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Brief report

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Mycoplasma genitalium and sexually transmitted infections: evidences and figures in a tertiary hospital

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ABSTRACT

Introduction. *Mycoplasma genitalium* is an emerging cause of sexually transmitted infections (STIs) and has been implicated in non-gonococcal urethritis in men and cervicitis in woman. The aim of this study is determinate the incidence and pathogenicity of *M. genitalium* within the diagnosis of STIs detected from clinical samples in a third level hospital.

Material and methods. A total of 8,473 samples from endocervix, urethra, vagina, rectum and others were processed applying Allpex STI Essential Assay. More than 190 records were reviewed to determinate *M. genitalium* pathogenicity.

Results. *M. genitalium* was detected in a rate 2.8%. Co-infections were detected in 20% of the patients.

Conclusions. *M. genitalium* is considered a STI emerging pathogen thanks to the renewal of multiplex-PCR tests although with a low incidence in our approach. Emerging from our experience and the institutional recommendations both detection of acid nucleic techniques (NAATs) and gonococcal culture might be implemented accurately and coexist to adequate prescriptions.

Keywords: *Mycoplasma genitalium*, sexually transmitted infections, coinfection

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Mycoplasma genitalium en el renovado diagnóstico de las infecciones de transmisión sexual: evidencias y cifras en un hospital terciario

RESUMEN

Introducción. *Mycoplasma genitalium* es un patógeno emergente causante de infecciones de transmisión sexual (ITS) y se ha relacionado con uretritis no gonocócica en hombres y cervicitis en mujeres. El objetivo de este estudio es determinar la incidencia y patogenicidad de *M. genitalium* en el seno del diagnóstico de ITS detectadas a partir de muestras clínicas en un hospital terciario.

Métodos. Se procesaron 8.473 muestras de endocérvix, uretra, vagina, recto y otros, aplicando Allpex STI Essential Assay. Se revisaron más de 190 historias clínicas para determinar la patogenicidad de *M. genitalium*.

Resultados. Se detectó *M. genitalium* en 2,8% de casos. Hubo coinfecciones en 20% de los pacientes.

Conclusiones. *M. genitalium* a pesar de la baja incidencia en nuestra revisión, actualmente es un patógeno de valor en alza gracias al desarrollo de técnicas moleculares como PCR-multiplex. A partir de nuestra experiencia y las recomendaciones institucionales, tanto las técnicas de detección de ácidos nucleicos (NAATs) como los cultivos para gonococo deberían implementarse y coexistir para adecuar los tratamientos.

Palabras clave: *Mycoplasma genitalium*, infección de transmisión sexual, coinfección

INTRODUCTION

Mycoplasma genitalium is the smallest known self-replicating bacterium that cause non-gonococcal urethritis in men and cervicitis in women. Co-infections with *M. genitalium* and other bacterial sexually transmitted infections (STIs) have fre-

quently reported. Its prevalence varies among sexually transmitted infection clinic attendees and the general population [1]. In our community, there is not a reference centre for attending STI patients and they are referred from Primary Care to specialities (dermatology, ginecology, infectious diseases) and directly to our microbiology lab at Miguel Servet Hospital (HUMS). The general purpose of this study was to determine the incidence and pathogenicity of *M. genitalium* within the STIs detected from clinical samples sent to our laboratory and discuss the renewal procedures and laboratory changes in the diagnosis of STI.

MATERIAL AND METHODS

A real-time PCR (Allplex STI Essential Assay by Seegene) was the detection method applied in vaginal, endocervical, and urethral samples. This assay detects simultaneously 7 microorganisms: *Chlamydia trachomatis*, *Mycoplasma genitalium*, *Mycoplasma hominis*, *Neisseria gonorrhoeae, Trichomonas vaginalis*, *Ureaplasma parvum*, *Ureaplasma urealyticum*. At the same time, samples were cultured on Columbia blood, Chocolate, VCA *Neisseria gonorrhoeae* and Sabouraud agar.

Antibiograms from positive cultures for *Neisseria gonorrhoeae* were done on GCII agar supplemented with Isovitalex (Becton-Dickinson) following the recommendations from EUCAST and using a control strain ATCC 49226.

From January 2019 to October 2020, 8,473 samples were processed from 6,058 patients. In this period, our hospital assisted a population of 586,835 inhabitants.

We reviewed the number of *M. genitalium* detected by PCR in this period and age, sex, co-infections and clinical evidence were analysed from the LIS records.

RESULTS

From 8,473 samples submitted to Allplex assay, *M. genitalium* was detected in 234 (2.8%) from 232 patients (106 males;126 females). The mean age was 29.8 years, being the group between 19 and 35 years old almost 70% of the cases. Samples were from endocervix (103), urethra (84), vagina (18), urine (16), rectum (11), others (2).

From the review of 194 available clinical records about *M. genitalium* isolates, 43 (22%) were clinically significant and were treated (52% azithromycin, 32% moxifloxacin, 16% doxycycline). The median cycle threshold- (*CT*) was 25.3 in the infected group and 30.3 in the non-infected group. Therefore, during this period, the prevalence of *M. genitalium* was 0.07‰ and the incidence density rate was 3.8 new cases/100 patients/year.

The incidence rate of *N. gonorrhoeae*, *C. trachomatis* and *T. vaginalis* in the same period is presented in table 1. Despite the decrease in the number of samples in 2020 compared to the previous years, there was an 11% of increase in the number of positive gonococcal cultures.

