www.jsstd.org

Journal of Skin and Sexually Transmitted Diseases

ScientificScholar® Knowledge is power
Publisher of Scientific Journals

IADVL 1973 IADVL KERALA

Review Article

Sexually transmitted infection by *Mycoplasma genitalium*: A short review

Sapna Harish

Department of Genitourinary Medicine and HIV, Chelsea and Westminster Hospital NHS Foundation Trust, Hammersmith, London, United Kingdom.

***Corresponding author:**
Sapna Harish,
Department of Genitourinary Medicine and HIV, Chelsea and Westminster Hospital NHS Foundation Trust, Hammersmith, London, United Kingdom.

sapnaharish768@gmail.com

Received : 14 February 2021
Accepted : 01 March 2021
Published : 06 April 2021

DOI
10.25259/JSSTD_14_2021

Quick Response Code:

ABSTRACT

Mycoplasma genitalium is identified as a pathogen causing sexually transmitted infection. Difficulty to culture the organism has been a major obstacle in understanding more about the pathogenesis. Lack of facility to diagnose the disease in many centers has led to syndromic management. Widespread treatment of asymptomatic individuals who test positive for the organism and syndromic management have resulted in emergence of drug-resistant strains.

Keywords: *Mycoplasma genitalium*, Sexually transmitted infection, Asymptomatic individuals, Diagnosis, Management

INTRODUCTION

Recent years have seen much interest in research and knowledge about *Mycoplasma genitalium* (*M. genitalium)* as a pathogen capable of causing sexually transmitted infection (STI). Centers for Disease Control and Prevention sexually transmitted diseases treatment guidelines, published in 2015, have placed *M. genitalium* under emerging issues.[1]

About 15%–20% of non-gonococcal urethritis (NGU) cases, 20%–25% of non-chlamydial NGU, and about 30% of recurrent or persistent urethritis are considered to be caused by *M. genitalium*.[1] In most settings, its prevalence is more than that of *Neisseria gonorrhoeae* but less common than that of *Chlamydia trachomatis*.[2] Although often the sole pathogen isolated, its coinfection with *C. trachomatis* is not uncommon.[2] *M. genitalium* is suggested as an independent risk factor for the acquisition of human immunodeficiency virus (HIV) infection.[2] Thus, it becomes essential for the clinicians to have awareness about the clinical presentation, diagnosis, and management guidelines of *M. genitalium* infection.

STRUCTURE

M. genitalium is the smallest known self-replicating organism with a genome size of only 580 Kb.[3] It belongs to the class *Mollicutes* (meaning soft skin).[4] *M. genitalium* lacks a cell wall which has provided the organism inherent resistance against antibiotics such as beta-lactams and penicillins that target cell wall synthesis.[2] This flask-shaped organism has a slightly curved terminal organelle. Ability for adhesion, gliding motility, and cell invasion aid it in pathogenesis.[3]

The organism is small enough to penetrate the surface of the agar medium, hence when viewed microscopically from above, the colonies give the characteristic "fried egg" appearance. The colonies appear as "flying saucers" when looked obliquely from beneath with adequate lighting.[5]

The organism has been detected in the genitourinary, rectal, and respiratory tract specimens, but is very rare in the throat.[6] It was first isolated in 1981 from the urethral samples of two men presenting with NGU.[1] Originally, it was isolated from a medium from which thallous acetate had been omitted. Thallous acetate is a chemical that is often incorporated in media for mycoplasma. This led to the conclusion that the organism is susceptible to thallous acetate.[5]

Younger age group, smoking, dark skin phenotype, and multiple partners are the common risk factors for acquiring this infection.[7-9] Most common route of transmission is by genital-genital contact. Penile-anal transmission has also been reported.[10] Oral sex is not considered to be significant in transmission.[11-13]

CLINICAL SIGNS AND SYMPTOMS

Majority of males infected with *M. genitalium* remain asymptomatic.[13] It is possible that <10% of males develop symptoms due to *M. genitalium*, though the exact proportion of those who develop symptoms remains unknown.[13] Urethral discharge, dysuria, urethral discomfort, or penile discomfort are seen in some of the affected men. Features of acute, recurrent, or persistent urethritis may be present. Anagrius *et al*. reported an association between *M. genitalium* and balanoposthitis.[14] It can also be associated with complications such as sexually acquired reactive arthritis (SARA) and epididymitis.[4,13,15] There are not enough data regarding the incidence of prostatitis in patients with *M. genitalium*.[6] In patients with proctitis, higher bacterial load of *M. genitalium* was noted, but its exact role in disease causation needs further elucidation.[6]

