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Prevalence and antibiotic susceptibility of *Mycoplasma hominis* and *Ureaplasma urealyticum* in pregnant women

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Spontaneous abortion;
Low birth weight;
Antibiotic susceptibility

Summary
Background: *Mycoplasma hominis* and *Ureaplasma urealyticum* are important opportunistic pathogens implicated in urogenital infections and complicated pregnancy. We aimed to study the role of these pathogens in symptomatic and asymptomatic pregnant women and determine their clinical significance and antibiotic susceptibility.
Methods: One hundred pregnant women were included in the study, 50 symptomatic patients and 50 asymptomatic controls. Duplicate endocervical samples were taken from each individual and analyzed using the Mycoplasma IST-2 kit and A7 agar medium. Antimicrobial susceptibility was tested against doxycycline, josamycin, ofloxacin, erythromycin, tetracycline, ciprofloxacin, azithromycin, clarithromycin, and pristinamycin using the Mycoplasma IST-2 kit.
Results: Twelve symptomatic pregnant women had spontaneous abortions. Of these, eight (66.7%) cases had been colonized with *M. hominis* and/or *U. urealyticum*. Of the pregnant women infected with *M. hominis* and/or *U. urealyticum*, 40.7% delivered a low birth weight infant. *M. hominis* was successfully cultured in five women (5%) and *U. urealyticum* in 27 (27%). Among positive cultures, 15.6% and 84.4% of isolates were *M. hominis* and *U. urealyticum*, respectively. *M. hominis* and *U. urealyticum* were uniformly susceptible to doxycycline, tetracycline, and pristinamycin, which may be successfully used in the empirical therapy of infected individuals.
Conclusions: It can be concluded that genital colonization with *M. hominis* and *U. urealyticum* may predispose to spontaneous abortion and low birth weight.

Introduction

Genital mycoplasmas represent a group of microorganisms that are commonly found in the genitourinary tract of preg-

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nant and non-pregnant women. They have been associated with various pathological conditions and intrauterine infections, including pyelonephritis, pelvic inflammatory disease, chorioamnionitis, endometritis, and postpartum fever, leading to important complications such as preterm birth, low birth weight, spontaneous abortion, stillbirth, premature birth, infertility, and perinatal mortality.[1–6] The genital mycoplasmas that contribute most to these conditions are *Mycoplasma hominis* and *Ureaplasma urealyticum*. They are most commonly present in the genital tract of sexually active women.[7–9] Colonization values worldwide for *M. hominis* range between 20% and 30% and for *U. urealyticum* range between 60% and 80%.[10] The prevalence of these organisms is significantly associated with socioeconomic conditions, such as poverty, and increasing number of sexual partners.[8,10] They pose a serious medical threat to the mother during gestation and to the fetus and neonate.[8] The role of mycoplasmas in the aetiopathogenesis of the urogenital system is still the subject of controversy.[11] Controversy regarding the association of genital mycoplasmas with bacterial vaginosis also exists; some investigators claim that there is a relationship between the two,[12] whereas others do not.[13]

Mycoplasmas lack a cell wall—the target of beta-lactam antibiotics and vancomycin. Tetracyclines, macrolides, and quinolones are the major antibiotics used in the treatment of urogenital infections caused by mycoplasmas.[8] However, their therapeutic efficacy may be unpredictable due to increasing resistance.[14] The extent of resistance varies geographically according to different antimicrobial therapy policies and the history of prior antimicrobial exposure in different populations.[6,8]

The aim of the present study was to detect the presence of *U. urealyticum* and *M. hominis* in symptomatic and control pregnant women, including an analysis by age group and gestation period. The association of these mycoplasmas with pregnancy complications and their antimicrobial susceptibility were also assessed.

