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Treatment of Mycoplasma Hominis and Ureaplasma Urealyticum in Pregnant Women

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Abstract: ***The purpose of this study was to investigate the antimicrobial susceptibility and resistance patterns of genital mycoplasmas in pregnant women attending antenatal care. The antimicrobial susceptibility testing included tetracycline, doxycycline, erythromycin, azithromycin, clarithromycin, josamycin, ofloxacin, ciprofloxacin, and pristinamycin. The development or absence of red color on the relevant part of the strip provided an index of resistance or susceptibility to each antimicrobial agent, respectively, according to the guidelines of the CLSI. To maintain a safe pregnancy, it is important to identify the isolates and use appropriate antibiotics immediately. Early pregnancy screening for genital mycoplasmas and following treatment may reduce preterm deliveries.***

Keywords: Women, Ureaplasma spp., Mycoplasma hominis, Antimicrobial susceptibility

1. Introduction

Mycoplasma hominis and Ureaplasma spp., including U. parvum and U. urealyticum, are collectively known as genital mycoplasmas and are found in the vaginal milieu of up to 80% of pregnant and non-pregnant women (1). The pathogenesis of genital mycoplasmas is still poorly understood. Damage related to genital mycoplasma infections might be the result of the induced immune- and inflammatory responses rather than the direct toxic effects of mycoplasma cellular components (2). Mycoplasma hominis is specifically associated with conditions such as endometritis and preterm birth (3). Ureaplasmas are reported to be more prevalent than other mycoplasmas in the female urogenital tract, with U. parvum found more often than U. urealyticum. During pregnancy, Ureaplasma spp. can cause chorioamnionitis, spontaneous abortion, stillbirth and preterm delivery. Although the pathogenic role of U. urealyticum in urogenital tract infections is widely recognised , the role of U. parvum in these infections is not that well established . Nonetheless, U. parvum might be present in bacterial loads leading to adverse pregnancy outcomes and produce asymptomatic infections of the upper genital tract in women as frequently as U. urealyticum. Out of the four U. parvum serovars (including serovars 1, 3, 6 and 14), serovars 3 and 14 have been isolated in more cases of genital tract infections than serovars 1 and 6 (4). The greater virulence reported for U. urealyticum in some conditions might be attributed to its superior capability of acquiring genes horizontally (5). Genital mycoplasmas display inherent resistance to beta-lactams and glycopeptides (e.g. vancomycin) because of the absence of a cell wall (6) Although macrolides are often the drugs of choice for treating these infections, M. hominis is intrinsically resistant to the C14 and C15 macrolides (e.g. erythromycin and azithromycin) (7). Ureaplasma species also have natural resistance to lincosamides (e.g. clindamycin) (8). Observed resistance to macrolides is associated with mutations in the 23S rRNA gene (9), while resistance to tetracyclines is associated with the presence of the moveable tet(M) genetic element (10). The administration of antimicrobial agents to pregnant women with preterm rupture of the membranes (PROM) may extend the gestation period and decrease the risks of associated complications and neonatal infections (11). The antimicrobial agent of choice should be considered carefully, as some agents are teratogens - i.e. the agent can cause malformation or functional damage to an embryo or foetus or may have toxic effects on the neonate (12). Macrolides are often used empirically (13) because of tetracyclines and fluoroquinolones being contraindicated in pregnancy (14). However, the amniotic sac is not effectively penetrated by erythromycin and ureaplasmas are not eradicated from the vagina or cervix by this agent (15). Newer macrolides (e.g. azithromycin and clarithromycin) allow for better tolerability and the once daily dosing benefit can increase compliance (16). Treatment with azithromycin is equally successful compared to erythromycin but with fewer side effects (17). To perpetuate the effective use of antimicrobial agents, the antimicrobial activities of such agents need to be monitored frequently. Speciation of bacteria may assist in elucidating the pathogenesis of specific medical conditions (18). The purpose of this study was to investigate the antimicrobial susceptibility and resistance patterns of genital mycoplasmas in pregnant women attending antenatal care.

2. Material and Methods

Using a sterile vaginal speculum vaginal swab was collected from lower one-third of the vaginal wall. The presence of *M. hominis and U. urealyticum*, as well as their antimicrobial susceptibilities, were investigated with the commercially available Mycoplasma IST 2 Kit (bioMérieux, Marcy-l'Étoile, France) as indicated by the manufacturer. Briefly, the endocervical cotton swab included in the kit was inoculated in R1 transport medium, inhibiting most of the Gram-negative and Gram-positive bacteria. The inoculated R1 medium was vortexed rapidly and 3 mL was added to the growth R2 medium, which contained 1 mL of lyophilized urea/arginine broth. After reconstitution and shaking, 55 µL

was dispensed into each of the 22 test wells on the strip. Two drops of mineral oil were added to each well. The remainder of the R2 medium and the inoculated strip were then incubated at 37°C and observed for colour changes at 24 and 48h. The antimicrobial susceptibility testing included tetracycline, doxycycline, erythromycin, azithromycin, clarithromycin, josamycin, ofloxacin, ciprofloxacin, and pristinamycin. The development or absence of red color on the relevant part of the strip provided an index of resistance or susceptibility to each antimicrobial agent, respectively, according to the guidelines of the CLSI.

