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ASSISTED REPRODUCTION

The prevalence of ureaplasma urealyticum, mycoplasma hominis, chlamydia trachomatis and neisseria gonorrhoeae infections, and the rubella status of patients undergoing an initial infertility evaluation

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Abstract

Purpose To determine the prevalence of positive test for Ureaplasma urealyticum (UU), Mycoplasma hominis (MH), Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG) infections, and their corresponding Rubella status when undergoing workup for infertility.

Methods Retrospective chart review to determine infection status for UU, MH, CT, and NG as determined by cervical swab, as well as the serum Rubella antibody titer.

Results A total of 46 patients of the patients reviewed were positive for UU (20.1%), three patients were positive for MH (1.3%), five patients were positive for CT (2.2%) and one patient was positive for NG (0.4%). Rubella immunity was confirmed in 90.3% of patients.

Conclusion Approximately one quarter of women presenting to an infertility clinic seeking to conceive were found to have a positive test for UU, MH, CT or NG infection. Additionally, almost 10% of the patients were Rubella non-immune at the time of presentation for infertility evaluation.

Keywords Chlamydia · Gonorrheae · Infertility evaluation · Mycoplasma · Rubella status · Ureaplasma

Determination of ureaplasma, mycoplasma, chlamydia and gonorrheae infections as well as rubella status in patients undergoing infertility treatment is important during the initial evaluation.

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Introduction

The evaluation of an infertile patient is broad and requires a detailed history, physical examination and laboratory analyses to determine the likely etiology of patient's problem. The infection panel included in the protocol for infertility evaluation in different institutions varies; many infertility clinics obtain Mycoplasma hominis and Ureaplasma urealyticum cultures in addition to Chlamydia trachomatis and Neisseria gonorrhoeae as part of the initial sexually transmitted disease screening. However, the exact prevalence of these infections in the couples undergoing work-up for infertility has not been established.

Chlamydia trachomatis is the most common agent of sexually transmitted genital infections [1–3]. C. trachomatis and N. gonorrhoeae cause similar clinical outcomes (Tubal factor infertility), but Chlamydia cervicitis tend to have few acute manifestations and more significant long-term complications. In one prospective study of a cohort of 14,322 individuals between the ages of 18 and 26 years, the prevalence of Chlamydia infection was 4.2% [4]. Approximately 30% of women with Chlamydia cervicitis will develop PID if left untreated or if treatment is delayed, and tends to be associated with high rates of subsequent infertility (17.8%) [5–7]. N. gonorrhoeae cervicitis is more acutely symptomatic and the long-term sequelae are similar to those caused by Chlamydia cervicitis.

In humans, both *Mycoplasma* and *Ureaplasma* species may be transmitted by direct contact between hosts (ie, venereally through genital-to-genital or oral-to-genital contact), vertically from mother to offspring (either at birth or in utero), or by nosocomial acquisition through transplanted tissues. Both organisms have been associated with

increased risk of recurrent pregnancy losses [8, 9], genitourinary tract infections which include pyelonephritis, pelvic inflammatory disease (PID), chorioamnionitis, postpartum and postabortal fever [10–13]. Whether these organisms cause involuntary infertility through fertilization or implantation impairment remains speculative.

Rubella virus causes German measles which develops subclinically in many cases but can cause significant birth defects if the disease occurs in first trimester of pregnancy. Maternal and fetal morbidity and mortality related to Rubella infection has been reduced drastically through universal and intensive vaccination program.

With this study, we sought to determine the prevalence of Ureaplasma urealyticum, Mycoplasma hominis, Chlamydia trachomatis and Neisseria gonorrhoeae infections as well as Rubella immunity in a group of women undergoing work-up for infertility.

Materials and methods

After obtaining the IRB approval from Wayne State University (WSU) Human Investigation Committee (HIC), we reviewed the charts of 236 previously unevaluated patients who presented for initial infertility evaluation between January 2001 and March 2007. Not all subjects completed their infertility work-up. Ureaplasma urealyticum, Mycoplasma hominis, Chlamydia trachomatis and Neisseria gonorrhoeae infections status determined by cervical swab was documented as either positive or negative. Similarly the serum Rubella antibody titer was documented as immune, indeterminate and non-immune as determined by the different laboratory reference values.