Subjects and methods

One hundred pregnant women (50 symptomatic patients and 50 asymptomatic controls) were studied at outpatient visits to the gynecology and obstetrics clinics of Turgut Ozal Medical Center, Inonu University Hospital, Malatya, Turkey from July 2006 to May 2007. A questionnaire was completed for each woman, recording personal data, sexual history, symptoms, and other obstetric and gynecologic disorders. Babies born weighing less than 2500 g were classified as low birth weight infants according to the World Health Organization criteria. The mean $\pm$ standard deviation age of the patients was 28.6 $\pm$ 5.3 years (range 18—41 years) and of controls was 28.6 $\pm$ 5.6 years (range 18—39 years). Enrolled subjects were sexually active pregnant women with a gestation period of $\leq$36 weeks.

The patient group experienced symptoms of vaginitis, abnormal vaginal discharge, and/or itching or burning in the genital area. Controls were those attending routine checkups and had none of the above symptoms. It was stipulated that all women participating in the study should not have taken any antimicrobial agent prior to sampling that could affect the growth of mycoplasmas. Women who did not meet the inclusion criteria were excluded from the study, hence they were not consecutive cases. The approval of the Ethics Committee of Inonu University was obtained. All women gave informed consent prior to enrolling.

M. hominis and *U. urealyticum* are not routinely detected by conventional bacteriological methods. For this study a commercial kit, Mycoplasma IST-2 (BioMerieux, Marcy l'Etoile, France), was used according to the manufacturer's instructions. The kit contains strips that give information on the presence or absence of *M. hominis* and *U. urealyticum* and also provide additional information on antibiotic susceptibility to doxycycline, josamycin, ofloxacin, erythromycin, tetracycline, ciprofloxacin, azithromycin, clarithromycin, and pristinamycin. In order to process specimens, two endocervical swabs were obtained from each individual. These were processed in the laboratory within 4 hours. One strip was placed directly into R1 tubes (transport medium) and subsequently delivered to the clinical laboratory for the identification of both *U. urealyticum* and *M. hominis* and to determine antimicrobial susceptibility. The other swab was cultured on blood, chocolate, and Sabouraud dextrose agars. A Gram stained smear was made. The presence of other organisms, such as *Gardnerella vaginalis*, was assessed according to Amsel's criteria and conventional microbiological techniques.[15,16]

Swabs in the R1 transport medium were processed according to the manufacturer's instructions. They were vortexed rapidly, and 3 ml of R1 was used to rehydrate the lyophilized growth medium R2 (provided in the Mycoplasma IST-2 kit). A Mycoplasma IST strip, consisting of 22 wells, was then inoculated with the rehydrated R2 growth medium (55 μl per well, overlaid with two drops of mineral oil). From the R2 positive tube, 0.1 ml was also inoculated onto A7 Mycoplasma agar plates (BioMerieux, Marcy l'Etoile, France) and incubated at 37 °C in an atmosphere of 5% CO_2 for checking characteristic colony morphology. All media and the inoculated strip were incubated at 37 °C in a CO_2 incubator and observed for color changes, and the results were interpreted after 24 and 48 h of incubation. Wells 1—5 provide information on the presence or absence of *M. hominis* and *U. urealyticum*, with an estimate of the density of each organism ($\geq 10^4$ CFU), and wells 6—22 show the antimicrobial susceptibilities to doxycycline, josamycin, ofloxacin, erythromycin, tetracycline, ciprofloxacin, azithromycin, clarithromycin, and pristinamycin. The A7 plates were examined with a microscope twice daily for up to 5 days for characteristic colonies. Colonies presenting with a fried egg appearance suggest the presence of *M. hominis*, whereas colonies that are brown and tiny indicate the presence of *U. urealyticum*. *M. hominis* ATCC 15488 and *U. urealyticum* ATCC 27813 strains were used as controls.

Statistical analysis was performed using SPSS version 11.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were analyzed by Chi-square test. *p*-Values of <0.05 were considered statistically significant.

