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Original article

# *Mycoplasma genitalium* screening in a specialized French unit: A retrospective study

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ABSTRACT

*Objective:* *Mycoplasma genitalium* (MG) infection accounts for 10–35% of non-gonococcal non-chlamydial (NGNC) urethritis. However, given that most people infected with MG do not develop symptoms and that antimicrobial resistance is increasing worldwide, there is no evidence of any benefits of screening asymptomatic individuals. We conducted this study to describe MG screening practices and outcomes at a French Sexually Transmitted Infections (STI) center in which MG testing was performed selectively and multiplex assays were not carried out [i.e., simultaneous screening for *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), and MG].

*Methods:* A retrospective, observational, single-center study was conducted at the STI unit of Saint-Louis Hospital in Paris. The records of all patients undergoing MG testing from January 1st, 2017, to December 31st, 2018, were reviewed. The primary aim of the study was to describe and evaluate the proportion of MG-positive (MG+) patients among those tested. Secondary objectives were determination of the prevalence of MG+ status among symptomatic patients, risk factors associated with MG infection, and therapeutic modalities and efficacy.

*Results:* Two hundred and forty-nine patients underwent MG testing, 28 (11%) of whom were positive (MG+). The prevalence of MG+ status among symptomatic NGNC patients was 12%. HIV-positive (HIV+) status was significantly associated with MG+ status in univariate and multivariate analyses (Odds Ratio = 7.3, 95% Confidence Interval 1.3-41.7; $P = 0.02$). Twenty-three patients (85%) received antibiotics. Eighteen (67%) received azithromycin for 5 days, but 7 had clinical resistance. No quinolone resistance was reported.

*Conclusion:* Despite unavailability of multiplex testing at our facility, which led to targeted-only screening for MG, its relatively high local prevalence is in keeping with what is generally observed at similar facilities across the world, where use of multiplex tests enables systematic screening for MG alongside NG and CT. This reinforces the current recommendations in Europe, France and the US against systematic MG testing or treatment in asymptomatic patients.



## 1. Introduction

*Mycoplasma genitalium* (MG) prevalence ranges from 1% to 2%, but recent studies have reported a prevalence in Sexually Transmitted Infections (STI) clinics of around 10% [1,2]. Risk factors associated with MG infection include HIV positivity (HIV+) in men who have sex with men (MSM), younger age, non-white ethnicity and a high number of sexual partners [1,3]. Although the proportion of infected patients who develop symptoms is unknown and probably low, MG is strongly associated with non-gonococcal non-chlamydial urethritis (NGNCU) and is the cause in 10-35% of cases [4,5]. In women, it is associated with increased risk of cervicitis, pelvic inflammatory disease, pre-term birth, and spontaneous

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abortion [6]. However, its role in infertility has not been demonstrated.

Since MG is a slow-growing bacterium, culture is not appropriate for diagnostic purposes. Use of nucleic amplification tests (NAAT) for diagnosis is now recommended [7]. Several NAATs are available, including multiplex assays allowing simultaneous screening for *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT) and MG. The European guideline advocates first-line treatment of MG infection with azithromycin 500 mg on day one followed by 250 mg once daily on days two to five [7]. Alternative azithromycin regimens are suggested in Australia (1 g on day one followed by 500 mg daily on days two to four) and in the UK (doxycycline 100 mg twice daily for 7 days followed by azithromycin 1 g on day one, then 500 mg once daily for two days) [8,9]. Macrolide-resistance (MacR) in MG is increasing worldwide, being reported in over 50% of sampled strains in some countries [10]. The European guideline recommends that all MG-positive (MG+) subjects should undergo assay to screen for MacR [7]. Moxifloxacin is given as second-line treatment or where MacR is detected [7]. However, cases of quinolone-resistance are also emerging [10].

