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*Mycoplasma genitalium* retrospective audit of Northern Territory isolates from 2022

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# Abstract

The Northern Territory (NT) has the highest rates of sexually transmitted infections (STI) in Australia; however, the local prevalence of *Mycoplasma genitalium* (*M. genitalium*) has not been previously determined. This study was designed to review *M. genitalium* detection, to determine the regional NT prevalence and macrolide resistance rates. In our study the NT background prevalence of *M. genitalium* is 13%, with the highest detection rates occurring in central Australia and in correctional facility inmates. Symptomatic patients attending sexual health clinics have a positivity rate of 12%, but very high macrolide resistance. The decision to screen for *M. genitalium* should be based on several factors, including the prevalence of the infection in the local population; the availability of effective treatments; and the potential benefits and risks of detection and therapy.

Keywords: *Mycoplasma genitalium*; STI; Northern Territory; sexually transmitted disease; infectious diseases

# Introduction

The Northern Territory (NT) has the highest rates of sexually transmitted infections (STI) in Australia; however, the local prevalence of *Mycoplasma genitalium* has not been previously determined.1 This study was designed to review the 2022 STI screening results, specifically looking at *M. genitalium*, to determine the regional NT prevalence and macrolide resistance rates. *M genitalium* is the smallest prokaryote, and detection by culture is challenging due to its slow growth and cell wall deficiency.2,3 Diagnosis is made via detection of *M. genitalium* DNA from nucleic acid amplification tests (NAAT).3,4 Infection by *M. genitalium* can cause nongonococcal urethritis (NGU) in men, and in women cervicitis or pelvic inflammatory disease (PID).2 In pregnancy, *M. genitalium* is associated with preterm birth.4 First pass urine for NAAT is less sensitive than patient- or healthcare-worker-collected cervical or vaginal swabs in women.2

In Australia, asymptomatic screening for *M. genitalium* is generally not recommended unless individuals have ongoing sexual contact with persons infected with *M. genitalium*.3 Testing for *M. genitalium* is indicated in patients with signs and symptoms of NGU, urethritis, PID, post coital bleeding or cervicitis.3 Treatment has become challenging with rising antimicrobial resistance.3 The Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) cite macrolide resistance as high as 60%; in men who have sex with men (MSM), resistance rates greater than 80% are documented.3

# Methods

In the NT we have undertaken a retrospective audit of all patients who have had STI testing performed (by swab or first stream urine) as a part of verification of the novel Alinity mSTI 4-in-1 multiplex assay for the detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis* and *Mycoplasma genitalium* (Abbott Alinity Chicago USA). The NT is separated into two distinct geographical regions, serviced by Top End Health Service (TEHS) and the Central Australian Health Service (CAHS) respectively. STI specimens were collected from individuals attending communicable disease clinics, from women’s antenatal visits, from correctional facility inmates, from hospital inpatients, and from general practice and community health clinics. The data was collected over a ten month period in 2022 (February to November). *M. genitalium* assays requested by clinicians were confirmed at a reference laboratory (PathWest Western Australia) and positive results underwent macrolide resistance testing. Macrolide resistance testing was performed at PathWest on the Resistance Plus MG FleXible assay (Cepheid USA). The communicable diseases clinics in the NT only request *M. genitalium* on symptomatic patients or in asymptomatic patients who have ongoing sexual contact with those diagnosed with *M. genitalium*.

During the verification period, all tests were confirmed at a reference laboratory. The tests performed on the Abbott Alinity mSTI 4-in-1 multiplex assay had 100% concordance with the results obtained by the reference laboratory.

This retrospective audit was designed to provide *M. genitalium* prevalence for the NT, in persons undergoing routine testing for other STIs and to compare with the prevalence among patients who exhibited symptoms consistent with *M. genitalium* infection. The authors have ethics approval for this study (HREC Reference number 2022-4284) from the NT Department of Health (NT Health) and Menzies School of Health Research.

# Results

A total of 12,178 *M. genitalium* tests from 9,805 unique patients were undertaken using the Alinity m STI 4-in-1 multiplex assay during the ten-month study period in 2022. Demographic data is shown in Table 1. *M. genitalium* assay demographics by gender were 54% female, 45% male, and 1% trans and gender diverse. Median ages were 29 years for females, 33 years for males, and 27 years for trans and gender diverse persons. These tests were undertaken from the following sources: communicable disease clinics (22%), correctional facility inmates (26%), antenatal patients (15%) and ‘other’ (38%), where contributions to ‘other’ include community health clinics, general practice, and hospital specimens.