In females, again majority of the infected, remain asymptomatic.[16] Although the exact proportion is not known, it is believed that <5% of infected women develop symptoms.[17,18] Post-coital bleeding, dysuria, intermenstrual bleeding (which can be painful), cervicitis, and lower abdominal pain are the manifestations reported in symptomatic cases.[18] Cervicitis most often presents as post-coital bleeding.[19] *M. genitalium* infection in females may be associated with complications such as pelvic inflammatory disease (PID), SARA, and preterm delivery.[19]

WHEN TO TEST PATIENTS FOR *M. genitalium?*

Testing for *M. genitalium* is recommended in men with NGU. It is recommended to consider testing for *M. genitalium* in patients with epididymitis and sexually acquired proctitis.[3]

In women, testing is recommended in patients with signs and symptoms of PID. Testing must be considered in people with signs or symptoms of mucopurulent cervicitis, especially those manifesting post-coital bleeding.[3]

Gram stain analysis of genital secretions cannot detect *M. genitalium* since it lacks a cell wall.[3] Culture is not the preferred diagnostic technique since the organism is very slow growing (about 6 months in culture) and fastidious in its growth requirements.[4] Nucleic acid amplification tests that detect specific deoxyribonucleic acid or ribonucleic acid of *M. genitalium* in samples are the test of choice.[20] Due to a high rate of macrolide resistance, it would be ideal to test all *M. genitalium* positive specimens for macrolide resistance as well.[20]

In men, first void urine is the most sensitive specimen, which is more sensitive than urethral swabs.[21-23] In women, vulvovaginal swabs (self-taken or clinician taken) are the most sensitive followed by the endocervical swabs.[22,24,25] Exact information regarding the incubation period or window period before which a laboratory test becomes positive is lacking.[13]

Management of patients involves detailed explanation of the condition, and advice to abstain from sexual intercourse for 14 days from the start of the treatment or till the resolution of symptoms, whichever is later.[13,26,27]

Macrolide-resistant *M. genitalium* is becoming more common worldwide. The prevalence of macrolide-resistant strains ranges from 30% to 100%.[28] Doxycycline as monotherapy [Table 1] has a low eradication rate for *M. genitalium*, but it is seen that treatment with doxycycline followed by an extended azithromycin regimen (an initial 500 mg dose followed by 250 mg daily for 4 days) can improve the success of treatment.[13,26,27] This could be because doxycycline reduces the load of the organism, thus bringing down the risk of macrolide resistance [Table 1].[13,26,27]

Moxifloxacin has been found to be very effective in Europe, but resistance seems to be increasing in Asia–Pacific region to the drug.[29,30] Therefore moxifloxacin as the first line treatment is not recommended.[31] Ten days are the recommended duration of optimal treatment.[31]

Pristinamycin, a streptogramin, that binds the 50S subunit of the bacterial ribosome is found useful against *M. genitalium*. The different regimens prescribed are 1 g 2 times a day or 1 g 4 times a day or a combination therapy of 1 g 3 times a day with doxycycline for 10 days.[3]

Although the mechanism of action remains unknown, minocycline at 100 mg twice a day for 14 days is found useful in treating *M. genitalium* infections that failed to respond to doxycycline and showed both macrolide and quinolone resistance mutations.[3]

Table 1: Treatment guidelines for infections due to *Mycoplasma genitalium*.

For uncomplicated infections
If macrolide sensitivity is unknown or if the organism is known to be macrolide sensitive – doxycycline 100 mg twice daily for 7 days followed by azithromycin 500 mg stat dose followed by 250 mg daily for 4 days
Infection by macrolide-resistant organism or in cases of treatment failure
Moxifloxacin 400 mg orally once daily for 10 days
For complicated cases (e.g., epididymitis, severe proctitis, and pelvic inflammatory diseases) – moxifloxacin 400 mg orally once daily for 14 days
Alternative treatment regimens
Doxycycline 100 mg twice daily for 14 days
Pristinamycin 1 g orally 4 times daily for 10 days
Doxycycline 100 mg twice daily for 7 days followed by pristinamycin 1 g 4 times daily for 10 days
Minocycline 100 mg twice daily for 14 days