Given that most people infected with MG do not develop symptoms and that antimicrobial resistance is increasing worldwide, to date there is no evidence of any benefits or cost-effectiveness of screening for asymptomatic individuals [11]. To address this issue, the French Society of Dermatology and the MG National Reference Center released a joint note in 2019 recommending against testing or treatment of asymptomatic patients [12].

The objective of this study was to describe MG screening practices and outcomes in a French STI center not using multiplex assays and thus with selective MG testing of patients before the note was published.

## 2. Methods

### 2.1. Study design and patients

We conducted an observational, retrospective, single-center study at the Sexually Transmitted Diseases unit of Saint-Louis Hospital, Paris. All patients seen at our clinic and undergoing MG testing from January 1st, 2017, to December 31st, 2018, were included.

Genital, anal and oral swabs as well as urine samples were collected at our clinic, and polymerase chain reaction (PCR) NAAT of MG was performed at the microbiology laboratory of Saint-Louis Hospital, Paris. Assay was performed using the Cobas 6800® system (Roche Diagnostics®).

### 2.2. Procedures

The following data were collected: dates of MG testing and test-of-cure (TOC) when this was performed (at least 3 weeks after treatment), age, gender, sexual orientation, symptoms, medical history of MG infection, STI co-infection, symptoms and infection of partner(s), and treatment modalities and efficacy.

### 2.3. Outcomes

The study objective was to describe all patients tested for MG. We then evaluated the prevalence of MG+ status among symptomatic patients, identified risk factors associated with MG infection, and described treatment modalities and efficacy.

### 2.4. Statistical analysis

Continuous variables were described using medians and ranges. Discrete variables were described using counts and percentages. Univariate logistic regression models were used to assess the association of covariates with MG positivity. The covariates examined were age, gender, sexual orientation (contrasting MSM with other sexual orientations), number of sexual partners per year (assessed as a continuous variable or as a binary variable using a threshold of 10 sexual partners per year), HIV+ status and symptoms (contrasting urethral discharge with other or no symptoms). A multivariate logistic regression model was applied to eliminate potential confounders. Covariates with *P*-values below 0.2 in the univariate analysis were included in the multivariate regression model. Age and number of sexual partners were included because of a known association with *M. genitalium* infection [1]. Symptoms were not included in the multivariate model since they constitute an intermediate variable between demographic and sexual characteristics and MG infection. For all statistical analyses, type 1 error was set at 5%. Statistical analysis was performed using RStudio Version 1.0.136 (RStudio Inc., Boston, MA, USA).

## 3. Results

### 3.1. Patient characteristics in the population screened for MG

Two hundred and forty-nine patients underwent MG testing (132 in 2017 and 117 in 2018). The records of three patients were lost, resulting in no demographic information. Among the 246 patients for whom clinical details were available, mean age was 34 years (range: 15-76 years). The sex ratio was 10.2 (224 men and 22 women). Fifty-six patients (23%) had had 10 or more sexual partners/year. Eighty-five patients (35%) were MSM and 13 (5%) were HIV+. NG and CT were detected in 7 (3%) and 12 (5%) patients, none of whom had concomitant MG+ status.

MG testing was performed secondarily after a negative CT or NG test in 139 patients (59%). Of these, 131 were re-tested for NG or CT, with 2 (1%) being NG+ and 8 (6%) CT+. Twenty-two patients (9%) were tested because of an MG+ partner. Among patients tested fo MG first-intention, 100 (93%) were also tested for NG and CT. Five were NG+ (5%), all of whom had clinical symptoms, and 4 were CT+ (4%), including 2 with clinical symptoms.

Thirty patients (12%) were asymptomatic. Others reported symptoms of urethritis (urinary pain, burning or itching), including 69 (28%) with urethral or vaginal discharge.

The complete characteristics are presented in Table 1.