Results

Of the 100 subjects, 29 (29%) were positive for *M. hominis* and/or *U. urealyticum*. Of these, 27 women were in the patient group (54%) and two were in the control group (4%). *U. urealyticum* was isolated alone from 22/50 (44%) patients and 2/50 (4%) controls ($p < 0.05$). The frequency of

Table 1 Prevalence of *Mycoplasma hominis* and *Ureaplasma urealyticum* among symptomatic and control women

Group[a]	*U. urealyticum*	*M. hominis*	*U. urealyticum* + *M. hominis*	Total
Patients (N = 50)	22 (44%)	2 (4%)	3 (6%)	27 (54%)
Controls (N = 50)	2 (4%)	0 (0)	0 (0)	2 (4%)
Total	24 (24%)	2 (2%)	3 (3%)	29 (29%)

Results are *n* (%).
[a] $p < 0.05$.

M. hominis detected alone in the patient group was 2/50 (4%); no *M. hominis* was detected in controls. Three women within the patient group (6%) were co-infected with both *M. hominis* and *U. urealyticum*. Thus 32 *M. hominis* and *U. urealyticum* were identified overall, 27 (84.4%) *U. urealyticum* and five (15.6%) *M. hominis* (Table 1).

The distribution of *M. hominis* and *U. urealyticum* according to age group is shown in Table 2. Of the symptomatic patients, six (12%) were aged 18—24 years, 12 (24%) were aged 25—29 years, six (12%) were aged 30—34 years, and three (6%) were over 35 years old. Significantly, approximately two thirds of *U. urealyticum* and *M. hominis* occurred in patients between the ages of 25 and 34 years ($p < 0.05$).

The distribution of *M. hominis* and *U. urealyticum* according to gestation period is shown in Table 3. Of the 32 mycoplasmas, 13 (48.1%) were seen in patients at between 33 and 36 weeks of gestation ($p < 0.05$).

Twelve women in the patient group had a spontaneous abortion at a gestation period of less than 36 weeks (Table 4). Of these, eight (66.7%) cases had been colonized with *M. hominis* and/or *U. urealyticum* and only three cases were simultaneously infected with *G. vaginalis*. Other organisms detected in the patient group are presented in Table 5. These were as follows: *G. vaginalis* (seven strains, five in the patient group and two in controls), beta-hemolytic streptococcus (*Streptococcus agalactiae*; two strains, both in patients), *Candida albicans* (22 strains, 12 in patients and 10 in controls), and 13 strains of other *Candida* species. Some of the patients were co-infected with *M. hominis* and/or *U. urealyticum* (11 cases) as follows: three (27.3%) with strains of *G. vaginalis*, two (18.2%) with *S. agalactiae*, and six (54.5%) with *C. albicans* (Table 5).

Among symptomatic patients with positive cervical mycoplasmas, 11 (40.7%) were associated with low birth weight (Table 4).

Antimicrobial susceptibilities were determined using the Mycoplasma IST-2 kit and are shown in Tables 6 and 7. All strains were susceptible to doxycycline, tetracycline, and pristinamycin. Multiple resistance to two antibiotics was rarely seen, even when mixed genital mycoplasmas were present. Among *M. hominis*, the highest drug resistance rate was 100% to erythromycin, while the highest drug resistance rates in *U. urealyticum* were 92.6% to ciprofloxacin and 85.2% to ofloxacin. No resistance was observed to josamycin, although some strains had intermediate resistance.

Table 2 Distribution of *Mycoplasma hominis* and *Ureaplasma urealyticum* in the different age groups

Age group (years)	*M. hominis*	*U. urealyticum*
18—24	1 (20%)	8 (29.6%)
25—29	3 (60%)	7 (25.9%)
30—34	1 (20%)	8 (29.6%)
35—39	0 (0)	3 (11.1%)
≥40	0 (0)	1 (3.7%)
Total	5 (100%)	27 (100%)

Results are *n* (%).