As doxycycline is used as first-line drug for uncomplicated NGU, a repeat treatment with doxycycline is not required if patient tests positive for *Mycoplasma genitalium* after standard treatment for NGU. Azithromycin should be given immediately after doxycycline and preferably within 2 weeks of completing doxycycline. NGU: Non-gonococcal urethritis

SPECIAL SCENARIOS

Pregnancy

Three-day course of azithromycin can be used for uncomplicated *M. genitalium* infection. In pregnant women with macrolide resistance or with upper genital tract involvement, treatment options are limited.[32] Moxifloxacin and doxycycline are contraindicated in pregnancy.[33] There are no data regarding the safety of pristinamycin in pregnancy. As the amount of azithromycin detected in breast milk is very low, it is considered to be of low risk in lactation.[34] An increased risk of pyloric stenosis has been reported in breastfed infants of mothers who had taken macrolides during the post delivery period of 0-13 days.[35] Doxycycline, moxifloxacin, and pristinamycin are contraindicated in lactation.

HIV infection

Treatment of *M. genitalium* in HIV-positive patients is the same as that for HIV-negative individuals.[2]

Treatment of asymptomatic individuals

There is no evidence to recommend screening and treatment of asymptomatic individuals for *M. genitalium*. This is based on the knowledge that there will be spontaneous clearance of infection in many of the affected. On the contrary, treatment of asymptomatic individuals may increase the risk of the organism acquiring antimicrobial resistance.[36]

Asymptomatic partners of patients who tested positive for *M. genitalium* should be tested and when found positive, should be treated using the same treatment regimen.[13] Testing of current partners is recommended so as to avoid reinfection in index case. This is contrary to the partner notification advised for most other STI pathogens, where contact tracing and treatment are offered to all sexual contacts of previous 3 months to prevent transmission in the community.[3]

Test of cure is recommended for all patients to confirm clearance of the organism.[2] If *M. genitalium* is detected after treatment with azithromycin or moxifloxacin, it strongly indicates antimicrobial resistance.[37,38] The time taken for eradication of the organism after treatment is variable. One study that used polymerase chain reaction to detect the organism reported 96% eradication within 8 days after treatment with azithromycin, but the same authors noted that after a period of negative results, the patient showed resistant strains. This suggested that test of cure should be delayed after treatment.[39] Test of cure is recommended for all patients and should be performed 5 weeks after the start of treatment.[39] However, others have questioned this recommendation stating that the treatment should aim at clinical cure, rather than microbiological eradication. It is argued that an asymptomatic infection may be non-pathogenic and attempt at microbiological eradication may lead to overtreatment.[3]

When facility is not available for diagnosing *M. genitalium* infection, an empirical treatment may be started in patients with persistent or recurrent NGU, or in those with PID, who show lack of response to treatment within 7–10 days.[1]

As per current knowledge, the most common cause of persistent or recurrent NGU (especially following treatment with doxycycline) is *M. genitalium*.[1] The possibility of disease caused by *M. genitalium* should be considered in PID cases not responding to treatment since the recommended treatment regimens for PID advise antibiotics that are ineffective against *M. genitalium*.[1]

It is advised that azithromycin 1 g orally should be given to men who manifest recurrent or persistent NGU after treatment with doxycycline. Higher doses of azithromycin were not found effective in such patients; hence, those who fail to respond to 1 g azithromycin should receive retreatment with moxifloxacin.[1] Moxifloxacin 400 mg/day for 14 days is the recommended treatment for PID patients who do not respond to standard treatment.[1]

ADVERSE EFFECTS OF DRUGS USED IN TREATMENT

Most common side effects with azithromycin, doxycycline, moxifloxacin, and pristinamycin are gastrointestinal problems.[40,41] Azithromycin and moxifloxacin can prolong

QT interval, so one must be cautious when prescribing it to patients who are on medications that can prolong QT interval.[42] Fluoroquinolone antibiotics can cause side effects affecting muscles, tendons, bones, or nervous system.[43]

CONCLUSION

Additional research can give valuable information on the disease pathogenesis and may help to improve the management of infections due to *M. genitalium*. In resource-poor settings, where diagnostic facilities are not available, patients who fail first-line treatment for urethritis, cervicitis, and PID should receive treatment for *M. genitalium* infection.

