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Prevalence of *Mycoplasma genitalium* infection and macrolide resistance in pregnant women receiving prenatal care

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Keywords

Mycoplasma genitalium ; pregnancy; resistance; sexually transmitted infection

Mycoplasma genitalium (MG) infection is an emerging sexually transmitted infection (STI). In women, it has been epidemiologically associated with cervicitis, pelvic inflammatory disease, and infertility[1,2]; however, most infections are asymptomatic.[3] Routine MG screening is not currently recommended[4] because of a lack of consistent evidence of reproductive sequelae from asymptomatic infection. Most MG prevalence estimates have come from nonpregnant populations; reported prevalence in pregnant women from a small number of studies ranges from 1% to 17%.[5–8] Limited studies evaluating the association of MG with adverse pregnancy outcomes have produced conflicting results.[2] Macrolides are the only MG treatment available in the United States that can be safely used during pregnancy, and their efficacy is declining as a result of the emergence of strains containing macrolide resistance–associated gene mutations (MRMs).[9]

Obtaining accurate estimates of MG infection prevalence and associated MRM frequency in pregnant women is critical for building a foundation for understanding morbidity associated with MG in pregnant women as well as for guiding future MG testing and treatment considerations in pregnant women. The current study's primary objective was to determine

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AUTHOR CONTRIBUTIONS

WMG, AS, and JD designed the study. WMG and AS supervised the clinical study procedures. MH, JPS, and WMG obtained consent from patients and collected data and specimens. BVDP performed the MG testing and LX conducted the MRM testing. KG provided logistical support for study procedures. WMG conducted data analyses. MH and WMG wrote the main manuscript draft. All authors reviewed and edited the manuscript.

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the prevalence of MG infection and associated MRMs among pregnant women; a secondary objective was to evaluate the association of MG with select perinatal outcomes.

We performed a prospective cross-sectional study of MG infection prevalence in pregnant women at any gestational age. Inclusion criteria were pregnant (confirmed by urine pregnancy test), age ≥ 18 years, and receiving routine prenatal care at one of three OB clinics at the University of Alabama at Birmingham (UAB): a clinic providing care to underserved women at risk for pregnancy complications (OB Complications Clinic), a maternal-fetal medicine clinic (MFM Clinic) serving primarily an insured population at risk for pregnancy complications, and a primary care obstetrics clinic serving an insured low-risk population (Prime Care Clinic). Exclusion criteria were reported macrolide use within the prior one month, not English speaking, and women who only had sex with women. The study was approved by the UAB institutional Review Board (number: IRB-300005789) before beginning. All participants provided written informed consent before participation.

At enrollment, the only study visit, participants were interviewed and provided a self-collected vaginal swab. Batch MG testing on swabs was performed using the cobas MG/TV assay (Roche Diagnostics). MG-positive swabs were tested for MRMs in domain V of the *23S rRNA* gene by real-time polymerase chain reaction.[10] For participants delivering at UAB, chart review was conducted to ascertain delivery outcomes. Associations of MG positivity and MG MRM frequency with participant characteristics and perinatal outcomes were evaluated using Fisher's exact, χ^2, or Wilcoxon rank-sum tests as appropriate, and the association with perinatal outcomes was also assessed by logistic regression.

Characteristics of the 224 women enrolled between November 2020 to February 2021, stratified by MG positivity status, are shown in Table 1. MG was detected in 18 (8.0%) women, more often in those who were younger, of Black race, or who reported prior trichomoniasis; 10 (55.6%) of the MG infections were detected in the third trimester. MRM genotyping was successfully performed for 17 MG strains. MRMs were detected in seven (41.2%): four had the A2071G mutation and three had the A2072G mutation (*Escherichia coli* numbering 2058 and 2059, respectively). MRM detection was only associated with younger age (median age, 22 years vs. 28 years; $P = 0.03$).

Data on maternal conditions and perinatal outcomes were available for 185 (82.6%) women (Table 2). Adverse pregnancy outcomes commonly occurred. Although MG was detected at a higher frequency in patients with an outcome of preterm birth (11.4% vs. 7.8%), small for gestational age (14.8% vs. 7.7%), or fetal growth restriction (15.4% vs. 8.2%), MG was not significantly associated with these outcomes.

In the current prospective study, we found that 8% of pregnant women receiving prenatal care at OB clinics in a Southeastern US urban medical center tested positive for MG, and MG positivity was associated with younger maternal age, black race, and prior trichomoniasis. Frequency of MRMs was high (41%), which is similar to the 31% MRM frequency reported in MG-infected pregnant women seen in Southwestern US sites.[8] The common detection of MG infection and high frequency of MRMs in this cohort underscores the great need for a better understanding of the clinical implications of untreated MG

infection in pregnant women to guide screening and treatment recommendations; should treatment be necessary for MG infection in pregnant women in the United States, then additional MG treatment options that are safe in pregnancy will be needed. We did not detect an association of MG with adverse perinatal outcomes, although our study was underpowered to detect these associations. Given the limited evidence suggesting that MG may be associated with adverse pregnancy outcomes,[2] further studies will be needed to determine the impact of MG and associated MRMs on pregnancy and neonatal outcomes and whether treatment of MG during pregnancy can prevent these outcomes.

