The Role of *Mycoplasma* and *Ureaplasma* in Adverse Pregnancy Outcomes

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KEYWORDS

• Genital mycoplasma • Ureaplasma • Mycoplasma • Preterm birth
• Chorioamnionitis • Endometritis • Bronchopulmonary dysplasia

KEY POINTS

- Both *Mycoplasma* and *Ureaplasma spp* cause inflammation leading to spontaneous preterm birth, preterm premature rupture of membranes, postdelivery infectious complications, and neonatal infections.
- Molecular detection methods now allow the distinction between the various species and biovars of both *Mycoplasma* and *Ureaplasma*.
- Genital mycoplasmas are frequently found as part of a polymicrobial infection which weakens the association between these organisms and associated outcomes.
- In vitro and animal model systems must be created to establish causality between the genital mycoplasmas and adverse perinatal outcomes.
- Polymerase chain reaction quantification allows an accurate measurement of organismal burden, which may distinguish between colonization and infection leading to a better assessment of the relationship to adverse perinatal outcomes.

INTRODUCTION

Mycoplasma and *Ureaplasma spp* are associated with multiple pregnancy and neonatal complications ranging from preterm labor to postpartum endometritis, and from low birth weight to bronchopulmonary dysplasia (BPD). In the almost half century since the association between these organisms and adverse perinatal outcomes was postulated,[1] the distinction between these organisms and their effects is incompletely understood. Until the past decade, their fastidious nature slowed investigation. Newer, molecular-based investigation techniques revitalized this field of research, allowing

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exploration into the pathogenic ability of these organisms, particularly their transition from commensal colonization to parasitic infection.

This paper is written to serve as a review of the effects *Mycoplasma* and *Ureaplasma* infection, with particular attention to disease prevalence, organism microbiology, perinatal outcomes, and disease treatment. Although not taxonomically correct, the term "genital mycoplasmas" is used to refer to *Mycoplasma spp* and *Ureaplasma spp* to facilitate discussion. When distinct evidence exists regarding separate species, a more accurate description will be specified.

PREVALENCE AND EPIDEMIOLOGY

Isolation of genital mycoplasmas initially proved difficult secondary to the extensive culture requirements for organism growth. To expand detection, early studies analyzed serum samples for antibodies directed against these organisms using enzyme-linked immunosorbent assay.[2] Although serologic testing increases the detection rate, it is unable to differentiate between previous and current infection. It was not until the advent of the polymerase chain reaction (PCR) that genital mycoplasmas could be reliably detected and easily screened.[3] Further development of PCR techniques, including nested PCR as well as random amplified polymorphic DNA PCR, allowed for increased sensitivity to lower organism counts as well as increased specificity and differentiation of species and subtypes.[4] In fact, PCR detection methods were shown to be superior to culture-based methods for detection of the presence of organisms.[5]

With the advent of highly sensitive and specific PCR detection techniques, more accurate estimates of the prevalence of genital mycoplasmas can be determined. Various studies have been performed across the world with surprising similarities between the rates of colonization. Initial studies on a low- to middle-income predominately white and Mexican-American population in Tucson, Arizona, revealed a 23.5% rate of *Mycoplasma* and a 72.3% rate of *Ureaplasma spp*.[6] These same authors found rates of 50% for *Mycoplasma* and approximately 80% for *Ureaplasma* in an America Indian population.[7] Similar rates were found in a Canadian population, including both family planning and prenatal patients.[8] Luton and colleagues[9] investigated *Mycoplasma* and *Ureaplasma* rates in equatorial Africa and similarly found rates of approximately 50% and 80%, respectively. Another study in Cote d'Ivoire, West Africa, in 2000 revealed somewhat lower rates of *Ureaplasma* (53%), but similar rates of *Mycoplasma* (51%).[10] Finally, a study of healthy pregnant women in Kuala Lumpur, Malaysia, revealed much lower colonization rates with only 18% of women colonized with *Mycoplasma* and 57% colonized with *Ureaplasma*. These studies indicate that genital mycoplasma colonization rates are similarly high across the world. Such high colonization rates make understanding these organism's contributions to the microbiome and particularly their interplay with adverse pregnancy and neonatal outcomes of the greatest importance (**Box 1**).

MICROBIOLOGY

Genital mycoplasmas are unique microorganisms, characterized by their fastidious nature and subsequently difficult identification.[11] The class Mollicutes is subdivided into 8 genera, leading to more than 200 different species with the majority belonging to the genus *Mycoplasma*. These organisms are derived from the ancestral clostridia bacteria via gene deletion and consequently have the smallest known genome of any free-living organism. The *Ureaplasma* genus is another clinically significant group of organisms.[12] Colloquially these are all referred to as mycoplasmas. They are