Co-infections were in 16/106 male patients with *M. genitalium* detected (9 *N. gonorrhoeae*, 6 *C. trachomatis*, 1 *T. vaginalis*) and in 31/126 female patients (23 *C. trachomatis*, 5 *T. vaginalis*, 3 *N. gonorrhoeae*). *M. genitalium* was detected together with *M. hominis* (5) and *U. urealyticum* (4) with an uncertain value not clinically related.

DISCUSSION

M. genitalium is a considered pathogen but in our experience, the incidence was low and less than 25% of patients with a positive sample was clinically significant and treated. Different consideration deserves the diagnosis of gonorrhoea established by the detection of *N. gonorrhoeae* at an infected site, either by nucleic acid amplification (NAATs) or by culture. Symptoms and signs of sexually acquired infection depend, in part, on the site of infection. One of the most important and scary pathogen, *N. gonorrhoeae*, is on an emerging trend since the last decade [2]. Co-existing infections such as *C. trachomatis, T. vaginalis, M. genitalium, Candida albican*s and conditions as bacterial vaginosis, are common and these should be considered for an optimal and efficacious treatment but its interpretation is often difficult [3].

The approach to diagnose any infectious diseases will be oriented by the clinical examination, but sexually transmitted diseases (STDs) need a more specific and in-depth oriented exam and interview of sexual behaviours [4].

Having fast NAAT tests allows a personalized, practical, preventive and predictive assistance. NAATs are more sensitive than culture, particularly for oropharyngeal and rectal

Table 1 **Prevalence and incidence rate of *M. genitalium*, *N. gonorrhoea*, *C. trachomatis* and *T. vaginalis* infections during the study period (2019-2020).**

	N. Cases	Population at risk	Prevalence ‰	Incidence rate %
M. genitalium	43	6,058	0.07	0.7
N. gonorrhoea	498	6,985	0.84	7.1
C. trachomatis	740	6,985	1.26	10.6
T. vaginalis	186	6,985	0.32	2.7

sites and they show high sensitivity (>95%) in both symptomatic and asymptomatic infection but indirectly these tests promotes the detriment and oblivion of classical tests (rapid wet mount smear or Gram stain, special media cultures ...). So that, it is assumed that the primary role of culture is not for diagnostic purposes but for antimicrobial susceptibility testing prior to prescribe any treatment.

In the study of Salmeron et al. [5], a prospective multicentre study in ten hospitals in Spain (including ours), only 49% of gonococcal infections had a positive culture available for antimicrobial susceptibility testing. Azithromycin resistance was found in 12% and high-level resistance (MIC>256 mg/L) was detected in 0.1% of all cases. As long as antimicrobial resistance in *N. gonorrhoeae* continues spreading, cultures will survive. Despite the decrease in the number of samples and patients in 2020, we detected an 11% of increase in the number of positive gonococcal cultures [6]. The rate of gonococcal resistance to azithromycin detected in our lab was between 19 and 24% of the isolates and 64% to ciprofloxacin. There was no isolate resistant to ceftriaxone. These are the reasons for the culture survival.

The detection of antimicrobial resistance genes enclosed in the multiplex PCR tests or the whole genome sequencing armamentarium threaten cultures to be banished. Nevertheless, the "multiplex" results of the NAATs must be interpreted cautiously, because bacteria as *M. genitalium, M. hominis, U. urealyticum and U. parvum* can pose confounding approaches, potential partner conflict and misuse of antibiotics. *M. genitalium* was detected in our study in a low rate 2.8% and a very low prevalence. From the review of near two hundred available clinical records, it was relevant in less than 25% of patients and treated.

Co-infections pose another growing barrier for specific implementation of prevention strategies. In our study, coinfections were detected in 47 patients (20%), mainly *M. genitalium* and *C. trachomatis* (29 cases), *or N. gonorrhoeae* (12 cases) or *T. vaginalis* (5 cases). In the article of Rob et al [7], the prevalence of co-infections in men who have sex with men (MSM) was significantly higher (20%) than in heterosexual men and women (4.2%), and it was significantly associated with HIV infection. Syphilis, HIV together with *N. gonorrhoeae and C. trachomatis* show how co-infections can be missed in rectal and pharyngeal localizations in asymptomatic patients, who can further spread these co-infections [7].

In agreement with the comments from Roland C. Merchant in Annals of Emergency Medicine [8], accurate point-of-care rapid tests would permit the more efficient use of antimicrobials and would reduce the inherent difficulties in attempting to notify patients of their test results after their emergency department visit.

Emerging from our experience and the institutional recommendations [9,10], both NAATs and primary and following cultures need to live together in good harmony and fitness to prevent the blind prescriptions from spreading fatal errors.

In a recent article published by Dumke et al. [11], about some important strategies to establish regional networks of laboratories that can perform gonococcal culture and resistant gene detection of *M. genitalium* (quinolones and macrolides), they highlight the importance of a good quality control mechanisms to detect treatment failures by developing a standard protocol of follow-up.

Our study has the limitation of the small number of patients with enough clinical data an also the default of a long follow-up of asymptomatic patients (just 3 months in symptomatic) and their partners to know the real prevalence and clinical impact of *M. genitalium*. Nevertheless, we did not take into account the positive samples of asymptomatic patients in accordance with recent publications and guidelines [12-14]. Screening of asymptomatic *M. genitalium* infection among women and men or extragenital testing for *M. genitalium* is not recommended.

In conclusion, *M. genitalium* is considered a STI pathogen thanks to the renewal of multiplex-PCR tests although with a low incidence in our approach.

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None to declare

CONFLICTS OF INTEREST

The authors declare no conflict of interest

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