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CONFLICT OF INTEREST

WMG reports having previously received honoraria as a speaker for Roche. BVDP reports receiving funding for research and honoraria for participation on advisory boards from Roche.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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TABLE 1

Baseline characteristics of the study participants by MG status

Characteristics	Total (*N* = 224)	MG positive (*n* = 18)	MG negative (*n* = 206)	*P* value[a]
Age	29 (18–44)	26 (21–35)	29 (18–44)	0.03
Race				0.08[b]
White	114 (50.9)	5 (27.8)	109 (52.9)	
Black	94 (42.0)	12 (66.7)	82 (39.8)	
Other	16 (7.1)	1 (5.6)	15 (7.3)	
Hispanic	10 (4.5)	0 (0.0)	10 (4.9)	1.00
Days since last vaginal sex	7 (0–270)	4 (1–210)	7 (0–270)	0.08
Reported STI history				
Chlamydia	61 (27.2)	7 (38.9)	54 (26.2)	0.25
Gonorrhea	18 (8.0)	2 (11.1)	16 (7.8)	0.64
Trichomoniasis	43 (19.2)	9 (50.0)	34 (16.5)	0.001
Gestational age at enrollment (weeks)	27.5 (6.2–40.0)	29.5 (7.0–37.4)	27.4 (6.2–40.0)	0.88
Enrollment site				0.16
Obstetrics Complications Clinic	123 (54.9)	14 (77.8)	109 (52.9)	
Maternal-Fetal Medicine Clinic	51 (22.8)	2 (11.1)	49 (23.8)	
Prime Care Clinic	50 (22.3)	2 (11.1)	48 (23.3)	

Notes: Values are given as median (range) or number (percentage). *N* = 1 missing for ethnicity from the MG-negative group.

N = 1 missing for days since last vaginal sex from the MG-negative group.

Abbreviation: STI, sexually transmitted infection.

[a] By Pearson χ^2, Fisher exact, or Wilcoxon rank-sum (Mann–Whitney) test, as appropriate.

[b] On analysis of individual race by *Mycoplasma genitalium* (MG) status, Black race was associated with MG positivity (*P* = 0.03).

TABLE 2

Select participant characteristics and perinatal outcomes among women who delivered at the University of Alabama at Birmingham by MG status

Characteristics	Total (*N* = 185)	MG positive (*n* = 16)	MG negative (*n* = 169)	*P* value[a]
Medical conditions				
Pregestational diabetes	31 (16.8)	4 (25.0)	27 (16.0)	0.32
Gestational diabetes	13 (7.0)	0 (0)	13 (7.7)	0.61
Chronic hypertension	39 (21.1)	2 (12.5)	37 (21.9)	0.53
Gestational hypertension	13 (7.1)	1 (6.3)	12 (7.1)	1.0
Pre-eclampsia	12 (6.5)	1 (6.3)	11 (6.6)	1.0
Severe pre-eclampsia	23 (12.5)	1 (6.3)	22 (13.1)	0.70
Macrolide use during pregnancy	19 (10.3)	5 (31.3)	14 (8.3)	0.01
Gestational age at delivery (weeks)	38.4 (20.4–41.4)	39.0 (33.1–41.4)	38.3 (20.4–40.5)	0.67
Perinatal outcomes[b]				
Preterm birth	44 (23.8)	5 (31.3)	39 (23.1)	0.54
Small for gestational age	27 (14.8)	4 (25.0)	23 (13.8)	0.26
Fetal growth restriction	13 (7.1)	2 (12.5)	11 (6.6)	0.32

Notes: Values are given as median (range) or number (percentage).*N* = 1 missing for gestational hypertension from the *Mycoplasma genitalium* (MG)–negative group.

N = 1 missing for pre-eclampsia from the MG-negative group.

N = 1 missing for severe pre-eclampsia from the MG-negative group.

N = 1 missing for gestational age at delivery from the MG-negative group.

N = 2 missing for small for gestational age from the MG-negative group.

N = 2 missing for fetal growth restriction from the MG-negative group.

[a]By Pearson chi-square, Fisher exact, or Wilcoxon rank-sum (Mann–Whitney) test, as appropriate.

[b]Preterm birth defined as a livebirth before <37 weeks of gestation but after >20 weeks of gestation; small for gestational age defined as birth weight < 10th percentile for gestational age; fetal growth restriction defined as an estimated fetal weight < 10th percentile.