The overall percentages of patients positive for each infection were calculated as well as the percentage of patients that were immune to Rubella virus. Patients were stratified by the following ages; 20–29, 30–39 and 40–49 years old for statistical evaluation.

Results

Twenty point one percent of the patients were found to be positive for Ureaplasma urealyticum, 1.3% for Mycoplasma hominis, 2.2% for Chlamydia trachomatis and 0.4% for Neisseria gonorrhoeae (Fig. 1). For seven patients (3.0%) results for Ureaplasma urealyticum and Mycoplasma hominis were not available, while five patients (2.1%) had no results for Chlamydia trachomatis and Neisseria gonorrhoeae.

All patients positive for U. urealyticum and M. hominis were treated with doxycycline for 7 days and test of cure was documented in all the treated patients. Only two patients who were initially positive for U. urealyticum required repeated cycle of treatment with doxycycline in order to have a negative culture for Ureaplasma urealyticum.

Rubella immunity was noted in 90.3% of patients tested (226); results were not available for ten patients (4.2%). Six of the patients had indeterminate Rubella status which was considered as non-immune in this study because they required additional vaccine to acquire Rubella immunity.

The mean age of the patients was 34 years old, using the previously established age distribution, 46 (19.5%) patients were in the 20–29, 146 (61.9%) in the 30–39 and 44 (18.5%) in the 40–49 years old group respectively. Approximately two thirds of U. urealyticum, M. hominis and C. trachomatis infections occurred in patients between the ages of 30 and 39 and almost two thirds of the patients non-immune to Rubella belongs to this same age group. Only two patients had concomitant U. urealyticum and M. hominis infections while one patient had concomitant N. Gonorrhoeae and C. trachomatis infections (Tables 1 and 2).

Discussion

Our findings suggest that almost one quarter of the patients presenting to an infertility clinic for an initial evaluation could either be positive for U. urealyticum, M. hominis, C. trachomatis or N. gonorrhoeae. The exact role of Ureaplasma and Mycoplasma in patients with infertility problem is not completely understood. According to Witkin et al., U. urealyticum, but not M. hominis, is present in the cervices of many culture-negative women. Its presence, however, does not influence IVF outcome subsequent to embryo transfer in women treated with tetracycline after oocyte retrieval [14]. Rodriguez et al. found 47.3% of their infertile population study group to be positive for at least one of the microorganism (with 12.9% being Chlamydia, 0.3% gonococal infection, 23.5% Ureaplasma, 4.8% Mycoplasma) and showed that Chlamydia and U. urealyticum were related to infertility [15]. Gump et al. and Nagata et al. failed to demonstrate any association between genital Mycoplasma and infertility [16, 17].

The percentage of women with vaginal colonization with M. hominis increases after puberty in fairly direct proportion to sexual experience, such as the number of lifetime sexual partners. This was illustrated in a study in which genital colonization with M. hominis was found in 1 of 91 women without a prior history compared to 15 of 97 women with multiple lifetime partners and genital colonization could also be linked to lower socio-economic status [18]. The rate of colonization with M. hominis increases more rapidly with increasing sexual experience in women than in men, suggesting that women are more susceptible to

