

SHORT COMMUNICATION

## Prevalence of *Mycoplasma genitalium* in early pregnancy and relationship between its presence and pregnancy outcome

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*Mycoplasma genitalium* is associated with cervicitis and pelvic inflammatory disease but little is known about its role in pregnancy. We investigated the prevalence of *M. genitalium* by polymerase chain reaction assay on urine specimens from 1216 pregnant women (mean age 31 years) presenting before 10 weeks of gestation in 32 general practices. The prevalence of *M. genitalium* was 0.7% (6/915, 95% CI 0.1–1.2). It was more common in women aged <20 years, women of Afro-Caribbean or black African ethnic origin, women in social classes 3–5 and single women. Only one woman with *M. genitalium* infection miscarried, and none of those followed up to term had a preterm birth, although the numbers were small. The low prevalence of *M. genitalium* infection suggests it is unlikely to be an important risk factor in adverse pregnancy outcome in healthy women in the community.

### Introduction

Little is known about the epidemiology of *Mycoplasma genitalium*.<sup>1</sup> It has been causally associated with non-gonococcal urethritis in men,<sup>2</sup> and linked with cervicitis,<sup>3</sup> endometritis<sup>4</sup> and pelvic inflammatory disease<sup>1,5,6</sup> in women. However, its role in pregnancy has been examined infrequently.<sup>7,8</sup> Although difficult to culture, the availability of the polymerase chain reaction assay for detection of *M. genitalium*<sup>9,10</sup> enables an expansion of screening. As part of a prospective study<sup>11</sup> of the role of *Chlamydia trachomatis* and bacterial vaginosis in adverse pregnancy outcome, we decided to test first-pass urine specimens obtained from newly pregnant women for *M. genitalium*. The aim was to investigate the prevalence and predictors of *M. genitalium* at <10 weeks of gestation, and to examine the relation between the mycoplasma, co-infections and pregnancy outcome.

### Methods

As described previously,<sup>11</sup> consecutive, pregnant women of <10 weeks of gestation who presented at 32 general practices and 5 family planning clinics in south London were invited to take part in the study. Those who agreed to participate were asked to provide a first-pass urine specimen and a self-administered vaginal swab and smear and to complete questionnaires about the pregnancy at 16 weeks and at term. First-pass urines and swabs were tested for *C. trachomatis* by a ligase chain reaction assay (Abbott Laboratories, Chicago, USA), and vaginal smears were Gram-stained and examined microscopically for bacterial vaginosis.<sup>12</sup> Ethical approval was obtained from Wandsworth Local Research Ethics Committee.

After sampling for *C. trachomatis*, urine specimens were frozen at –20°C and transported within three years on dry ice to Denmark for examination by a polymerase chain reaction assay.<sup>13</sup> Urine specimens were centrifuged and the pellet lysed by boiling in 20% wt/vol Chelex as previously described.<sup>14</sup> An inhibitor controlled polymerase chain reaction assay detecting the 16S rRNA gene of *M. genitalium* was used.<sup>13</sup> All positive results were confirmed by a second polymerase chain reaction detecting the MgPa adhesin gene.<sup>9</sup> The *M. genitalium* DNA load in the positive specimens was determined by TaqMan quantitative polymerase chain reaction procedure targeting a conserved part of the MgPa adhesin gene. The results were expressed in terms of genome equivalent (geq) per mL of urine.

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## Results

Between June 1998 and July 2000, 1216 pregnant women of mean age 31 years (range 16–48 years) were recruited. The mean gestation time was 49 days (range 12–69 days). Of 1107 women who responded, 78% described their ethnicity as white, 7% as Afro-Caribbean, 4% as black African, 6% as of Indian subcontinent origin and 5% as other ethnic groups. Sixty percent (626/1045) were in social classes 1 or 2, and 91% (1009/1105) were married or cohabiting.

