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Molecular Diagnostics Update for the Emerging (If Not Already Widespread) Sexually Transmitted Infection Agent *Mycoplasma genitalium*: Just About Ready for Prime Time

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MINIREVIEW

Molecular Diagnostics Update for the Emerging (If Not Already Widespread) Sexually Transmitted Infection Agent *Mycoplasma genitalium*: Just About Ready for Prime Time

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ABSTRACT *Mycoplasma genitalium* is an important and emerging agent of sexually transmitted infection in females and males, carrying the potential for postinfection genital tract sequelae. Past efforts to identify this organism on a routine basis, which were problematic due to the fastidious nature of the bacterium and its antigenic intricacies, have recently become supplemented by molecular diagnostics. A number of these assays are available commercially. This minireview describes the format and performance indices of a number of *M. genitalium* DNA- and RNA-based amplification assays; many of these assays have contributed to an improved clinical and epidemiologic understanding of this organism.

KEYWORDS *Mycoplasma genitalium*, PCR, molecular diagnostics, transcription-mediated amplification

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In 1981, the first report of recovery and identification of *Mycoplasma genitalium*, the smallest free-living microorganism capable of reproduction, was published (1). However, the fastidious nature of this intracellular bacterium significantly limits its ability to be cultivated in an *in vitro* setting (2). Attempts at serologic diagnosis have been confounded by antigenic variation of *M. genitalium* (3) and immunogenic analogs observed in other *Mollicutes*, such as *Mycoplasma pneumoniae* (4). These paradigms are unfortunate because of the long-standing association of *M. genitalium* with nongonococcal and nonchlamydial urethritis in males (2) and an emerging collection of literature implicating the organism in cervicitis, pelvic inflammatory disease, preterm birth, and spontaneous abortion (5). Other investigators have reported promotion of HIV acquisition (6) and shedding (7) by antecedent *M. genitalium* infection.

Initial efforts to alleviate the gap in laboratory diagnosis of *M. genitalium* infection involved molecular assays performed in research settings. Hooton et al. (8) utilized a radiometric dot hybridization assay to detect *M. genitalium* DNA from 30 of 203 male urethral swabs. Jensen et al. (9) targeted the *M. genitalium* 140-kDa adhesion protein gene (MgPa) in 150 urogenital specimens that were originally collected for *Chlamydia trachomatis* culture. Restriction digestion and hybridization identified the target in 6.7% of specimens. MgPa nomenclature will be used in this paper in reference to genetic derivatives of the adhesion protein gene frequently used in assay development.

In an attempt to highlight *M. genitalium* diagnostic advancements, a PubMed primary literature search (U.S. National Library of Medicine and the National Institutes of Health), conducted on 8 May 2017, selected 417 in-print English language citations from the years 1991 to 2017 (Fig. 1). Ten additional manuscripts had a status of electronic publication ahead of print. Nearly 27% of the aforementioned publications entered the literature between 2006 and 2011, perhaps coinciding with some of the