Table 3 Distribution of *Mycoplasma hominis* and *Ureaplasma urealyticum* in the different gestation periods

Gestation period (weeks)	*M. hominis*	*U. urealyticum*
21—24	2 (40%)	1 (3.7%)
25—28	2 (40%)	6 (22.2%)
29—32	1 (20%)	7 (25.9%)
33—36	0 (0)	13 (48.1%)
Total	5 (100%)	27 (100%)

Results are *n* (%).

Discussion

In our study, 27 women (54%) in the patient group were positive for *M. hominis*, *U. urealyticum*, or both mycoplasmas. In controls, two women (4%) yielded only *U. urealyticum* ($p < 0.05$). None of the controls yielded *M. hominis*. Three cases (6%) were infected with both *M. hominis* and *U. urealyticum*. The highest prevalence of *M. hominis* and/or *U. urealyticum* was seen in pregnant women in the 18—34 years age group (Table 2). In comparing our findings with those of

Table 4 Numbers and percentages of pathological conditions observed in control and symptomatic pregnant women and their possible association with mycoplasmas

	Patients (*N* = 50)	Mycoplasmas (*N* = 27)	Controls (*N* = 50)	Mycoplasmas (*N* = 2)
Spontaneous abortion	12 (24%)	8 (29.6%)	3 (6%)	0 (0)
Low birth weight	14 (28%)	11 (40.7%)	13 (26%)	0 (0)
Still birth	3 (6%)	1 (3.7%)	3 (6%)	0 (0)

Results are *n* (%).

Table 5 Co-infections of *Mycoplasma hominis* and/or *Ureaplasma urealyticum* with others pathogens

Pathogens	Patients	Controls	Co-infection with mycoplasmas in patients, *n* (%)
Gardnerella vaginalis (*n* = 7)	5	2	3 (27.3%)
Candida albicans (*n* = 22)	12	10	6 (54.5%)
Beta-hemolytic Streptococcus (*n* = 2)	2	0	2 (18.2%)
Total	19	12	11 (100%)

many previous studies, which have reported between 10% and 50% of women to be colonized with *U. urealyticum* but colonization rates with *M. hominis* of less than 30%,[11,12,17] we found a distinct disproportion in the incidence of these two mycoplasmas. *U. urealyticum* was more commonly detected than *M. hominis* in both the patients and controls. Our findings are fairly consistent with those of other studies conducted in Poland[9] and Greece,[18] but distinctly different to those of studies from the highlands of Papua New Guinea,[10] Portugal,[11] and Japan.[19]

The presence of genital mycoplasmas is associated with an increased risk of developing certain pathologic conditions of pregnancy, such as spontaneous abortion, preterm labor, and low birth weight.[10,20] In the present study, 40.7% of pregnant women infected with *M. hominis* and/or *U. urealyticum* delivered a low birth weight infant. Moreover, eight out of 12 (66.7%) spontaneous abortion cases had been colonized with *M. hominis* and/or *U. urealyticum*. Although, it has been reported that *U. urealyticum* is associated with premature onset of labor,[19,21] the exact role of mycoplasmas in such cases is not fully understood.

Simultaneous colonization with both *M. hominis* and *U. urealyticum* was not common (6% in symptomatic patients), but has been found to be as low as 2.92% in one population[18] and as high as 60% in another.[10] This discrepancy may be due to variations in socioeconomic conditions and living standards.

A change in vaginal pH (e.g., bleeding in pregnancy, sexual intercourse, or vaginal douching) may predispose to an overgrowth of potential pathogens.[6,20,22] Both *M. hominis* and *U. urealyticum* have been suggested to have an uncertain role in bacterial vaginosis.[2,23] As shown in Table 5, some potential pathogens were frequently associated with mycoplasmas. The exact reason for the simultaneous detection of these potential pathogens remains unclear;[8] it may be associated with sexual activity, vaginal environment, sexual education, socioeconomic status, poor hygiene, and altered immune status.[8,9] Urogenital diseases are not only caused by mycoplasmas but also by other pathogens. It is usually impossible to define which pathogen is responsible in mixed infections, hence the antibiotic sensitivity of these pathogens must be taken into account when empirical therapy is prescribed.[2]

