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Lack of macrolide resistance in *Mycoplasma genitalium* infections in a cohort of pregnant women in South Africa

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Macrolide resistance in *Mycoplasma genitalium* infection is emerging worldwide and is largely driven by use of azithromycin in STI treatment. South Africa has used azithromycin in its syndromic management regimen of male urethritis and vaginal discharge since 2015, but prevalence of macrolide resistance in *M. genitalium* remains largely unknown.

This study determined azithromycin resistance in *M. genitalium* in remnant vulvovaginal specimens that had been obtained from pregnant women in Cape Town, South Africa, between November 2017 and February 2019.[1] In brief, vulvovaginal swabs were self-collected at participants' first antenatal care (ANC), third trimester ANC and postnatal care visits. In-facility GeneXpert testing (Cepheid, Sunnyvale, California) for *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis* was done, followed by treatment if indicated. The Aptima Vaginal Swab Specimen Collection Kit (Hologic, San

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Contributors RPHP conceptualised the study, analysed the data and wrote the draft and final version of the manuscript. HS-J performed the laboratory work, analysed the data and provided comments on the manuscript. MMK and LM provided supervision to the evaluation and commented on the manuscript. JK and DJD organised funding, led the clinical study and commented on the manuscript.

Competing interests We received donation of diagnostic kits for the detection of *Mycoplasma genitalium* (Hologic, San Diego, CA) and the determination of macrolide resistance (SpeedX, Australia).

Ethics approval The study was approved by the human research ethics committee at the University of Cape Town (#454/2017).

Diego, California) was used to collect a second swab that was stored at −20°C at the National Institute for Communicable Diseases for batched testing of *M. genitalium* using the Aptima *M. genitalium* Assay (Hologic) after study completion.

All specimens with a positive Aptima assay result were evaluated for presence of macrolide resistance mutations using the ResistancePlus *M. genitalium* assay (SpeeDx, Australia) as per manufacturer's instructions at the University of Pretoria.

M. genitalium was detected with the Aptima Assay in 84 specimens from 38 women in the study cohort. The median age of these women at baseline was 28 years (range 19–40 years); 24 (63%) were HIV infected and 19 (50%) had another STI: *C. trachomatis* (n=9), *N. gonorrhoeae* (n=2) and *T. vaginalis* (n=10). Resistance testing with the ResistancePlus assay was successful in 64/84 (76%) specimens; these had been obtained from 34/38 women (89%) with *M. genitalium* infection detected at either first ANC (26/35, 74%), third-trimester ANC (22/26, 85%) and postnatal visit (16/23, 70%). Wild-type *M. genitalium* was detected in all 64 (100%) specimens.

Specimen degradation likely influenced the recovery rate for resistance testing in our study because *M. genitalium* is generally a low-load infection, and macrolide resistance testing was done after 14 months of specimen storage (median, IQR 11–16 months) and after 6 months and at half the input volume of the Aptima assay. Differences in assay sensitivity might also play a role. To our knowledge, *M. genitalium* bacterial load and macrolide resistance are not associated, so we consider selection bias unlikely.

This study confirms that macrolide resistance is uncommon in *M. genitalium* infections in South Africa despite the use of azithromycin for syndromic STI management since 2015.[2–5] It is the first data point from the Southern part of the country, >1000 km away from the settings of previous studies (table 1), suggesting that geographical differences in resistance are not present in the country. Nevertheless, continuous surveillance is warranted as emergence of resistant *M. genitalium* could undermine the effectiveness of syndromic STI management.

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Table 1

Overview of studies of macrolide resistance in genital *Mycoplasma genitalium* infection stratified by inclusion of azithromycin in the syndromic management regimen for genital discharge in South Africa

Study	Year	Location	Study population	Detection of resistance*†
Syndromic management regimen without azithromycin				
Muller *et al*[2]	2007–2014	Johannesburg (urban)	Symptomatic adults participating in STI national screening and HIV-infected individuals	0/266
Hay *et al*[3]	2011–2012	Mopani District (rural)	Women visiting PHC facilities for any reason	2/52 (4%)
Ong *et al*[4]	2011–2012	Johannesburg (urban)	HIV-infected women attending for cervical cancer screening	0/43
Syndromic management regimen with azithromycin				
Laumen *et al*[5]	2015–2019	Johannesburg (urban)	Men accessing sexual health services at three PHC facilities	1/9 (11%)
Laumen *et al*[5]	2016–2017	Pretoria (urban)	HIV-infected women attending ANC at three PHC facilities	0/44
Laumen *et al*[5]	2016–2018	Mopani District (rural)	Women accessing a mobile clinic and individuals with STI-associated symptoms mobilised for STI services	0/37
This study	2018–2019	Cape Town (urban)	Pregnant women attending antenatal and postnatal care at a PHC	0/64

*Number of macrolide-resistant strains per total number of strains tested.

†Studies using endocervical, urethral, urine or vaginal specimens were included.

ANC, antenatal care; PHC, primary healthcare.