Background prevalence rates separated by region, gender, and screening categories are presented in Table 2.

Overall, *M. genitalium* positivity, among samples tested, was 13%. *M. genitalium* positivity for both asymptomatic and symptomatic patients was 12% in females, 14% in males, and 13% in trans and gender diverse persons.

This audit demonstrates a marked difference between the regions of the NT: prevalence was 9% within TEHS and 20% within CAHS. The NT communicable diseases clinics accounted for 22% of all swabs, with a positivity rate of 7% (TEHS and CAHS). Patients who underwent testing whilst as a correctional facility inmate had a 21% positivity rate; positivity among correctional centre inmates was higher in CAHS (26%) than in TEHS (17%). The positivity rate among NT antenatal patients was 7%. The overall higher positivity of tests performed on specimens from patients in CAHS than those in TEHS was also apparent in tests on antenatal patients and those attending other clinics, and among both females and males, as well as among correctional facility inmates as noted above (see Table 2).

Table 3 details the results of symptomatic patients who underwent targeted *M. genitalium* testing.

In total, during the ten-month period February–November 2022, there were 276 targeted *M. genitalium* requests on symptomatic patients (223 in TEHS, 43 in CAHS), with an overall positive rate of 11%. There were no positive results obtained in the targeted antenatal cohort. Most tests were requested by the TEHS communicable diseases clinics. The communicable diseases clinics in both TEHS and CAHS requested *M. genitalium* in 156 patients and had a combined positivity rate of 12%.

Resistance testing was successfully performed in 23 of 28 Top End Health symptomatic patient samples. In this cohort, 16/23 (70%) were detected as having macrolide resistance. Resistance testing was unsuccessful on 5/28 samples, due either to low signal strength of *M. genitalium* or to a swab greater than 7 days from collection, a factor known to be associated with a reduction in the sensitivity of the resistance assay. Macrolide resistance was detected on the following samples: urine samples 9/16 (56%) and vaginal swab samples 7/56 (44%). Vaginal swabs received included healthcare-collected high vaginal swabs and cervical/endocervical swabs as well as self-collected vaginal swabs. Of the positive macrolide resistance tests, 10/16 (62.5%) were requested by communicable disease clinics on patients who live in the TEHS region; the remainder of samples were received from TEHS clinics or hospital inpatients.

Table 1: Demographic details of *M. genitalium* assay undertaken in the Northern Territory

| Parameter | Demographic | Top End | Central Australia | Total |
| --- | --- | --- | --- | --- |
| N | %a | Median ageb | IQR (age)c | N | %a | Median ageb | IQR (age)c | N | %a | Median ageb | IQR (age)c |
| Sex | Female | 4,665 | 56 | 29 | 24–35 | 1,986 | 52 | 29 | 22–36 | 6,651 | 54 | 29 | 23–35 |
| Male | 3,653 | 44 | 33 | 26–43 | 1,821 | 48 | 33 | 25–41 | 5,474 | 45 | 33 | 26–42 |
| Trans and gender diverse | 46 | 1 | 29 | 21–36 | 7 | < 1 | 27 | 26–34 | 53 | 1 | 27 | 21–36 |
| Category | Communicable disease clinics | 2,237 | 27 | — | — | 458 | 12 | — | — | 2,695 | 22 | — | — |
| Correctional facility inmates | 1,661 | 20 | — | — | 1,442 | 38 | — | — | 3,103 | 26 | — | — |
| Antenatal | 1,542 | 18 | — | — | 225 | 6 | — | — | 1,767 | 15 | — | — |
| Other | 2,924 | 35 | — | — | 1,689 | 44 | — | — | 4,613 | 38 | — | — |
| Totald |  | 8,364 | 69 | — | — | 3,814 | 31 | — | — | 12,178 | 100 | — | — |

a Unless otherwise indicated, the percentage shown is percentage of total assays tested within the indicated region.

b Median age in years for the indicated demographic.

c IQR: inter-quartile range.

d Percentage of total tested.