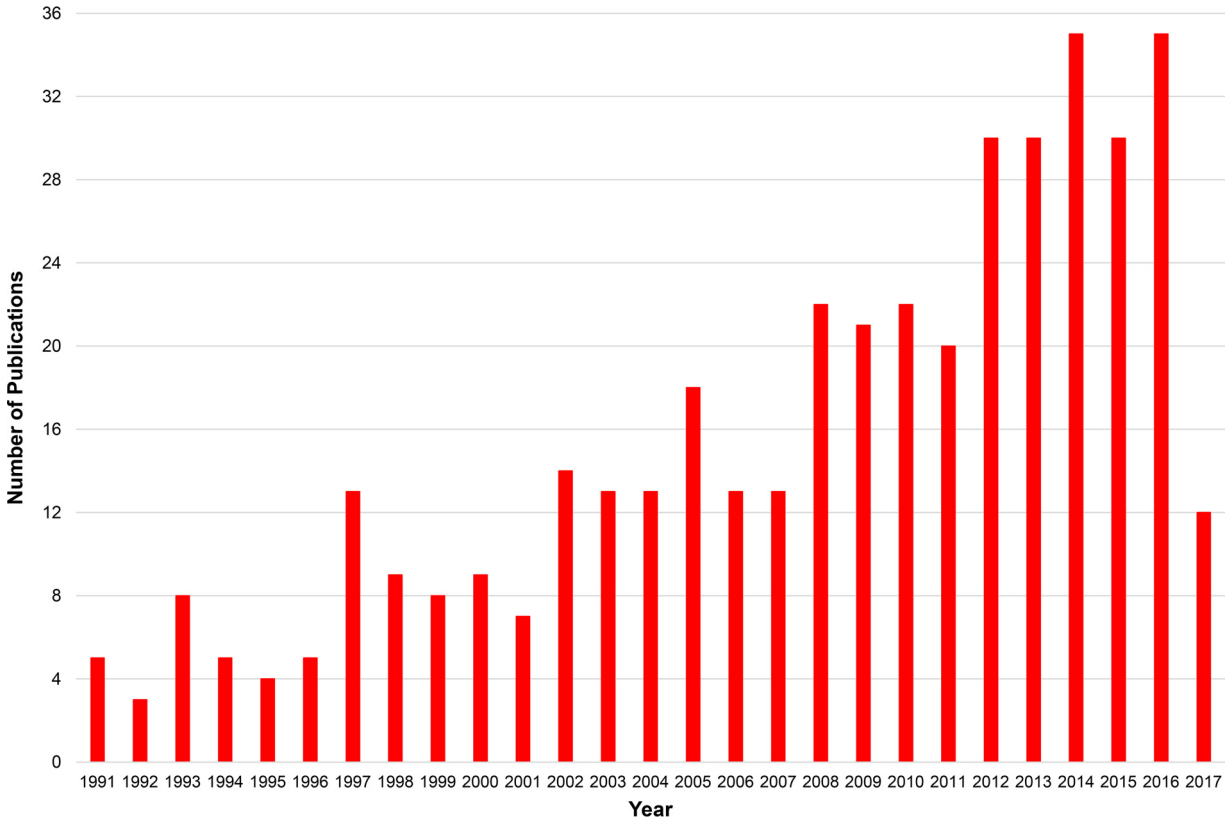

FIG 1 Frequency of *Mycoplasma genitalium* molecular diagnostics publications in English from 1991 to 2017 as determined by the search parameter "*Mycoplasma genitalium*" filtered by the possibilities of "molecular diagnostics," "molecular testing," "NAAT," "nucleic acid amplification testing," "PCR," "LAMP," "TMA," or "transcription-mediated amplification."

first commercial attempts at assay development; over 41% have been published since 2012, which may be in line with increasing reports of clinical macrolide treatment failure and concomitant development of molecular assays to alert clinicians to this possibility. This brief commentary, with a focus largely on literature published within the past 2 years, provides an update on *M. genitalium* molecular diagnostics and suggests that these assays may soon become commonplace for the clinical microbiologist.

COMMERCIALLY DEVELOPED DNA AMPLIFICATION ASSAYS

A number of commercially produced *M. genitalium* DNA amplification modalities have been described. *M. genitalium*-specific dual-priming oligonucleotide primers have been incorporated into a multiplex PCR assay for six sexually transmitted infection (STI) agents, with subsequent detection of end products via auto-capillary electrophoresis (Seeplex STD6 ACE; Seegene, Seoul, South Korea). One evaluation (10), performed on 739 urogenital specimens, was limited by utilization of a monoplex PCR (using the same primer sets) to confirm positive results and by *M. genitalium* DNA being detected from only two specimens. Kweon et al. (11) evaluated a PCR microarray capable of detecting 13 agents of genitourinary tract infection (STDetect Chip; LabGenomics, Seongnam, South Korea) using a combination of prospective vaginal and urine specimens that was augmented by archived specimens. When compared to direct sequencing of PCR products generated by primers to the MgPa operon, the assay yielded concordance and sensitivity values of 99.4% and 98.1%, respectively, in this study set with an 11% *M. genitalium* detection rate. The method required independent nucleic acid extraction and demonstrated 100% concordance with results of the Seeplex STD6 ACE within a subset of 87 specimens.