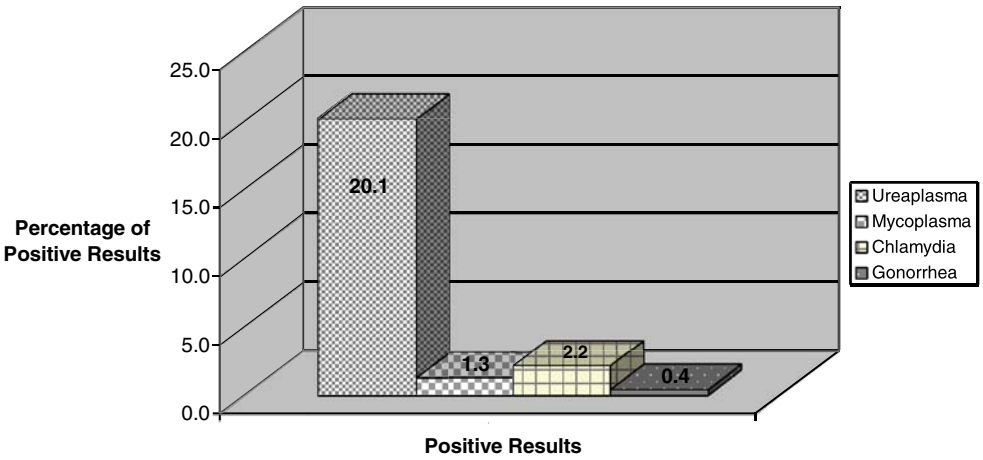

Fig. 1 The prevalence of U. urealyticum, M. hominis, C. trachomatis and N. gonorrhoeae infections in patients undergoing an initial infertility evaluation

colonization [19]. However, sexually active men are frequently asymptomatically colonized with M. hominis (25% in one series of 99 men attending a clinic for sexually transmitted diseases) [20].

It can be argued that the presence of any microorganism in the upper female reproductive tract, either acute or chronic can adversely affect fertilization, implantation and capacity to keep the embryo because of the inflammatory reactions generated by the presence of these microorganisms. The majority of the patients treated with doxycycline because of positive Ureaplasma and Mycoplasma cultures responded positively, indicating their susceptibility to this class of antibiotics. The presence of N. gonorrhoeae and/or C. trachomatis in a patient undergoing infertility evaluation or treatment could give us some information about the possible cause of her infertility problem, especially when tubal factor is found to be present in the patient. Although this was not the main objective of this study, we think screening for these infections in patients undergoing infertility evaluation is warranted, especially considering the fact that Mycoplasma hominis and Ureaplasma urealyticum are often concomitant with Chlamydia trachomatis and may have a role in subclinical infection and tuboperitoneal infertility [21]. We had two patients with concomitant U. urealyticum and M. hominis infections and one patient with concomitant N. Gonorrhoeae and C. trachomatis infections in our study.

In our study, approximately 10% of the patients, who presented for initial infertility evaluation and treatment, were Rubella non-immune. Even though there is no indication for termination of pregnancy or prenatal diagnosis following inadvertent vaccination during pregnancy [22], the recommendation with the currently available vaccine is to avoid pregnancy for at least 1 month after vaccination [23]. The acknowledgement of the Rubella status of the patients in advance would avoid unnecessary worries or intervention.

Our study is one of the first which estimates the prevalence of U. urealyticum, M. hominis, C. trachomatis and N. gonorrhoeae infections in infertile patients in the United States of America. However, an important limitation is that it is a retrospective chart review, and the sample size is relatively small for a cross sectional study.

Conclusion

The number of infertile patients who tested positive for U. urealyticum, M. hominis, C. trachomatis and N. gonorrhoeae in our study is high. The higher-than-expected prevalence of these microorganisms and the impact they have in female reproduction suggests a role for routine screening and treatment before undergoing infertility

Table 1 Age distribution and prevalence of U. urealyticum, M. hominis, C. trachomatis and N. gonorrhoeae infections in patients undergoing an initial infertility evaluation

Age groups (years)	% of patients per age group	Ureaplasma	Mycoplasma	Chlamydia	Gonorrhoeae
20–29	19.5	10	1	2	0
30–39	61.9	32	2	3	1
40–49	18.6	4	0	0	0
Total	100	46	3	5	1

Table 2 Age distribution and Rubella Status of patients undergoing an initial infertility evaluation

Age groups (years)	# of patients per age group	Immune	Nonimmune
20–29	46	42	4
30–39	138	124	14
40–49	42	38	4
Total	226	204	22

treatment. As part of the evaluation, the Rubella status should also be determined, as almost 10% were non-immune and could be vaccinated before initiating attempts for conception, thus reducing the potential exposure threat to the embryo/fetus and potentially reduce birth defects resulting from Rubella exposure in utero.

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