### 3.2. Characteristics of MG+ patients

In the total population, 28 patients were MG+ (11%). Among the 27 patients whose clinical data were available, 13 (48%) were MSM and 5 (19%) were HIV+. Fourteen (52%) were first-intention. Only 3 (11%) were asymptomatic, and symptoms were not specified for 1. One patient with anal MG+ had mild symptoms of proctitis, without discharge. Four (15%) had an MG+ partner. The complete characteristics are presented in Table 1.

### 3.3. Prevalence of symptomatic MG+ patients

Following exclusion of asymptomatic NG+ and CT+ patients ($n = 197$), 23 (12%) had MG+ NGNC symptomatic infection (174 symptomatic patients were NGNC MG−). Seventeen (74%) infections were detected in urine samples, 5 by genital swab, and 1 by anal swab.

### 3.4. Determinants of MG+ infection

In the univariate and multivariate analyses, HIV+ status was significantly associated with MG+ (OR = 7.25, 95%CI = 1.31–41.73, $P = 0.02$ after adjustment for age, sexual orientation and number

**Table 1**
Characteristics of MG+ and MG- patients.

| Characteristics | MG+ ($n$ = 27) | MG− ($n$ = 219) |
|---|---|---|
| Age in years, mean (range) | 28 (18–61) | 31 (15–76) |
| Gender, male (%) | 24 (89) | 200 (91) |
| Sexual orientation, $n$ (%) | | |
| WSM[a] | 1 (4) | 15 (7) |
| WSW[b] | 2 (7) | 2 (1) |
| MSW[c] | 11 (41) | 120 (55) |
| MSM[d] | 13 (48) | 72 (33) |
| Unknown | 0 (0) | 10 (5) |
| ≥ 10 sexual partners/year, $n$ (%) | 9 (33) | 47 (21) |
| HIV+, $n$ (%) | 5 (19) | 8 (4) |
| HIV prophylaxis use (PrEP), $n$ (%) | 2 (7) | 11 (5) |
| Personal history of MG+, $n$ (%) | 5 (19) | 8 (4) |
| Partner MG+, $n$ (%) | 4 (15) | 18 (8) |
| Symptoms, $n$ (%) | | |
| Urethral or vaginal discharge | 13 (48) | 56 (26) |
| Other (pain, burning, itching, etc.) | 10 (37) | 134 (61) |
| Asymptomatic | 3 (11) | 27 (12) |
| Unknown | 1 (4) | 2 (1) |
| Sample collection method, $n$ (%) | | |
| Urine | 19 (70) | 190 (87) |
| Genital swab | 5 (19) | 31 (14) |
| Anal swab | 3 (11) | 12 (5) |
| Oral swab | 0 (0) | 8 (4) |

MG = *Mycoplasma genitalium*; PrEP = Pre-exposure prophylaxis. Three patients were not described since their medical records were lost (1 MG+ and 2 MG−).
[a] WSM = women who have sex with men.
[b] WSW = women who have sex with women.
[c] MSW = men who have sex with women.
[d] MSM = men who have sex with men.

of sexual partners). Age, gender, sexual orientation and number of sexual partners were not associated with MG+ (Table 2). MG+ patients had significantly more urethral or vaginal discharge than MG− patients in the univariate analysis (OR = 2.88, 95%CI = 1.25–6.63, $P$ = 0.01).

### 3.5. Treatment of MG+ patients

Twenty-three patients (85%) received antibiotics. Most patients ($n$ = 18, 67%) received azithromycin for 5 days as first-line treatment, in accordance with the European guideline [7]. Two patients received moxifloxacin as first-line treatment, including one due to detection of MacR MG in their sexual partner. Four patients (15%) received no treatment (2 were lost to follow-up and for the 2 others, their physicians provided no information), and 3 received doxycycline, azithromycin 1 day or ofloxacin for 14 days with no rationale being provided by the practitioners. The efficacy of azithromycin was documented in 5 patients, contrasting with 7 presenting clinical MacR, and 6 were lost to follow-up. Among patients with MacR, 3 received moxifloxacin as second-line treatment with good efficacy (3 negative TOC) and 3 received doxycycline (1 negative TOC, 2 clinical resistance). One patient with positive TOC two months after first-line azithromycin did not receive any further treatment and exhibited spontaneous clearance of MG with negative a TOC 4 months later.