Additional attempts to detect *M. genitalium* DNA have come in the context of assays

designed for genital *Mycoplasmataceae*. Takanashi et al. (12) applied PCR target amplification and Invader-based signal amplification (InvaderPlus; LSI Medience Corporation, Tokyo, Japan) to detection of *M. genitalium*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, and *Ureaplasma parvum* from male first-void urine samples. Detection specificity emanates from triple-stranded hybridization complexes and Cleavase enzyme activity. When compared to a research PCR microtiter plate hybridization assay, a kappa value of 0.961 was attained for InvaderPlus in the context of 15 positive specimens. Incorporation of internal control nucleic acid revealed endogenous inhibition within 12 of 171 specimens. Kriesel et al. (13) assessed a research-use-only nested multiplex PCR assay for detection of *M. genitalium*, *U. urealyticum*, and seven other STI agents (FilmArray STI panel; BioFire Diagnostics, Salt Lake City, UT) with 295 clinical specimens and used standard-of-care laboratory offerings as reference methods. However, with respect to *M. genitalium*, no reference was employed since testing for this organism was not offered to clinicians at that time. *M. genitalium* DNA was detected in 3% of specimens (five urine samples, one genital swab, one rectal swab, one pharyngeal swab). Kappa values of $\geq$0.97 were attained with FilmArray STI panel assessment of *Neisseria gonorrhoeae* and *C. trachomatis* infections when compared to FDA-cleared Amplicor assays (Roche Molecular Diagnostics).

The LightMix *Mycoplasma genitalium* kit (TIB Molbiol, Berlin, Germany) is a commercially available real-time PCR assay that requires nucleic acid extraction apart from the kit. The assay, targeting a 224-bp *gap* sequence, was applied to the cobas z 480 analyzer (14). In a study of 104 archived urogenital DNA extracts, kit-provided internal control was amplified in all instances. When compared to a research *M. genitalium* PCR reference standard, sensitivity and specificity of the LightMix *Mycoplasma genitalium* kit were 92.6% and 100%, respectively.

A number of *M. genitalium* DNA amplification assays have received Conformité Européene *in vitro* diagnostic (CE) marking. The Bio-Rad Dx CT/NG/MG assay (Bio-Rad, Marnes-la-Coquette, France) is a multiplex PCR assay that incorporates an internal control and provides a lysis reagent for manual nucleic acid extraction. The assay is CE-marked for performance on vaginal, cervical, and urethral swabs as well as female and male first-void urine samples. *M. genitalium* MgPa amplification and detection occur in manufacturer-provided instrumentation. When compared to research MgPa PCR results, the Bio-Rad Dx CT/NG/MG assay exhibited 100% sensitivity from 658 female and male urogenital specimens acquired from 453 French STI clinic patients (15). However, just 11 specimens had detectable *M. genitalium* DNA using the evaluated method, one of which (vaginal swab collection) was classified as a false-positive result.

The Hyplex STD *Mycoplasma* test system (Amplex BioSystems, Lich, Germany) is a CE-marked multiplex PCR for detection of *M. genitalium*, *M. hominis*, *U. urealyticum*, and *U. parvum*. A prototype of this assay was reported to have 87% sensitivity and 96% specificity for detection of *M. genitalium* MgPa (16). Khatib et al. (17) utilized this assay (in concert with commercial RNA methods for *C. trachomatis*, *N. gonorrhoeae*, and *Trichomonas vaginalis* detection) for assessment of symptomatic males in the United Kingdom. *M. genitalium* DNA was detected in 11 of 83 (13.3%) first-void urine specimens and was the only agent detected in six of those specimens. All positive findings were confirmed by research *M. genitalium* PCR. A total of 42.2% of specimens in this report had no detectable nucleic acid specific to *C. trachomatis*, *N. gonorrhoeae*, *T. vaginalis*, *M. genitalium*, or *U. urealyticum*.

The AmpliSens N. gonorrhoeae/C. trachomatis/M. genitalium/T. vaginalis-Multiprime-FRT assay (InterLabScience, Moscow, Russia) is a CE-marked real-time PCR assay containing an internal control that requires independent nucleic acid extraction. Amplification and detection of *M. genitalium gyrB* is facilitated by an open-channel platform. Rumyantseva et al. (18) evaluated this assay using 1,261 frozen specimens originally collected from Swedish STI clinic attendees in transport medium specific to a commercial RNA amplification system. AmpliSens *M. genitalium* data were compared to those of two reference commercial RNA amplification assays. Overall AmpliSens sensitivity

was 81.9%, with a range of 76.5% to 84.8% among vaginal specimens and first-void urine samples from both genders. No false-positive results were derived from the AmpliSens assessment; 59 patients yielded detectable *M. genitalium* RNA within this study.

