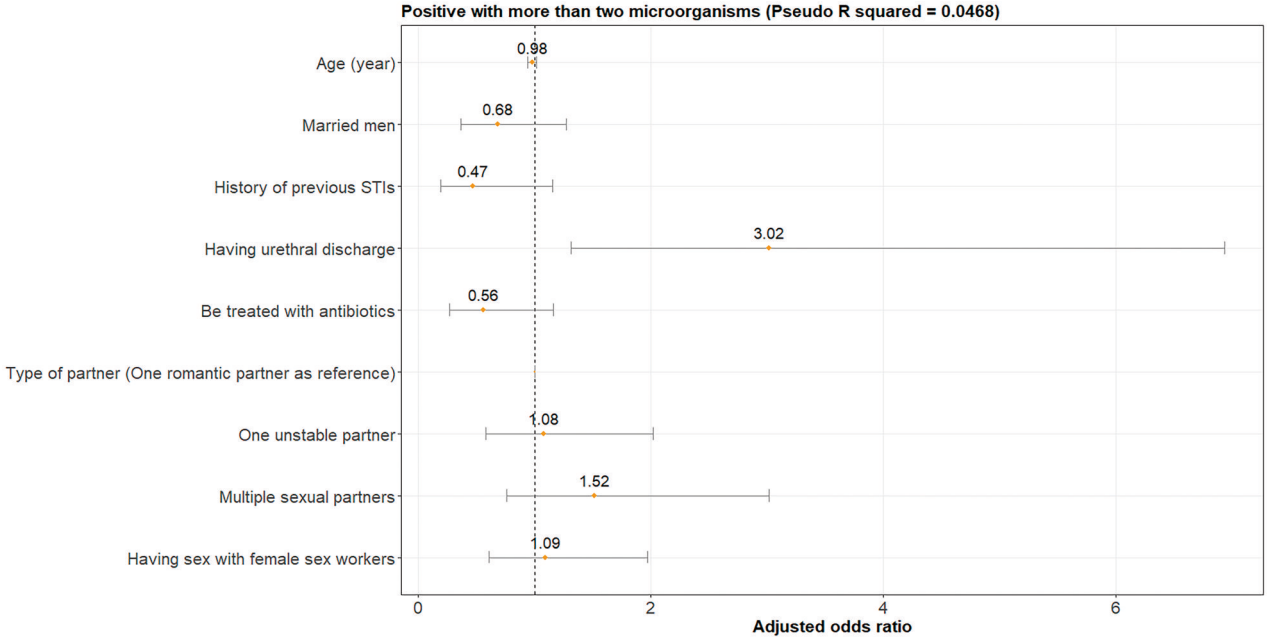

Figure 4. The multivariate logistic regression predicting the possibility of detecting more than two microorganisms ($n = 349$).

high rates, specifically in 14% of men with urethritis in Japan [19,21] but accounts for only 1.2% in the present study. Besides *G. vaginalis*, the prevalence of *C. albicans*, HSV2, and HSV1 are also minimal. These findings are similar to other studies [5,22]. On the other hand, with no positive case of *T. pallidum*, this study suggests that urethritis may not be an acute symptom of this pathogen. Indeed, *T. pallidum* is more likely to be detected in patients with serologic confirmations and other locations, particularly in ulcers, rather than in the urethra [23]. Findings from this study provide a deep understanding of microorganisms causing urethritis in men which is essential in clinical practice since multiplex PCR is not always available and accessible in Vietnam.

Coinfections are significant with a prevalence of more than 40% and are more likely to be detected in patients with urethral discharge. Since the number of coinfections depends on how many microorganisms were tested, findings from different studies are not identical. The rate was high at 37.4% in a Japanese study where 13 causative pathogens of symptomatic

urethritis were examined [5]. On the other hand, only 19.7–25.8% of samples were positive with more than two microorganisms of the four most common ones tested, including *N. gonorrhoeae, C. trachomatis, T. vaginalis,* and *M. genitalium,* in studies conducted in African countries [16,17]. With the acceleration in the antibiotic resistance of *N. gonorrhoeae* [24] and the relatively high treatment failure rate of non-gonococcal urethritis with the initial treatment [25,26], coinfection, which is a challenge for clinicians, should be acknowledged.

This study indicates that *C. trachomatis* is the most common pathogen detected in heterosexual men with urethritis, followed by *N. gonorrhoeae*, *M. genitalium*, and others. Several studies in Vietnam have explored the prevalence of STIs in different study populations. However, they used PCR tests with a small number of pathogens, mainly focusing on *C. trachomatis* and *N. gonorrhoeae* [7,9–12]. Noticeably, despite the differences in study subjects, *C. trachomatis* was consistently found with the highest proportion among STIs tested by multiplex PCR, which varied at 4.3% among married women [7,11], 3.2% among men who have sex with men (MSM) [12], and 11.9–48.4% among female sex workers (FSW) [9,10]. In a study on 192 men with the symptoms of STIs, Le et al. detected the DNA of *C. trachomatis* and *N. gonorrhoeae* in 19.8% and 10.9% of urethral samples using loop-mediated isothermal amplification (LAMP) [8]. With the predominance of *C. trachomatis* in reproductive tract infections of both men and women, this bacteria needs to be prioritized in STIs-controlling programs in Vietnam. On the contrary, while testing only *C. trachomatis* and *N. gonorrhoeae*, the role of other microorganisms appears as having been underestimated in previous studies. Indeed, we found that the number of non-gonococcal and non-chlamydial urethritis is considerable, accounting for 20.9% of all cases. Therefore, screening for all possible pathogens using the wide-ranging test is required to optimize urethritis treatment, especially in men. Furthermore, the microbial etiology in women and other high-risk populations needs to be further investigated to provide health authorities and policymakers with accurate information on STIs to finely adjust their priorities and approaches.