A total of 1014 urine specimens were available for examination, but 97 of the labels were unclear and two specimens contained polymerase chain reaction inhibitors. Six of the remaining 915 specimens tested positive for *M. genitalium*, a prevalence of 0.66% (95% CI 0.13 to 1.18). *M. genitalium* was detected most often in urine from women aged <20 years, women of Afro-Caribbean or black African ethnic origin, women in social classes 3–5 and those who were single, widowed or divorced (Table 1). None of 20 chlamydia-positive women was *M. genitalium*-positive. However, *M. genitalium* was associated with bacterial vaginosis. Thus, it was present in 3 of 128 women who were positive for bacterial vaginosis (Nugent score 7–10), 1 of 45 women who had smears graded as 'intermediate' (Nugent score 4–6) and 2 of 731 women who were negative for bacterial vaginosis (Nugent score 0–3;  $\chi^2$  for trend,  $P = 0.01$ ). However, the *M. genitalium* DNA load carried by the infected women in the three groups was similar: 70, 140 and 770 geq, respectively, for the three women with bacterial vaginosis; 2835 geq for the woman with vaginal flora of intermediate grade; and 35 and 910 geq for the two women with normal flora. None of four women with *M. genitalium* who responded to the question gave a history of pelvic inflammatory disease.

Of six women for whom *M. genitalium* was detected at <10 weeks of gestation, one miscarried before 10 weeks and the remaining five were still pregnant when followed

up at 16 weeks. Three of these five delivered at term, one was lost to follow up and one returned an incomplete questionnaire at term (Table 1).

## Discussion

This is the first community-based prospective study of *M. genitalium* and its association with pregnancy outcome and has the strength of being a study of a large number of normal women recruited much earlier in pregnancy than in hospital-based studies.<sup>7,8</sup> This required the use of routine general practice specimen storage and transport facilities. Whether this influenced in a detrimental way the detection of *M. genitalium* is a moot point. Also unknown, but possible, is whether the low prevalence of mycoplasma infection could be due, at least partly, to the fact that specimens were defrosted to test for *C. trachomatis* in the UK before being refrozen and transported to Denmark. But an unpublished laboratory study suggests this is unlikely to reduce the detection rate by more than 25% (JS Jensen, personal communication). Unlike previous studies,<sup>7,8</sup> this was a cohort of pregnant women at lower risk of sexually transmitted infections: older, mainly in stable partnerships and the majority from social classes 1 and 2. Although the prevalence of *M. genitalium* was low at about 1%, it was found to be more common in women who were young, black, single or in social classes 3–5. Whether exclusion of 97 specimens, which could not be identified due to labelling problems in transit, had an effect on the results is not clear, but the association of *M. genitalium* with the normal risk factors for sexually transmitted infections<sup>15</sup> lends the results credibility. The number of women with *M. genitalium* was too small to assess any relationship with adverse pregnancy outcome, but the low prevalence also suggests the infection is unlikely to be a major risk factor in healthy women.

There have been two previous reports of *M. genitalium* infection in pregnancy. Lu *et al.*<sup>7</sup> found *M. genitalium* at mid-trimester in the vagina of 5 (3.9%) of 124 women (ages

**Table 1.** Demographic characteristics, co-infection and outcome of pregnancy in 915 pregnant women according to *M. genitalium* status at <10 weeks of gestation.