Regarding antibiotic sensitivity, the results show that the sensitivity to various antibiotics in *U. urealyticum* infection was different from that of *M. hominis* infection. *U. urealyticum* was more sensitive to macrolides and *M. hominis* was more sensitive to quinolones. Antibiotics such as pristinamycin (streptogramin group) and josamycin (a novel antibiotic belonging to the newly developed macrolides), which are unavailable in our local pharmacies and not prescribed in our clinics, were tested in this study. They had potent activity against both *U. urealyticum* and *M. hominis*. Although pristinamycin, josamycin, doxycycline, and tetracycline resistance has been reported for both *U. urealyticum* and

Table 6 Antimicrobial susceptibility of the total identified mycoplasmas determined using the Mycoplasma IST-2 kit

Antimicrobial agent	Susceptible	Intermediate	Resistant
Doxycycline	32 (100%)	0 (0)	0 (0)
Josamycin	29 (90.6%)	3 (9.4%)	0 (0)
Ofloxacin	4 (12.5%)	2 (6.3%)	26 (81.3%)
Erythromycin	16 (50%)	5 (15.6%)	11 (34.4%)
Tetracycline	32 (100%)	0 (0)	0 (0)
Ciprofloxacin	5 (15.6%)	0 (0)	27 (84.4%)
Azithromycin	17 (53.1%)	7 (21.9%)	8 (25%)
Clarithromycin	27 (84.4%)	1 (3.1%)	4 (12.5%)
Pristinamycin	32 (100%)	0 (0)	0 (0)

Results are *n* (%).

Table 7 Susceptibility of *Mycoplasma hominis* and *Ureaplasma urealyticum* to nine different antimicrobials

Antimicrobial agent	*M. hominis* (*n* = 5)			*U. urealyticum* (*n* = 27)		
	S	I	R	S	I	R
Doxycycline	5 (100%)	0 (0)	0 (0)	27 (100%)	0 (0)	0 (0)
Josamycin	4 (80%)	1 (20%)	0 (0)	25 (92.6%)	2 (7.4%)	0 (0)
Ofloxacin	1 (20%)	1 (20%)	3 (60%)	3 (11.1%)	1 (3.7%)	23 (85.2%)
Erythromycin	0 (0)	0 (0)	5 (100%)	16 (59.3%)	5 (18.5%)	6 (22.2%)
Tetracycline	5 (100%)	0 (0)	0 (0)	27 (100%)	0 (0)	0 (0)
Ciprofloxacin	3 (60%)	0 (0)	2 (40%)	2 (7.4%)	0 (0)	25 (92.6%)
Azithromycin	2 (40%)	1 (20%)	2 (40%)	15 (55.6%)	6 (22.2%)	6 (22.2%)
Clarithromycin	3 (60%)	0 (0)	2 (40%)	24 (88.9%)	1 (3.7%)	2 (7.4%)
Pristinamycin	5 (100%)	0 (0)	0 (0)	27 (100%)	0 (0)	0 (0)

S, susceptible; I, intermediate; R, resistant. Results are *n* (%).

M. hominis,[18] they were found to be the most active agents against these pathogens in the current work, and could be used in empirical therapy. *M. hominis* is naturally resistant to erythromycin whereas *U. urealyticum* is moderately susceptible to macrolides but is resistant to quinolones.[14,24,25] The significant difference related to susceptibility to macrolides and quinolones has been reported before.[26] Resistance to quinolones such as ofloxacin and ciprofloxacin has been observed in our clinical isolates of *U. urealyticum*. Higher resistance of mycoplasmas to antimicrobials is due to mutations in antibiotic targets and may suggest their relation to higher pathogenicity.[6,8,27]

Empirical therapy is important in the treatment of mycoplasmas since culture and identification methods are not routinely used for the detection of mycoplasmas in Turkish clinical laboratories. This is of paramount importance for successful therapy and clinicians recommend early administration of antibiotics for a good pregnancy outcome and to prevent the occurrence of complications. However, limitations of this study are the small number of samples and that we could not investigate other potential pathogens such as *Ureaplasma parvum*, since this was not available in the commercial kit used in the present study.