Le Roy et al. (14) evaluated the CE-marked *Mycoplasma genitalium* real-time PCR kit targeting *mg219* (Diagenode, Seraing, Belgium) using a cobas z 480 open-channel system. Performance indices from 104 archival nucleic acid extracts included 100% specificity when compared to research *M. genitalium* PCR results and 87% sensitivity (seven false-negative results). Kit-provided internal control was amplified in all cases. A newer generation assay allows for simultaneous detection of *M. genitalium* and *T. vaginalis*. This S-DiaMGTV kit (Diagenode) was subjected to a 1,569-specimen evaluation from STI clinic and general practice patients in the Netherlands (19). The assay was facilitated by open-channel amplification and detection; DNA extraction apart from the kit was required. All positive *M. genitalium* results, along with 100 negative results, were verified by reference laboratory *M. genitalium* PCR. No *M. genitalium* testing discrepancies were reported. The study, undertaken to generate point prevalence data and address empirical treatment guidelines, revealed *M. genitalium* and *T. vaginalis* detection rates of 4.0% and 1.3%, respectively.

Using the same assay, Pereyre et al. (20) reported an *M. genitalium* detection rate of 3.4% and a *T. vaginalis* detection rate of 1.7% from 2,652 consecutive female and male urogenital specimens collected in 16 French university hospitals. Of the 88 patients that were positive for *M. genitalium* DNA, 38.6% were coinfected with *C. trachomatis*, *N. gonorrhoeae*, or *T. vaginalis*. Within a subset of 34 males with detectable *M. genitalium* DNA, close to 6% prevalence was noted in a 35- to 44-year-old demographic. A total of 70.9% of patients across both genders with detectable *M. genitalium* DNA were asymptomatic.

Fast-track diagnostics (Sliema, Malta) produces a number of CE-marked multiplex qualitative PCR assays for STI agents that allow for *M. genitalium* MgPa detection from first-void urine, genital, and rectal collections. The assays include an internal control and require additional instruments for DNA extraction and target amplification/detection. However, a paucity of peer-reviewed studies exists comparing assay performance to other molecular diagnostic modalities. Gossé et al. (21) adapted the FTD Urethritis basic assay to a quantitative PCR format to investigate a test-of-cure paradigm for azithromycin therapy. Using daily first-void urine specimens over the course of 14 days, the authors concluded that fluctuations in bacterial counts hypothetically result in false-negative tests of cure. Consequently, the authors advocated *M. genitalium* mutation analysis at time of organism detection as an optimal means of addressing therapeutic options.

The CE-marked ResistancePlus MG kit (SpeeDx, Sydney, Australia) utilizes PlexZyme/PlexPrime technology for real-time quantitative PCR (qPCR) detection of *M. genitalium* on an open-channel platform. The multiplex assay includes an internal control and can identify mutations in 23S rRNA sequences encoding macrolide resistance. An assay prototype was described by Tabrizi et al. (22) using an Australian cohort of 254 *M. genitalium*-infected patients during clinical follow-up. In a collection of 400 urine/urethral swab, cervical/vaginal swab, and anal swab specimens, the evaluated assay achieved 99.0% concordance in comparison to a research 16S rRNA gene qPCR reference. Four noted discrepant specimens each contained a low *M. genitalium* copy number. With respect to organism detection by the ResistancePlus MG kit, a retrospective assessment of 206 urogenital specimens produced a kappa value of 0.98 when compared to a combined research PCR and S-DiaMGTV reference standard (23). One ResistancePlus MG result was false-negative (98.9% sensitivity), and internal control amplification failure occurred at a rate of 0.48%. Taken together, this assay may be positioned to address current and future conundrums of clinical *M. genitalium* resistance.