Table 2: *M. genitalium* positivity by location, gender and screening category

| Parameter | Demographic | Top End | Central Australia | Total |
| --- | --- | --- | --- | --- |
| na | %b | na | %b | na | %b |
| Sex | Female | 418 | 9 | 373 | 19 | 791 | 12 |
| Male | 368 | 10 | 374 | 21 | 742 | 14 |
| Trans and gender diverse | 6 | 13 | 1 | 14 | 7 | 13 |
| Category | Communicable disease clinics | 159 | 7 | 34 | 7 | 193 | 7 |
| Correctional facility inmates | 279 | 17 | 381 | 26 | 660 | 21 |
| Antenatal | 78 | 5 | 49 | 22 | 127 | 7 |
| Other | 276 | 9 | 284 | 17 | 560 | 12 |
| Total |  | 792 | 9 | 748 | 20 | 1,540 | 13 |

a Number of specimens testing positive for *M. genitalium* among those tested within the indicated demographic.

b Percentage positivity among those specimens tested within the indicated demographic.

Table 3: *M. genitalium* demographics and positivity rates in specimens from symptomatic patients

| Parameter | Demographic | Top End | Central Australia | Total |
| --- | --- | --- | --- | --- |
| Na | %b | nc | %d | Na | %b | nc | %d | nc | %d |
| Sex | Female | 129 | 55 | 13 | 10 | 34 | 79 | 1 | 3 | 14 | 9 |
| Male | 100 | 43 | 14 | 14 | 9 | 21 | 0 | 0 | 14 | 13 |
| Trans and gender diverse | 4 | 2 | 1 | 25 | 0 | 0 | 0 | 0 | 1 | 25 |
| Category | Communicable disease clinics | 142 | 61 | 19 | 13 | 14 | 33 | 0 | 0 | 19 | 12 |
| Correctional facility inmates | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Antenatal | 7 | 3 | 0 | 0 | 2 | 5 | 0 | 0 | 0 | 0 |
| Other | 84 | 36 | 9 | 11 | 27 | 63 | 1 | 100 | 10 | 9 |
| Total |  | 233 | 100 | 28 | 12 | 43 | 100 | 1 | 3 | 29 | 11 |

a Number of specimens from symptomatic patients in indicated demographic and region.

b Percentage within indicated demographic classification, of all specimens from symptomatic patients in indicated region.

c Number of specimens from symptomatic patients testing positive for *M. genitalium* infection in indicated demographic and region.

d Percent positivity within specimens from symptomatic patients in indicated demographic and region.

# Discussion

The NT has high rates of STIs compared to the rest of Australia.1 In this study, the NT background prevalence of *M. genitalium* was 13%, with the highest rates in central Australia and in correctional centre inmates. CAHS has higher STI rates than the rest of the NT and this is replicated in the *M. genitalium* data.1 Symptomatic patients attending communicable diseases clinics had a positivity rate of 12% but very high macrolide resistance. The global estimated prevalence of *M. genitalium* in the general population is 1.3%.5 In 2018, Trevis et al reviewed a cohort of backpackers in far North Queensland and found this transient population had a background prevalence of 1.8%.6 This contrasts to a meta-analysis in 2020 by Latimer et al which reviewed the prevalence of *M. genitalium* in MSM and found urethral swabs had a higher prevalence at 7.1% compared to 2.2% on rectal swabs.7 This same meta-analysis by Latimer *et al* demonstrated symptomatic patients had a higher prevalence rate of 16.1% compared to 7.5% in asymptomatic patients, and in HIV-positive MSM the rate of *M. genitalium* was higher than among HIV-negative MSM (respectively 7.0% and 3.4%).7

The Australian STI Guidelines quote Australian macrolide resistant *M. genitalium* as exceeding 60%.3 In a Melbourne-based study, data from 2017–2018 found *de novo* macrolide resistance in 4.6% of the cases.8 In a meta-analysis published by Lancet in 2020, it was noted that in 2010 the portion of samples positive for the mutations associated with azithromycin resistance was 10%, but by 2016–2017 that prevalence had jumped to 51%.9 The same meta-analysis found the macrolide resistance rate was 68% in the WHO Western Pacific region.10 A study in the United States of America (USA) in 2020 found a prevalence of macrolide resistance mutations of 59.1%.11 In a 2022 study by Tickner et al, they discuss that rates of fluoroquinolone resistance are increasing globally, and this is due to mutations in the *parC* gene which is leading to fluoroquinolone clinical treatment failure.12 In our study, we had small numbers of specimens for which resistance testing was undertaken; however, the prevalence rate of macrolide resistance was high at 70%, in line with other Australian studies.

