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Brief report

Mycoplasma genitalium in Spain: prevalence of genital infection and frequency of resistance to macrolides



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ABSTRACT

Introduction: The aim of this study was to determine the prevalence of *Mycoplasma genitalium* infection and the resistance to macrolides within a general population in Madrid in 2015.

Methods: We collected 359 urine samples from a general population with symptoms of sexually transmitted infections (STIs). All samples underwent a real-time PCR. For the detection of macrolide resistance, a 283 bp fragment of region V of the 23S rRNA gene of *M. genitalium* was amplified and sequenced.

Results: We found a prevalence of 3.34% of *M. genitalium* and a macrolide resistance rate of 20%. In males, the prevalence was 6.62% and in women 0.96%, being significantly higher in males.

Conclusions: The prevalence obtained shows that it is a pathogen to consider in our environment. These findings stress the need for routine testing of *M. genitalium* infections and would seem to suggest the advisability of resistance testing.

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Mycoplasma genitalium en España: prevalencia de infección genital y frecuencia de resistencia a macrólidos

RESUMEN

Introducción: El objetivo de este estudio fue determinar en 2015 en una población general de Madrid la prevalencia de infección por *Mycoplasma genitalium* (*M. genitalium*) y la resistencia a macrólidos.

Métodos: Se recogieron 359 muestras de orina procedentes de una población general con síntomas de infección de transmisión sexual. A todas las muestras se les realizó una PCR a tiempo real. Para la detección de resistencias a macrólidos, se amplificó y secuenció un fragmento de 283 pb de la región v del gen 23S rRNA de *M. genitalium*.

Resultados: Se encontró una prevalencia de un 3,34% de *M. genitalium* y un 20% de resistencia a macrólidos. En varones la prevalencia fue del 6,62% y en mujeres del 0,96%, siendo significativamente superior en varones.

Conclusión: La prevalencia obtenida muestra que es un patógeno a considerar en nuestro entorno. Estos hallazgos hacen hincapié en la necesidad de realizar pruebas de rutina de infección por *M. genitalium* y argumentan que es recomendable realizar pruebas de resistencia.

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Table 1
Prevalence of *M. genitalium* in the 359 samples studied.

	MG	CT	NG	CT+NG
Men	10/151 (6.62%)	18/151 (11.92%)	10/151 (6.62%)	5/151 (3.31%)
Women	2/208 (0.96%)	12/208 (5.77%)	0/208 (0%)	1/208 (0.48%)
Total	12/359 (3.34%)	30/359 (8.36%)	10/359 (2.78%)	6/359 (1.67%)

MG: *Mycoplasma genitalium*, CT: *Chlamydia trachomatis*, NG: *Neisseria gonorrhoeae*.

Mycoplasma genitalium is a fastidious organism found in the urogenital tract of humans now recognized as a common cause of nongonococcal urethritis in men. In addition, it is associated with increased risk for cervicitis, pelvic inflammatory disease, and spontaneous abortions in women.^{1–3}

Routine diagnostic detection is based on nucleic acid amplification methods.

The recommended treatment for *M. genitalium* is a single dose of 1 g azithromycin, but in certain environments this pathogen responds poorly, having declined the eradication rate over the years.^{4,5} This has been associated with the development of resistance to macrolides,⁶ predominantly based on single point mutations in the V-region of the 23S rRNA gene.^{6,7}

There are still a limited number of studies related to the prevalence of *M. genitalium* in the world, that can widely differ depending on both the geographic location and the population tested; there are less studies related to resistance to azithromycin. The aim of this study was to determine the prevalence of *M. genitalium* infection and the resistance to macrolides in a symptomatic general population of two separate areas of the Community of Madrid, Spain.

Between May and September 2015, 359 urine samples of patients attending general inquiries or emergency departments with symptoms suggestive of sexually transmitted infections (STIs) were collected from two separate areas of the Community of Madrid: the Getafe area with a population of 210,133 inhabitants (3.29% of the population of Madrid), and the La Paz area with 500,445 inhabitants (7.83% of the population of Madrid). 151 were from men (42.1%) and 208 from women. 7.52% of patients were aged between 0 and 20 years, 66.29% between 21 and 40 years, 20.89% between 41 and 60 years, and 2.2% were over 60 years. The samples underwent a technique of real time PCR in the Cobas 4800 (Roche®) to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* (Cobas 4800 CT/NG Test, Roche®) and *M. genitalium* (*M. genitalium* EC LightMix Kit, Roche®) as per manufacturers protocol.

For the detection of macrolide resistance, a 283 bp fragment of region V of the 23S rRNA gene of *M. genitalium* were amplified and sequenced.⁷

Of the 359 urine samples tested, 12 were found PCR-positive for *M. genitalium*, representing 3.34% of prevalence (95% CI, 1.48%–5.20%). In males, it was 6.62% (95% CI, 4.05%–9.19%) (10/151) and in women 0.96% (95% CI, 0%–1.97%) (2/208) (Table 1). Prevalence was significantly higher in males ($p = 0.003$). The age range of infected patients was 21–40 (11/12) and 41–60 (1/12).

In the 359 samples studied, only *C. trachomatis* was detected in 30 (8.36%), only *N. gonorrhoeae* was detected in 10 (2.78%), and in 6 (1.67%) both agents were detected (Table 1).

Regarding the resistance results, we were able to determine it for 10/12 *M. genitalium* positive samples. Of these, 2 (20%) carried mutations that would render them resistant to macrolides: one of them had a mutation in the position A2058T and the other in A2059G.