| Characteristic  | No. (%) with characteristic | Prevalence of <i>M. genitalium</i> in women with characteristic | Prevalence of <i>M. genitalium</i> in women without characteristic | P value (Fisher's exact test) |
|---|-----------------------------|---|--|-------------------------------|
| Age <20 ( $n = 915$ )                                     | 33 (3.6)                    | 3/33 (9.0)  | 3/882 (0.3)  | 0.002                         |
| Bacterial vaginosis positive ( $n = 859$ )                | 128 (14.9)                  | 3/128 (2.3)   | 2/731 (0.3)  | 0.051                         |
| Chlamydia-positive ( $n = 914$ )                          | 20 (2.2)                    | 0/20 (0)  | 6/894 (0.7)  | NS                            |
| Past history of pelvic inflammatory disease ( $n = 661$ ) | 9 (1.4)                     | 0/9 (0)   | 4/652 (0.6)  | NS                            |
| Afro-Caribbean or black African ethnicity ( $n = 827$ )   | 86 (10.3)                   | 3/86 (3.4)  | 3/741 (0.4)  | 0.034                         |
| Social class 3–5 ( $n = 789$ )                            | 309 (39.2)                  | 6/309 (1.9)   | 0/480 (0)  | 0.007                         |
| Single, widowed divorced ( $n = 829$ )                    | 67 (8.1)                    | 3/67 (4.5)  | 3/762 (0.4)  | 0.017                         |
| Miscarried at <16 weeks ( $n = 894$ )                     | 92 (10.3)                   | 1/92 (1.1)  | 5/802 (0.6)  | NS                            |
| Preterm birth at <37 weeks ( $n = 699$ )                  | 39 (5.6)                    | 0/39 (0)  | 3/660 (0.5)  | NS                            |

not given) who subsequently had a spontaneous preterm birth and suggested that *M. genitalium*, as in the current study, was unlikely to be an important contributory factor. Labbè *et al.*<sup>8</sup> found a larger proportion (6.2%) of 1014 pregnant women infected with *M. genitalium* in their study in Guinea-Bissau. These women were relatively young (66% aged <25 years), and with high prevalences of sexually transmitted infection (9% had HIV, 8% had *N. gonorrhoeae*). In this study as well, infection with *M. genitalium* was not associated with a poor pregnancy outcome. These studies differed from ours in the specimen used for *M. genitalium* analysis. We used first-pass urine, which may be less sensitive than physician-taken high vaginal<sup>7</sup> or cervical swabs.<sup>8,16,17</sup> Similarly, for detection of *C. trachomatis*, we used ligase chain reaction assay which has sensitivities of 78% in urine, 89% in self-taken vaginal swabs and 96% in endocervical swabs.<sup>18</sup> As previously indicated, the low prevalence of *M. genitalium* found in our study may be an under-estimate.

In agreement with the findings in many other studies, predominantly those of men with or without urethritis,<sup>5</sup> *M. genitalium* was found independently of *C. trachomatis*. However, in a study, such as the current one, where the number of chlamydia-positive results was small and those of *M. genitalium* even smaller, the chance of coexistence is also likely to be small. Nevertheless, outside pregnancy, however, *M. genitalium* has pathogenic potential in women, being associated with cervicitis,<sup>3</sup> histologically confirmed endometritis<sup>4</sup> and pelvic inflammatory disease.<sup>1,5,6</sup> In none of these small studies, however, was an association found between *M. genitalium* and concomitant bacterial vaginosis. Furthermore, the association with bacterial vaginosis in the current study is at variance with observations in young women attending genitourinary clinics in the UK<sup>16</sup> and USA.<sup>17</sup> Keane *et al.*<sup>16</sup> noted that while *Mycoplasma hominis* was strongly associated with the occurrence of bacterial vaginosis, *M. genitalium* was not associated. Similarly, in a larger study of women recruited in the 1980s, Manhart *et al.*<sup>17</sup> found *M. genitalium* was associated with mucopurulent cervicitis, young age and multiple partners, but not with bacterial vaginosis. However, the association with bacterial vaginosis in the current study is qualitative rather than quantitative in that the *M. genitalium* DNA load in women with bacterial vaginosis was not obviously greater than in those without the condition. Thus, *M. genitalium* is apparently not behaving like *M. hominis* where the number of organisms may increase 10,000-fold in women with bacterial vaginosis compared with those without vaginosis.<sup>19</sup> It seems that the discrepancy between this and previous studies is less than appears at first sight.

## Conclusion

Although the prevalence of *M. genitalium* in this large community-based cohort was low, this is the first report in pregnant women of the association of the infection with

demographic factors. However, the low prevalence also suggests that *M. genitalium* is unlikely to be an important contributor to adverse pregnancy outcome in normal women.

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