COMMERCIALLY DEVELOPED RNA AMPLIFICATION ASSAYS

Over 10 years have passed since the initial formulation of RNA amplification assays specific to *M. genitalium* 16S rRNA using transcription-mediated amplification (TMA; Hologic, San Diego, CA). Hardick et al. (24) determined the sensitivity of research multitarget PCR (16S rRNA gene, MgPa) and TMA for *M. genitalium* detection to be 88.8% and 100.0%, respectively, from 286 male urine specimens. *M. genitalium* prevalence exceeded 13% in this U.S. STI clinic demographic. Wroblewski et al. (25) assessed 352 male urine specimens from U.S. STI clinic attendees by research MgPa PCR and TMA, reporting detection rates of 7.4% and 6.8%, respectively. A preliminary TMA investigation in females (24) yielded 96.9% sensitivity and 98.4% specificity from 321 self-collected vaginal swabs in a population with 19.6% *M. genitalium* prevalence. Analogous values for multitarget PCR were 93.8% and 99.2%. The other report (25) noted sensitivity values of *M. genitalium* TMA (relative to a standard of a patient yielding a positive research PCR or TMA result) from vaginal and cervical specimens as being 84% and 60%, respectively. Comparative values for research PCR were 91% and 53%. Prevalence rates derived from these specimen sources ranged from 9% to 14%.

Wroblewski et al. (25) introduced the prospect of alternative specimen sources for female screening. Sensitivity values of MgPa PCR and TMA assays on female first-void urine samples (relative to a standard of a patient being positive for either test) were calculated at 65% and 58%, respectively. The authors did not provide information regarding urine preservation, other than the fact that specimens were archived at −80°C prior to analysis. These data come with the additional caveat that cell wall-deficient microbes, such as *M. genitalium*, are likely more susceptible to lytic activities or components endogenous to urine (25). Data concerning another STI pathogen, *T. vaginalis*, may be extrapolated into the potential value of first-void urine samples as a noninvasive screen for *M. genitalium* in females using TMA. Using a molecular-resolved algorithm, Nye et al. (26) determined the sensitivity values of commercial *T. vaginalis* TMA on 296 first-void female urine, endocervical, and vaginal specimens to be 87.5%, 89.8%, and 96.6%, respectively. Analogous values derived from PCR were 76.1%, 80.9%, and 83.0%. These data further provide evidence for the enhanced analytical sensitivity of commercial TMA versus conventional DNA amplification methods. Potential explanations for this difference (oligonucleotide-based target capture for removal of endogenous inhibitors, differences in nucleic acid target quantity), which may further promote the value of urine screening efforts, have been discussed in a previous review (27).

TMA-based detection of *M. genitalium* has subsequently been adapted to an analyte-specific reagent (ASR) format on automated analyzers. In a study of males from an STI clinic and community care settings (apart from the STI clinic) in a high-prevalence U.S. STI community (28), residual contents of 2,750 consecutive first-void urine samples, preserved in Aptima urine specimen transport tubes (Hologic) within 24 h of primary void, were subjected to *M. genitalium* ASR on TIGRIS automation. The *M. genitalium* ASR detection rate (6.84%) nearly equaled that generated by *C. trachomatis* TMA (6.87%) and exceeded those of *N. gonorrhoeae* TMA and laboratory-validated *T. vaginalis* TMA. *M. genitalium* distribution, when delineated by patient age, was similar to distributions exhibited by *N. gonorrhoeae* and *C. trachomatis*.

STI phenotype can be defined as *M. genitalium*, *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis* distribution within a given health care encounter that yields detection of at least one STI agent. This measure essentially denotes the probability that a given agent is the etiology of the STI diagnosed during that encounter. In the aforementioned study (28), a dichotomy of STI prevalence emerged when comparing STI phenotypes involving *M. genitalium* and *T. vaginalis* (Table 1). Sole detection of *M. genitalium* was documented in 36.5% of STI clinic visits that yielded at least one STI; this frequency was 22.0% within community care encounters ($P = 0.0007$). Overall detection of *M. genitalium* STI phenotype occurred in 47.4% of STI clinic visits that generated at least one STI; that value was 29.7% within community care encounters. In contrast, while 5.3% of STI clinic visits that yielded at least one STI involved sole detection of *T. vaginalis*, 18.7%

TABLE 1 Sexually-transmitted infection phenotype determined by transcription-mediated amplification specific for *Mycoplasma genitalium*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* within screened males who were positive for at least one STI[a]