Conclusions

This study shows a low prevalence of mycoplasmas in pregnant women in our population, since this population is generally conservative and there is mostly one sex partner. The prevalence of genitourinary infections due to *U. urealyticum* was considerably higher as compared to *M. hominis* infection. The prevalence of *U. urealyticum* and *M. hominis* was significantly correlated with age and gestation period. *M. hominis* and *U. urealyticum* may be associated with spontaneous abortion and low birth weight. In inflammatory and pathological states of pregnancy, testing for the presence of mycoplasmas is necessary for a safe pregnancy outcome and should be included in the diagnostic protocol. Our results also indicate that doxycycline, tetracycline, and pristinamycin are the first choice drugs when empirical therapy is required.

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Conflict of interest: No conflict of interest to declare.

References

1. Cassell GH, Waites KB, Watson HL, Crouse DT, Harasawa R. *Ureaplasma urealyticum* intrauterine infection: role in prematurity and disease in newborns. *Clin Microbiol Rev* 1993;**6**:69–87.
2. Taylor-Robinson D, Furr PM. Update on sexually transmitted mycoplasmas. *Lancet* 1998;**351**(Suppl 3):12–5.
3. Daxboeck F, Zitta S, Stadler M, Iro E, Krause R. *Mycoplasma hominis* and *Ureaplasma urealyticum* in patients with sterile pyuria. *J Infect* 2005;**51**:54–8.
4. Patai K, Szilágyi G, Hubay M, Szentmáriay IF, Paulin F. Severe endometritis caused by genital mycoplasmas after Caesarean section. *J Med Microbiol* 2005;**54**:1249–50.
5. Witt A, Berger A, Gruber CJ, Petricevic L, Apfalter P, Worda C, et al. Increased intrauterine frequency of *Ureaplasma urealyticum* in women with preterm labor and preterm premature rupture of the membranes and subsequent cesarean delivery. *Am J Obstet Gynecol* 2005;**193**:1663–9.
6. Pararas MV, Skevaki CL, Kafetzis DA. Preterm birth due to maternal infection: causative pathogens and modes of prevention. *Eur J Clin Microbiol Infect Dis* 2006;**25**:562–9.
7. van Belkum A, van der Schee C, van der Meijden WI, Verbrugh HA, Sluiters HJ. A clinical study on the association of *Trichomonas vaginalis* and *Mycoplasma hominis* infections in women attending a sexually transmitted disease (STD) outpatient clinic. *FEMS Immunol Med Microbiol* 2001;**32**:27–32.
8. Waites KB, Katz B, Schelonka RL. Mycoplasmas and ureaplasmas as neonatal pathogens. *Clin Microbiol Rev* 2005;**18**:757–89.
9. Zdrodowska-Stefanow B, Kłosowska WM, Ostaszewska-Puchalska I, Bułhak-Kozioł V, Kotowicz B. *Ureaplasma urealyticum* and *Mycoplasma hominis* infection in women with urogenital diseases. *Adv Med Sci* 2006;**51**:250–3.
10. Clegg A, Passey M, Yoannes M, Michael A. High rates of genital Mycoplasma infection in the highlands of Papua New Guinea determined both by culture and by a commercial detection kit. *J Clin Microbiol* 1997;**35**:197–200.
11. Domingues D, Távora Tavira L, Duarte A, Sanca A, Prieto E, Exposto F. Genital mycoplasmas in women attending a family planning clinic in Guiné-Bissau and their susceptibility to antimicrobial agents. *Acta Trop* 2003;**86**:19–24.
12. Keane FE, Thomas BJ, Gilroy CB, Renton A, Taylor-Robinson D. The association of *Mycoplasma hominis*, Ureaplasma urealyticum and Mycoplasma genitalium with bacterial vaginosis: observations on heterosexual women and their male partners. *Int J STD AIDS* 2000;**11**:356–60.
13. Arya OP, Tong CY, Hart CA, Pratt BC, Hughes S, Roberts P, et al. Is Mycoplasma hominis a vaginal pathogen? *Sex Transm Infect* 2001;**77**:58–62.
14. Kenny GE, Cartwright FD. Susceptibilities of *Mycoplasma hominis*, *M. pneumoniae*, and *Ureaplasma urealyticum* to GAR-936, dalfopristin, dirithromycin, evernimicin, gatifloxacin, linezolid, moxifloxacin, quinupristin–dalfopristin, and telithromycin compared to their susceptibilities to reference macrolides, tetracyclines and quinolones. *Antimicrob Agents Chemother* 2001;**45**:2604–8.
15. Amsel R, Totten PA, Spiegel CA, Chen KC, Eschenbach D, Holmes KK. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. *Am J Med* 1983;**74**:14–22.
16. Egan ME, Lipsky MS. Diagnosis of vaginitis. *Am Fam Physician* 2000;**62**:1095–104.
17. Grattard F, Soleihac B, De Barbeyrac B, Bebear C, Seffert P, Pozzetto B. Epidemiologic and molecular investigations of genital mycoplasmas from women and neonates at delivery. *Pediatr Infect Dis J* 1995;**14**:853–8.
18. Kechagia N, Bersimis S, Chatzipanagiotou S. Incidence and antimicrobial susceptibilities of genital mycoplasmas in outpatient women with clinical vaginitis in Athens, Greece. *J Antimicrob Chemother* 2008;**62**:122–5.
19. Kataoka S, Yamada T, Chou K, Nishida R, Morikawa M, Minami M, et al. Association between preterm birth and vaginal colonization by mycoplasmas in early pregnancy. *J Clin Microbiol* 2006;**44**:51–5.
20. McDonald HM, O'Loughlin JA, Jolley PT, Vigneswaran R, McDonald PJ. Changes in vaginal flora during pregnancy and association with preterm birth. *J Infect Dis* 1994;**170**:724–8.
21. Kundsin RB, Leviton A, Allred EN, Poulin SA. *Ureaplasma urealyticum* infection of the placenta in pregnancies that ended prematurely. *Obstet Gynecol* 1996;**87**:122–7.