In the past, urethral discharge played a crucial role in predicting gonococcal or chlamydial urethritis with high sensitivities at 100% for the former and 74% for the latter [27]. Using multiple logistic regression, Horner et al. reported an aOR of 12.3 (95%CI 2.39–63.5) being positive with *C. trachomatis* in patients with urethral discharge [28]. However, the result should be considered carefully since the above study was conducted decades ago with a high standard error in its analysis. In the present study, the probability of finding *C. trachomatis* in urethritis patients without discharge is higher than in those having this symptom after controlling for other factors. It suggests an increase in the number of atypical chlamydial urethritis without discharge that is easy to disregard or misdiagnosed.

In this study, *M. genitalium* is the third common pathogen found in urethritis men. Moreover, patients who reported using antibiotics before attending our clinic are more likely to be positive for *M. genitalium* than others. This bacterium had a high rate of treatment failure due to increased antimicrobial resistance and insufficient management of urethritis [25]. It is especially true for Vietnam where antibiotics can be bought in every pharmacy over the counter. The limitation of this study is that we could not identify the exact type, dose, and duration of antibiotics, which were not stored in the systems. In Vietnam, since *M. genitalium* is not well-reported as a critical pathogen of urethritis in men, using antibiotics without microbial evidence may be ineffective. Since the antibiotic susceptibility profile of *M. genitalium* is limited, further studies are required to fulfill this knowledge gap.

Interestingly, this study shows associations between exposures to female sex workers (FSWs) and the rates of detecting *N. gonorrhoeae, C. trachomatis,* or *M. genitalium* in patients. Men with only one romantic sex partner are less likely to be positive with *N. gonorrhoeae* but are more likely to be positive with *C. trachomatis* and *M. genitalium* compared with those having sex with FSW. These findings can be explained by the difference in transmission rate per sex act of these bacteria and the natural characteristics of sexual partner types. While there is a lack of information related to M. genitalium transmission [25], the estimated female-to-male transmission rates of *N. gonorrhoeae* and *C. trachomatis* were 20% and 3.75–15.4% per sex act, respectively [29,30]. *N. gonorrhoeae* transmits at a high rate than *C. trachomatis* [31]. Moreover, the transmission rate of *C. trachomatis* is even lower if the female partners were asymptomatic [29]. Since the likelihood of sex again with the same partner is low in casual sex or prostitution [32], men do not frequently contact FSW or one-off partners which explained their higher risk of being infected with *N. gonorrhoeae*. On the other hand, for microorganisms with low transmission rates, such as *C. trachomatis* and *M. genitalium*, accumulated sexual episodes with the infected partners are required to get an infection which is the case

for men with only one stable partner. Condom use is a key strategy in the management of STIs, from a "harm reduction" perspective [33]: however, the prevalence of condom use is not available in our data. While the type of sexual intercourse (anal, vaginal, or oral sex) may influence the transmission rate of specific STIs and the ability to detect them, this data is not assessed in our study. Since patients might have multiple sexual encounters before getting exposed to the STI, it was a challenge to correctly record this information. Therefore, more studies are required to support our findings.

Another limitation of our study is the lack of information on how STIs affected sexual function. To investigate this, prospective studies using validated questionnaires, such as the International Index of Erectile Function (IIEF) [34], the Premature Ejaculation Diagnostic Tool (PEDT) [35], and the Orgasmometer [36], would be needed. However, these studies are difficult to plan, as the risk of contracting STIs cannot be predicted and some STIs could be asymptomatic for a long time before the onset of clinical manifestations. Lastly, as the present study was conducted in the Andrology clinic, only data from sexually active men were investigated; prevalence and clinical phenotype of female STIs were thus not investigated, despite STIs being far more prevalent in women [37].

Conclusions

This study provides the microbial etiology of urethritis in men, which is still lacking in Vietnam. Besides some well-known pathogens like *C. trachomatis* and *N. gonorrhoeae*, other microorganisms also play important roles in causing urethritis in men, especially *M. genitalium*. Since the coinfection rate is quite high, targeted treatment with clear microbial evidence should be considered rather than empiric antimicrobial therapy. With limitations coming from the use of secondary data, further studies are required to explore associations between type of sexual partners and chances of detecting *C. trachomatis, N. gonorrhoeae,* or *M. genitalium*.

Author contributions

Bac Hoai Nguyen: conceptualization. Bac Hoai Nguyen and Long Hoang: data collection. Chau Minh Tran: sample processing in the laboratory. Quan Minh Pham and Andrea Sansone: formal analysis. Bac Hoai Nguyen, Andrea Sansone, Emmanuele A. Jannini, and Quan Minh Pham: drafting the article. Bac Hoai Nguyen and Emmanuele A. Jannini: critical revision and supervision.

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