STI phenotype[b,c]				No. (%) of patients delineated by healthcare setting		
M. genitalium	*C. trachomatis*	*N. gonorrhoeae*	*T. vaginalis*	STI clinic	Community care	*P* value
+	−	−	−	97[d] (36.5)[e]	46 (22.0)	0.0007
+	+	−	−	17 (6.4)	10 (4.8)	0.45
+	−	+	−	9 (3.4)	2 (1.0)	0.08
−	+	−	−	69 (25.9)	67 (32.1)	0.14
−	+	+	−	10 (3.8)	13 (6.2)	0.22
−	−	+	−	44 (16.5)	26 (12.4)	0.21
−	−	−	+	14 (5.3)	39 (18.7)	<0.0002
Any *M. genitalium* detection				126 (47.4)	62 (29.7)	0.0002
Any *C. trachomatis* detection				97 (36.5)	92 (44.0)	0.10
Any *N. gonorrhoeae* detection				68 (25.6)	43 (20.6)	0.20
Any *T. vaginalis* detection				19 (7.1)	44 (21.1)	<0.0002

[a]Adapted from reference 28 with permission from Elsevier.
[b]+, positive transcription-mediated amplification screen; −, negative transcription-mediated amplification screen.
[c]Phenotypes that were observed in <1.5% of patients at both the STI clinic and community care are not included in this table. No significant difference was noted within each of these comparisons.
[d]This value indicates the number of phenotypes.
[e]This value indicates the percentage of phenotypes per clinic distribution.

of community care visits that generated at least one STI demonstrated sole detection of *T. vaginalis*. A total of 7.1% of STI clinic encounters with at least one detectable STI agent yielded *T. vaginalis*, while the analogous value in community care was 21.1%.

A community-wide study (with broad demographic and acuity-of-illness coverage) in the same U.S. high-prevalence STI community assessed *M. genitalium* ASR using 2,478 residual female specimens submitted for routine laboratory screening of *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis* (29). The *M. genitalium* detection rate was 11.4% and exceeded those of the other STI agents ($P \leq 0.005$). Sufficient material following primary *M. genitalium* ASR performance allowed for repeat testing of 208 *M. genitalium*-positive specimens; 207 (99.5%) yielded a positive result. Furthermore, a subset of 242 specimens was subjected to *M. genitalium* TMA with an alternative target. A 98.8% overall concordance of results was observed, including a 99.5% concordance rate among 213 specimens that initially yielded a negative *M. genitalium* ASR result. Age distribution of females with detectable *M. genitalium* mirrored those of females infected with *C. trachomatis* and *N. gonorrhoeae*.

M. genitalium detection rates, stratified by specimen source, ranged from 10.1% (first-void urine) to 13.8% (vaginal swab). As only 138 vaginal specimens were assessed on the basis of this representative, retrospective collection, the 13.8% vaginal swab detection rate was not significantly increased over that of urine ($P = 0.23$). The cervical swab detection rate from 1,896 specimens (11.5%) demonstrated no significant difference versus those of first-void urine and vaginal swab ($P \geq 0.41$). These data were limited by all specimens being collected in routine clinical practice, during which multiple patient samplings did not occur.

Nonutilization of the *M. genitalium* ASR would result in significant missed opportunities for STI detection. Of the 282 overall *M. genitalium* detections, *M. genitalium* was the sole STI agent detected in 203 (72.0%) of these instances (Table 2). In this high-prevalence population, one specific patient demographic demonstrated a greater proclivity for this organism. When compared to highly prevalent *T. vaginalis* (9.0% overall detection rate), *M. genitalium* detection rates from inpatient obstetric/gynecologic (OB/GYN), suburban family care, urban family care, and emergency room (ER)/urgent care settings showed little variation ($P \geq 0.37$) (Table 2). However, the *M. genitalium* detection rate from 1,032 outpatient OB/GYN clinic patients (10.3%) was elevated versus that of *T. vaginalis* (6.4%; $P = 0.001$). Moreover, relative to the *M. genitalium* sole detection paradigm, 80.2% of outpatient OB/GYN clinic patients with

TABLE 2 Female *Mycoplasma genitalium* and *Trichomonas vaginalis* transcription-mediated amplification detection frequencies delineated by health care setting[a]