## 4. Discussion

Our study was conducted to describe patients undergoing MG NAAT in a unit that does not perform multiplex assay, prior to publication of French recommendations regarding screening and treatment for MG [12]. This study reflects real-life practice regarding MG screening, with MG detection being left to the appreciation of the clinician, and not all patients presenting at our clinic were thus tested. We found a prevalence of MG+ infections of 12% among symptomatic NGNC patients, in keeping with the majority of studies [5,7]. Most patients were tested for MG after negative CT and NG testing, as would eventually be recommended. Of the 23 patients tested due to an MG+ partner, only 4 were themselves MG+. This data reinforces the notion of low sexual transmission of MG. Some countries recommend screening of contact partners, but this measure remains controversial [7,9,12]. Indeed, we showed that clinicians already seemed to test only selected patients, and the spread of multiplex assays inclusive of MG thus carries a risk of overdiagnosis.

As described in previous reports, HIV+ status is strongly associated with MG+ status [13,14]. Immunosuppression due to HIV or increased transmission of HIV because of MG urethritis could account for this association. However, neither the number of sexual partners in the previous year nor younger age were associated with MG+ status. Lack of statistical power due to the small number of MG+ patients compared to previous published data or possible recall bias concerning the number of partners could account for these results [2,15].

Most (85%) patients were treated but not all received the recommended antibiotics [7]. At least 39% of our patients had clinical MacR, which is higher than levels reported in western European countries but concordant with published French data (43% MacR in 2017 and 2018 – *Centre National de Référence des Infections Sexuellement Transmissibles Bactériennes, Bordeaux*) [10,16]. Although different assays exist to screen for MacR through amplification and sequencing of the 23S rRNA gene, none was available in our unit at the time of the study. Resistance-guided treatment will be helpful in trying to overcome these issues [7]. A recent trial recommended the use of doxycycline as first-line treatment, followed by azithromycin or moxifloxacin depending on MacR status, with high (> 90%) cure rates [17]. Some authors have hypothesized that despite low cure rates with doxycycline alone, its use as first-line treatment could reduce bacterial burden and improve cure rates with azithromycin or moxifloxacin.

In conclusion, despite targeted-only screening for MG, its relatively high local prevalence is in keeping with what is generally observed at similar facilities across the world. This reinforces the

**Table 2**
Univariate and multivariate analysis of factors associated with MG.

| | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| Characteristics | OR | 95% CI | $P$-value | OR | 95% CI | $P$-value |
| Age | 0.98 | (0.94–1.02) | 0.36 | 0.981 | (0.939–1.019) | 0.12 |
| Gender, men | 0.76 | (0.24–3.38) | 0.67 | | | |
| Sexual orientation, MSM* | 1.77 | (0.78–3.98) | 0.17 | 1.77 | (0.78–3.98) | 0.52 |
| Number of sexual partners/year | | | | | | |
| Continuous variable | 1.01 | (0.99–1.02) | 0.24 | 1 | (0.978–1.018) | 0.96 |
| ≥ 10 | 1.78 | (0.70–4.33) | 0.21 | | | |
| HIV+ | 6.16 | (1.72–20.33) | 0.003 | 7.25 | (1.31–41.73) | 0.02 |
| Urethral or vaginal discharge | 2.88 | (1.25–6.63) | 0.01 | | | |

OR: odds ratio; CI: confidence interval.
* MSM = men who have sex with men.

current recommendation in Europe, France and the US against routine testing and treatment for MG and casts doubt on the relevance of multiplex assays beyond CT and NG, particularly in asymptomatic patients.

## Disclosure of interest

The authors declare that they have no competing interest.

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