In the antenatal patient cohort, international reviews in South Africa and Papua New Guinea found a prevalence rate of 12%, whereas in the USA, prevalence ranged from 5.7 to 8.0%.13 In the NT, we found a positivity rate of 7% in antenatal patients; however, when reviewing regional NT, patients from CAHS had a higher positivity rate (22%). Some studies associate *M. genitalium* with preterm birth; while our numbers are low from this cohort, we would recommend further investigation into this finding by our obstetric colleagues, particularly in Central Australia. *M. genitalium* testing in symptomatic MSM patients is established; however, the decision to perform routine screening for *M. genitalium* amongst antenatal patients and inmates undergoing symptomatic STI testing is more complex.

The decision to screen for *M. genitalium* during pregnancy should be based on several factors, including: the prevalence of the infection in the local population; the availability of effective treatments; and the potential benefits and risks of screening. *M. genitalium* has a potential link with adverse pregnancy outcomes, including preterm birth, low birth weight, and spontaneous abortion.2,3,4 Our findings provide local prevalence data in a setting with known background high STI rates and high-risk pregnancy rates; this is a finding for consideration by obstetric staff. Resistance testing in pregnancy is vital, with the need to determine if the infection has macrolide susceptibility, as the alternative agents for treatment, doxycycline and moxifloxacin, are not recommended in pregnancy as per the Australian Medical Handbook Pty Ltd.2,3

Currently the *Australian Management of STI Guidelines for Primary Care* suggest that all people entering the Australian justice system should be offered screening for STIs and blood borne viruses; this is not mandatory.3 The finding of high rates of *M. genitalium* in central Australian correctional facility inmates, in particular, raises the question of whether inmates should be screened for all STIs. This is a topic that raises ethical, legal, and public health considerations.10

There are six areas to be considered:

1. **Public health concerns**: correctional facilities are considered high-risk environments for the transmission of infectious diseases, including STIs, due to factors such as overcrowding, limited access to healthcare, and potentially risky behaviours within the correctional facility population.10 STI screening can help identify and treat infections, thus reducing the risk of further transmission both within the prison and after release back into the community.10
2. **Consent**: any screening program, including STI screening, should be conducted with the informed consent of the individuals involved. This is especially important in a prison setting, where inmates may have limited autonomy and face unique power imbalance.10
3. **Human rights**: inmates, like all individuals, have a right to healthcare and should have access to appropriate medical services, including STI screening and treatment.10 Any screening program must adhere to human rights principles and must be conducted with dignity and respect.
4. **Cost-effectiveness**: screening programs need to be evaluated for their cost-effectiveness, to ensure resources are being used efficiently in addressing public health concerns.
5. **Treatment and follow-up**: STI screening should be accompanied by access to appropriate treatment and follow-up care to address positive cases effectively, including the identification, testing and treatment of contacts.
6. ***Mycoplasma genitalium***: testing should be undertaken in residents who are symptomatic or who are a contact of a known case, with treatment guided by resistance testing and consideration of test of cure post treatment.

The decision to implement STI screening in correctional facilities should involve collaboration between public health authorities, correctional facility administrations and healthcare professionals.11 It should also consider the specific context of the correctional system in question and the available resources. Ultimately, the goal is to strike a balance between public health protection, individual rights, and ethical considerations.10

Limitations of this study are the low number of samples sent for resistance testing. An indication for testing was not always placed on the request form. All requested detected samples were sent for resistance testing at an interstate reference laboratory. Some samples failed testing due to prolonged storage and interstate transportation leading to a degradation in the DNA; this study was undertaken during the NT coronavirus disease 2019 (COVID-19) Omicron wave, which resulted in delay in transportation of samples interstate. We did not review co-infections with other STIs which would have been important to consider, noting that in instances of co-infection between *M. genitalium* and *Chlamydia*, single-dose azithromycin for treatment may help fuel resistance. Some patients had multiple assays performed, so this study was based on assay numbers not patient numbers.

# Conclusion

The NT has higher rates of STI than the rest of the country, this was mirrored in this study showing high prevalence of 13% for *M. genitalium*, in groups undergoing STI screening. The unexpected findings were increased prevalence in central Australia, in patients who underwent testing whilst in the correctional system, and in the antenatal cohort. As a result of these findings, we will be recommending that, in the NT, *M. genitalium* testing is considered in symptomatic patients in pregnancy and in those in at-risk pregnancy categories.

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