3. Results

Antibiotics were administered in 83 (92.2%) of pregnant women with M. hominis and in 112 (94.1%) pregnant women with U. urealyticum (table 1). Because genital mycoplasmas lack a cell wall, they are resistant to antimicrobial agents that are active against this structure. Therefore penicillins, cephalosporins and vancomycin are ineffective in the treatment of conditions caused by these microorganisms. Antimicrobial susceptibility of genital mycoplasmas are shown in figure 1. Mycoplasmas are susceptible to agents that inhibit protein synthesis. Macrolides are often used empirically in pregnant women, as several agents are teratogens, such as tetracyclines and fluoroquinolones, which are the drugs of choice (19,20). There are a limited number of drugs available against genital mycoplasmas in pregnant women. Agents like β-lactams are completely inactive against U. urealyticum and M. hominis due to the lack of a cell wall. Tetracyclines and quinolones are the drugs of choice against genital mycoplasmas (21). However, macrolides are empirically used for pregnant women, as tetracyclines and quinolones are contraindicated in pregnancy. However, their therapeutic eficacy may be unpredictable due to increasing resistance. The rate of antimicrobial resistance varies geographically according to different antimicrobial therapy policies and history of prior use of antimicrobial agents (22). The antimicrobial susceptibility of genital mycoplasmas has changed over time and is different by geographic area (23). It is important to know the antimicrobial susceptibilities of genital mycoplasmas in a specific geographic region for the successful treatment.

4. Conclusions

To maintain a safe pregnancy, it is important to identify the isolates and use appropriate antibiotics immediately. Early pregnancy screening for genital mycoplasmas and following treatment may reduce preterm deliveries. Additionally, culture identification and antibiotic susceptibility tests should be used routinely in clinical laboratories. The method of administration of the treatment and its duration will depend on the location and the severity of the infection. Since tetracyclines and macrolides have only bacteriostatic activity against mycoplasmas, the course of the treatment must be sufficiently long. Clinical improvement is the first element and major criterion for evaluation. Partner testing and treatment of identified infections should be considered.

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Table 1: Frequency of antibiotic administration

Antibiotic administration	N	%
M. hominis	83	92.2
U. urealyticum	112	94.1

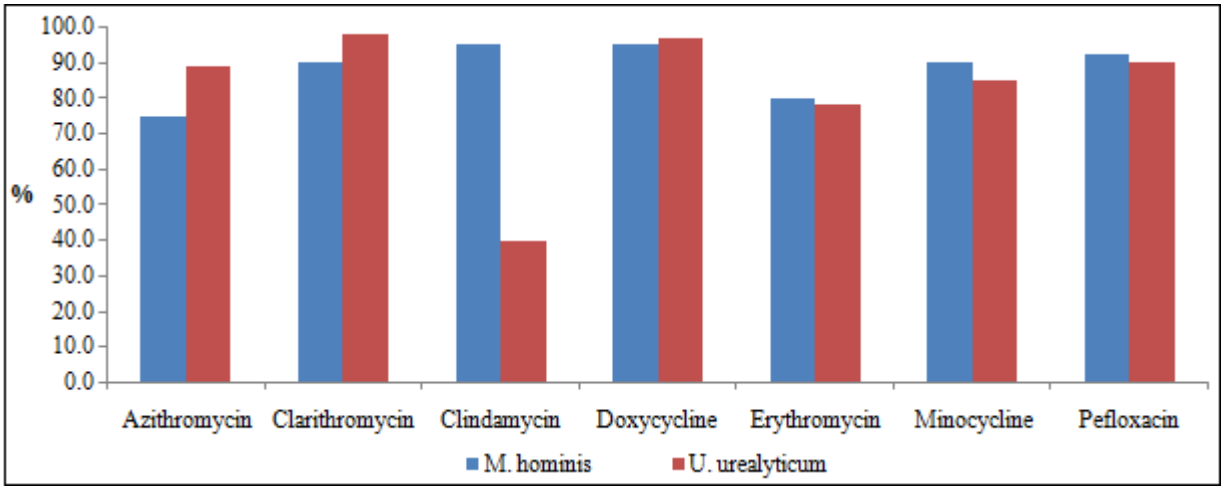

Figure 2: Susceptibility pattern of M. hominis and U. urealyticum