Declaration of patient consent

Not required as there are no patients in this article.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64:1-137.
2. Munoz JL, Goje OJ. *Mycoplasma genitalium*: An emerging sexually transmitted Infection. Scientifica (Cairo) 2016;2016:7537318.
3. Gnanadurai R, Fifer H. *Mycoplasma genitalium*: A review. Microbiology (Reading) 2020;166:21-9.
4. Taylor-Robinson D, Furr PM, Tully JG. Serological cross-reactions between *Mycoplasma genitalium* and *M. pneumoniae*. Lancet 1983;1:527.
5. Taylor-Robinson D. The Harrison Lecture. The history and role of *Mycoplasma genitalium* in sexually transmitted diseases. Genitourin Med 1995;71:1-8.
6. Taylor-Robinson D, Jensen JS. *Mycoplasma genitalium*: From chrysalis to multicolored butterfly. Clin Microbiol Rev 2011;24:498-514.
7. Andersen B, Sokolowski I, Østergaard L, Kjølseth Møller J, Olesen F. *Mycoplasma genitalium*: Prevalence and behavioural risk factors in the general population. Sex Transm Infect 2007;83:237-41.
8. Manhart L, Holmes K, Hughes J, 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. Sonnenberg P, Ison CA, Clifton S, Field N, Tanton C, Soldan K, *et al*. Epidemiology of *Mycoplasma genitalium* in British men and women aged 16–44 years: Evidence from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). Int J Epidemiol 2015;44:1982-94.
10. Edlund M, Blaxhult A, Bratt G. The spread of *Mycoplasma genitalium* among men who have sex with men. Int J STD AIDS 2012;23:455-6.
11. Bradshaw C, Fairley C, Lister N, Chen SJ, Garland SM, Tabrizi SN. *Mycoplasma genitalium* in men who have sex with men at male-only saunas. Sex Transm Infect 2009;85:432-5.
12. Deguchi T, Yasuda M, Yokoi S, Nakano M, Ito SI, Ohkusu K, *et al*. Failure to detect *Mycoplasma genitalium* in the pharynges of female sex workers in Japan. J Infect Chemother 2009;15:410-3.
13. Horner PJ, Martin DH. *Mycoplasma genitalium* infection in men. J Infect Dis 2017;216:S396-405.
14. Anagrius C, Loré B, Jensen J. Treatment of. observations from a Swedish STD clinic. PLoS One 2013;8:e61481.
15. Gaydos C, Maldeis NE, Hardick A, Hardick J, Quinn TC. *Mycoplasma genitalium* as a contributor to the multiple etiologies of cervicitis in women attending sexually transmitted disease clinics. Sex Transm Dis 2009;36:598-606.
16. Lis R, Rowhani-Rahbar A, Manhart L. *Mycoplasma genitalium* infection and female reproductive tract disease: A meta-analysis. Clin Infect Dis 2015;61:418-26.
17. Bradshaw CS, Jensen JS, Waites KB. New horizons in *Mycoplasma genitalium* treatment. J Infect Dis 2017;216:S412-9.
18. Horner P, Ingle SM, Garrett F, Blee K, Kong F, Muir P, *et al*. Which azithromycin regimen should be used for treating *Mycoplasma genitalium*? A meta-analysis. Sex Transm Infect 2018;94:14-20.
19. Unemo M, Bradshaw C, Hocking J, de Vries HJ, Francis SC, Mabey D, *et al*. Sexually transmitted infections: Challenges ahead. Lancet Infect Dis 2017;17:e235-79.
20. Gaydos CA. *Mycoplasma genitalium*: Accurate diagnosis is necessary for adequate treatment. J Infect Dis 2017;216:S406-11.
21. Jensen J, Björnelius E, Dohn B, Lidbrink P. Comparison of first void urine and urogenital swab specimens for detection of *Mycoplasma genitalium* and *Chlamydia trachomatis* by polymerase chain reaction in patients attending a sexually transmitted disease clinic. Sex Transm Dis 2004;31:499-507.
22. Tabrizi SN, Tan LY, Walker S, Twin J, Poljak M, Bradshaw CS, *et al*. Multiplex assay for simultaneous detection of *Mycoplasma genitalium* and macrolide resistance using PlexZyme and PlexPrime technology. PLoS One 2016;11:e0156740.
23. Dize L, Barnes P Jr., Barnes M, Hsieh YH, Marsiglia V, Duncan D, *et al*. Performance of self-collected penile-meatal swabs compared to clinician-collected urethral swabs for the detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, and *Mycoplasma genitalium* by nucleic acid amplification assays. Diagn Microbiol Infect Dis 2016;86:131-5.
24. Wroblewski J, Manhart L, Dickey K, Hudspeth MK, Totten PA. Comparison of transcription-mediated amplification and PCR assay results for various genital specimen types for detection of *Mycoplasma genitalium*. J Clin Microbiol 2006;44:3306-12.
25. Lau A, Bradshaw C, 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.