22. McGregor JA, French JI. Bacterial vaginosis in pregnancy. *Obstet Gynecol Surv* 2000;**55**(Suppl 1):S1—19.
23. Chaim W, Mazor M, Leiberman JR. The relationship between bacterial vaginosis and preterm birth. *Arch Gynecol Obstet* 1997;**259**:51—8.
24. Taylor-Robinson D, Bebear C. Antibiotic susceptibilities of mycoplasmas and treatment of mycoplasmal infections. *J Antimicrob Chemother* 1997;**40**:622—30.
25. Semra Z, Rosenberg S, Soffer Y. In vitro susceptibility of *Mycoplasma hominis* clinical isolates to tetracyclines, quinolones and macrolides. *Diagn Microbiol Infect Dis* 2002;**44**:359—61.
26. Ullmann U, Schubert S, Krausse R. Comparative in vitro activity of levofloxacin, other fluoroquinolones, doxycycline and erythromycin against *Ureaplasma urealyticum* and *Mycoplasma hominis*. *J Antimicrob Chemother* 1999;**43**(Suppl C): 33—6.
27. Bebear CM, Renaudin H, Charron A, Gruson D, Lefrancois M, Bebear C. In vitro activity of trovafloxacin compared to those of five antimicrobials against mycoplasmas including *Mycoplasma hominis* and *Ureaplasma urealyticum* fluoroquinolone-resistant isolates that have been genetically characterized. *Antimicrob Agents Chemother* 2000;**44**:2557—60.