Health care setting	No.	Comparative detection frequency (%)		*P* value	Instances (%) of sole *Mycoplasma genitalium* detection[b]
		Mycoplasma genitalium	*Trichomonas vaginalis*		
Outpatient OB/GYN	1,032	106 (10.3)	66 (6.4)	0.001	85 (80.2)
Inpatient OB/GYN	46	7 (15.2)	5 (10.9)	0.54	5 (71.4)
Suburban family care	261	18 (6.9)	14 (5.4)	0.47	12 (66.7)
Urban family care	384	41 (10.7)	39 (10.2)	0.81	26 (63.4)[c]
ER/urgent care	755	110 (14.6)	98 (13.0)	0.37	75 (68.2)[d]

[a]Adapted from reference 29.
[b]This indicates *M. genitalium* detections not involving codetection with another STI agent.
[c]$P = 0.03$ versus instances of sole *M. genitalium* detection from outpatient OB/GYN.
[d]$P = 0.04$ versus instances of sole *M. genitalium* detection from outpatient OB/GYN.

detectable *M. genitalium* did not exhibit STI codetection (Table 2). This rate was elevated over those for ER/urgent care patients (68.2% *M. genitalium* sole detection) and urban family care patients (63.4% *M. genitalium* sole detection; both $P \leq 0.04$).

A retrospective, seven-center U.S. study (30) confirmed and extended several of the findings from the previous two studies. *M. genitalium* and *C. trachomatis* prevalence rates (17.2% and 17.8%, respectively) were equally high among males. The female *M. genitalium* ASR detection rate (16.3%) was significantly higher than those of *C. trachomatis* and *N. gonorrhoeae* but less than that of *T. vaginalis*. Significant associations were made between *M. genitalium* detection and non-Hispanic ethnicity, African American race, younger age, and female symptomatic status. Moreover, a high frequency of single-agent infection was demonstrated.

Tabrizi et al. (31) evaluated an *M. genitalium* TMA assay on the automated Panther platform (Hologic) in comparison to a composite molecular standard comprised of an alternative target TMA assay, 16S rRNA gene PCR, and MgPa PCR. Sensitivity and specificity values for the CE-marked assay were 100% and 93.6%, respectively, from 1,080 urine specimens collected from a diverse clinical population with nearly 9% *M. genitalium* prevalence. Sensitivity values for the two PCR assays ranged from 89.1% to 91.3%. These data extend earlier findings (18, 24, 26) regarding the improved potential of STI agent detection using TMA modalities.

OUTLOOK

The field of molecular diagnostics, particularly in the last 8 to 10 years, has strived to fulfill an unmet clinical need with respect to this fastidious organism. Differences in *M. genitalium* prevalence exist throughout the world (references 10, 13, 15, and 18 to 20 discuss low prevalence; references 17, 24, 25, and 28 to 33 discuss high prevalence), which may influence local routine screening decisions. The possibility does exist that the lower sensitivity of DNA amplification testing may result in an underestimation of prevalence. However, concern for macrolide-resistant strains of *M. genitalium* may supersede some of these lower-prevalence data in providing impetus for clinical screening. Less-invasive means of specimen collection, such as first-void urine or self-collected vaginal swab options, may promote a higher screening frequency, particularly in scenarios that do not require a physical examination. Furthermore, Dize et al. (32) reported that *M. genitalium* ASR performed on self-collected penile-meatal swabs (investigated in a U.S. STI clinic with 14% *M. genitalium* prevalence) yielded performance indices equivalent to those derived from clinician-collected urethral swabs.

As clinical microbiologists encounter the increased availability of *M. genitalium* molecular diagnostics, including those ultimately receiving FDA clearance, additional studies will be necessary to ascertain the optimal specimen source in terms of performance characteristics and patient accessibility. Moreover, a recent report suggests that inclusion of multiple analytes and specimen source collections significantly increases detection of STI carrier status (33). Further investigations may be necessary to indicate

targeted demographics (20, 28–30) should a fully comprehensive screening approach not be advocated in a given locale. Consideration of *M. genitalium* molecular diagnostics within an STI screening algorithm may ultimately realize public health benefits and improved clinical management.

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