26. Read TR, Fairley CK, Murray GL, Jensen JS, Danielewski J, Worthington K, *et al*. Outcomes of resistance-guided sequential treatment of *Mycoplasma genitalium* infections: A prospective evaluation. Clin Infect Dis 2019;68:554-60.
27. Horner P, Blee K, O'Mahony C, Muir P, Evans C, Radcliffe K. 2015 UK National Guideline on the management of non-gonococcal urethritis. Int J STD AIDS 2016;27:85-96.
28. Pitt R, Fifer H, Woodford N, Alexander S. Detection of markers predictive of macrolide and fluoroquinolone resistance in *Mycoplasma genitalium* from patients attending sexual health services in England. Sex Transm Infect 2018;94:9-13.
29. Gesink D, Mulvad G, Montgomery-Andersen R, Poppel U, Montgomery-Andersen SM, Binzer A, *et al*. *Mycoplasma genitalium* presence, resistance and epidemiology in Greenland. Int J Circumpolar Health 2012;71:1-8.
30. Manhart L, Jensen J, Bradshaw C, Golden MR, Martin DH. Efficacy of antimicrobial therapy for *Mycoplasma genitalium* infections. Clin Infect Dis 2015;61:S802-17.
31. Li Y, Le WJ, Li S, Cao YP, Su XH. Meta-analysis of the efficacy of moxifloxacin in treating *Mycoplasma genitalium* infection. Int J STD AIDS 2017;28:1106-14.
32. Briggs GG. Drug effects on the fetus and breast-fed infant. Clin Obstet Gynecol 2002;45:6-21.
33. Czeizel AE, Rockenbauer M. Teratogenic study of doxycycline. Obstet Gynecol 1997;89:524-8.
34. Kelsey JJ, Moser LR, Jennings JC, Munger MA. Presence of azithromycin breast milk concentrations: A case report. Am J Obstet Gynecol 1994;170:1375-6.
35. Lund M, Pasternak B, Davidsen RB, Feenstra B, Krogh C, Diaz LJ, *et al*. Use of macrolides in mother and child and risk of infantile hypertrophic pyloric stenosis: Nationwide cohort study. Br Med J 2014;348:1908.
36. Jensen J, Orsum R, Dohn B, Uldum S, Worm AS, Lind K. *Mycoplasma genitalium*: A cause of male urethritis? Genitourin Med 1993;69:265-9.
37. Ito S, Shimada Y, Yamaguchi Y, Yasuda M, Yokoi S, Ito SI, *et al*. Selection of *Mycoplasma genitalium* strains harbouring macrolide resistance-associated 23S rRNA mutations by treatment with a single 1 g dose of azithromycin. Sex Transm Infect 2011;87:412-4.
38. Manhart LE, Gillespie CW, Lowens MS, Khosropour CM, Colombara DV, Golden MR, *et al*. Standard treatment regimens for nongonococcal urethritis have similar but declining cure rates: A randomized controlled trial. Clin Infect Dis 2013;56:934-42.
39. Falk L, Enger M, Jensen JS. Time to eradication of *Mycoplasma genitalium* after antibiotic treatment in men and women. J Antimicrob Chemother 2018;70:3134-40.
40. Conway R, Cook S, Soni S. Antibiotic treatment of *Mycoplasma genitalium* infection. Pharm J 2019;303:7928.
41. Read TR, Jensen JS, Fariley CS, Grant M, Danielewsky JA, Su J, *et al*. Use of pristinamycin for macrolide-resistant Mycoplasma genitalium infection. Emerg Infect Dis 2018;24920:328-35.
42. Lu ZK, Yuan J, Li M, Sutton SS, Rao GA, Jacob S, *et al*. Cardiac risks associated with antibiotics: Azithromycin and levofloxacin. Expert Opin Drug Saf 2015;14:295-303.
43. Scavone C, Mascolo A, Ruggiero R, Sportiello L, Rafaniello C, Berrino L, *et al*. Quinolones-induced musculoskeletal, neurological, and psychiatric ADRs: A pharmacovigilance study based on data from the Italian spontaneous reporting system. Front Pharmacol 2020;11:428.

How to cite this article: Harish S. Sexually transmitted infection by *Mycoplasma genitalium*: A short review. J Skin Sex Transm Dis 2021;3(1):46-50.