To our knowledge there are no publications on the prevalence of *M. genitalium* in Spain, our study aimed to assess it in a general population of Madrid. The prevalence obtained, 3.34%, shows that it is a pathogen to consider in our environment in patients with symptoms suggestive of STIs. Infection with *M. genitalium* is generally assumed to result in more frequently clinical signs in males and this is supported by our finding that the prevalence was significantly

higher in men than in women. The prevalence is in the range of other agents of STIs commonly searched for. However, testing for *M. genitalium* is not common, and in our opinion routine screening for this pathogen is advisable.

The studies carried out to date in other countries show different data. In the US, a national study in healthy young people, 1714 men and 1218 women, obtained a prevalence of 1%.⁸ In Sweden, in a heterogeneous population of 5519 women attending a gynecological clinic *M. genitalium* was found in 2.1%.⁹ In the UK, in 216 men with urethritis and without urethritis attending a genitourinary medicine clinic, the prevalence was 10.2%, higher in patients with urethritis.¹⁰ However, in France, in a study of 301 patients younger than 31 years who went to the emergency room with symptoms, a prevalence of 0.3%¹¹ was found. In Denmark, 28,958 patients attending specialists and general hospitals were studied between 2006 and 2010, and the prevalence obtained, according to the year, was 2.4%–3.8% in women and 7.9%–10.3% in men.¹² In Spain, there is no publication that discusses the prevalence of this organism, which makes this study of prevalence, co-infection, and macrolide resistance innovative. The findings in our study are similar to those obtained in the Denmark study¹² that was also performed in the general population, but differs from other studies carried out in specific and selected population.

Data of macrolide resistance in other countries are also diverse and range from 14.2% to 43%.^{7,12,13} The data obtained in our study indicate an average rate of resistance compared to other studies.

After the rate of resistance to macrolides obtained, we thought that detection of macrolide resistance is required to guide the clinician in the choice of antibiotic and limiting the selection and propagation of resistances,⁶ and thus avoiding therapeutic failures. As an alternative, we propose a test of cure (test of cure) on day 14 or later, due to the low probability of detecting nonviable DNA and its association if it is positive with resistance to azithromycin.^{5,14}

Conflict of interest

None.

References

1. Anagrus C, Loré B, Jensen J. *Mycoplasma genitalium*: prevalence, clinical significance and transmission. *Sex Transm Infect.* 2015;81:458–62.
2. Taylor-Robinson D, Jensen JS. *Mycoplasma genitalium*: from Chrysalis to multi-colored butterfly. *Clin Microbiol Rev.* 2011;24:498–514.
3. McGowan CL, Anderson-Smits C. *Mycoplasma genitalium*: an emerging cause of sexually transmitted disease in women. *PLoS Pathog.* 2011;7:e1001324.
4. Lau A, Bradshaw CS, Lewis D, Fairley CK, Chen MY, Kong FY, et al. The efficacy of azithromycin for the treatment of genital *Mycoplasma genitalium*: a systematic review and meta-analysis. *Clin Infect Dis.* 2015;61:1389–99.
5. Bissessor M, Tabrizi SN, Twin J, Abdo H, Fairley CK, Chen MY, et al. Macrolide resistance and azithromycin failure in a *Mycoplasma genitalium*-infected cohort and response of azithromycin failures to alternative antibiotic regimens. *Clin Infect Dis.* 2015;60:1228–36.
6. Jensen JS, Bradshaw CS, Tabrizi SN, Fairley CK, Hamasuna R. Azithromycin treatment failure in *Mycoplasma genitalium*-positive patients with nongonococcal urethritis is associated with induced macrolide resistance. *Clin Infect Dis.* 2008;47:1546–53.
7. Nijhuis RH, Severs TT, Van der Vegt DS, Van Zwet AA, Kusters JG. High levels of macrolide resistance-associated mutations in *Mycoplasma genitalium* warrant antibiotic susceptibility-guided treatment. *J Antimicrob Chemother.* 2015;70:2515–8.

8. Manhart LE, Holmes KK, Hughes JP, Houston LS, Totten PA. *Mycoplasma genitalium* among young adults in the United States: an emerging sexually transmitted infection. *Am J Public Health*. 2007;97:1118–25.
9. Bjartling C, Osseir S, Persson K. *Mycoplasma genitalium* in cervicitis and pelvic inflammatory disease among women at a gynecologic outpatient service. *Am J Obstet Gynecol*. 2012;206:e1–8.
10. Pond MJ, Nori AV, Witney AA, Lopeman RC, Butcher PD, Sadiq ST. High prevalence of antibiotic-resistant *Mycoplasma genitalium* in nongonococcal urethritis: the need for routine testing and the inadequacy of current treatment options. *Clin Infect Dis*. 2014;58:631–7.
11. Bayette J, Jreige R, Marchandin H, Laurens C, Joullie F, Clarivet B, et al. Prevalence of *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma genitalium* infections in the emergency department. *Pathol Biol (Paris)*. 2013;61:245–9.
12. Salado-Rasmussen K, Jensen JS. *Mycoplasma genitalium* testing pattern and macrolide resistance: a Danish nationwide retrospective survey. *Clin Infect Dis*. 2014;59:24–30.
13. Touati A, Peuchant O, Jensen JS, Bébér C, Pereyre S. Direct detection of macrolide resistance in *Mycoplasma genitalium* isolates from clinical specimens from France by use of real-time PCR and melting curve analysis. *J Clin Microbiol*. 2014;52:1549–55.
14. Falk L, Enger M, Jensen JS. Time to eradication of *Mycoplasma genitalium* after antibiotic treatment in men and women. *J Antimicrob Chemother*. 2015;70:3134–40.