Have *Ureaplasma urealyticum* and *Mycoplasma hominis* infections any significant effect on female fertility?

*Ureaplasma urealyticum e Mycoplasma hominis svolgono un ruolo nella infertilità femminile?*

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**INTRODUCTION**

Sexually transmitted diseases (STDs) act on genital systems and may affect female and male reproductive functions in three different ways, through the obstruction of either male or female reproductive ducts, a significant contribution to perinatal morbidity, mortality, and pregnancy wastage [1]. *Ureaplasma urealyticum* and *Mycoplasma hominis* are known as sexually transmitted agents. Although *U. urealyticum* and *M. hominis* are found in genital tract flora of many sexually active men and women who have no obvious clinical diseases or abnormalities [2], they have been associated with a variety of clinical conditions, including bacterial vaginosis, infertility, pelvic inflammatory disease (PID), premature birth and low birth weight infants, spontaneous abortion and stillbirth, chorioamnionitis, and postpartum infections [3-10]. *U. urealyticum* and *M. hominis* jeopardize male fertility [11, 12].

However, it is unclear whether these infections significantly contribute to female infertility. Some studies suggest that *U. urealyticum* and *M. hominis* may have potential adverse effects on fertility in women [13, 14], but in other studies there are controversial results which do not confirm a definitive pathogenic role for these agents in female infertility [15-17].

These organisms reduce the success rate of highly specialized infertility treatments including intrauterin artificial insemination (IUAI), gamet intrafallopian transfer (GIFT), in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI) [18-21]. In this controlled study we aimed to establish whether *M. hominis* and *U. urealyticum* are risk factors for female fertility and evaluate the prevalence of infection from these agents in patients attending our infertility clinic.

**MATERIALS AND METHODS**

A total of 96 married women were enrolled in this prospective study; the infertile (study) group consisted of 50 women (mean age: 27.16 ± 4.73) and the fertile (control) group comprised 46 women (mean age: 31.57 ± 5.44). The women that had at least two pregnancies in their gestational histories and still used one of the contraceptive methods were enrolled as fertile subjects. In the study group, infertile couples that had any etiologic factors and contributing causes were excluded. None of the women in the study and control groups had any symptoms or signs of infection with *U. urealyticum* and *M. hominis* or any other pathogens at the time of the examination.

All women in this study were selected from the middle and upper socio-economic classes. All participants gave informed consent.

The patients were searched for the presence of *U. urealyticum* and *M. hominis* by a micro-liquid culture method, Mycofast (IM, France). This method is very convenient in that it gives rapid results and has a good correlation with conventional agar culture method. During the sample collection from the endocervical area, first the
excess secretion was removed and then the specimen including mucous lining was collected with a dacron swab. Immediately, the swab was inoculated in a growth liquid medium. This liquid specimen was dispensed in wells covering indicators that contain urea and arginine and reflect the growth of putative agents. The existence of U. urealyticum or M. hominis was detected by a colour change following overnight incubation. The second step was performed for identification and colony forming units in similar wells for positive specimens. Subsequently, the detection of 10^4 cfu/ml growth or over was accepted as positive result for the agents.

Statistical analysis was made with Pearson Chi-Square and Fisher’s Exact Test. The data are expressed as means ± SE (Standard Error). Statistical significance was set at p < 0.05 and the categorical variables were expressed as percentages. Data were collected in a Windows-based relational database (Microsoft Excel 2000) and analyzed with the SPSS (Statistical Package for the Social Science, version 10.0) for Windows 98 (Microsoft Corp.).

### RESULTS

There was no statistically significant difference between the two groups in mean age (p>0.05). In the study group, mean duration of infertility was 5.48 ± 0.77 years. While in the study group 28 of 50 (56%) women were evaluated as positive for U. urealyticum colonization of the endocervical canal, 18 of 46 (39%) women proved positive for it in the control group. The difference between the study and control groups was not statistically significant for U. urealyticum colonization of the endocervical canal (p>0.05).

M. hominis was cultured from 4 of 50 (8%) women in the study group. The four women in question already proved positive for U. urealyticum colonization of the endocervical canal. None of the women in the control group yielded a culture positive for M. hominis. No statistically significant difference was found between the study and control groups in M. hominis colonization of the endocervical canal (p > 0.05) (Table 1).

### DISCUSSION

Infertility associated with U. urealyticum infection was first reported by Kundsin [22], and subsequently supported by other studies which demonstrated a high frequency of U. urealyticum and M. hominis positive culture in cervical secretions and semen in infertile couples [23, 24]. However, there is a controversy as to whether M. hominis and U. urealyticum contribute to reproductive failure in women [15-17].

Gnarpe and Friberg isolated U. urealyticum from the cervix of 90% of primary infertile women and from the semen of 86% of their husbands [23]. In the other studies the isolation rate of U. urealyticum from the endometrium or lower genital tract was found significantly higher in infertile women than fertile women [2, 5, 13, 25]. In contrast to the studies mentioned above, Marais et al. evaluated 40 infertile women and found the low prevalence of U. urealyticum and M. hominis colonization of the endocervical canal as 0.0% and 7.5%, respectively [14]. de Louvuis et al. reported that the prevalence of M. hominis was 14.7% in infertile couples and 13.2% in fertile couples [15]. Gump did not find any correlation between these agents and infertility [17].

Whether U. urealyticum and M. hominis could account for a small proportion of infertility cases or whether the relation was only coincidental remains unanswered.

Some serotypes of these agents accused of male infertility were reported in some studies [26-28]. According to the previous studies these agents attach to sperm and may reach the up-

<table>
<thead>
<tr>
<th>Groups</th>
<th>N.</th>
<th>Mean age</th>
<th>U. urealyticum Positive</th>
<th>U. urealyticum Negative</th>
<th>M. hominis Positive</th>
<th>M. hominis Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study group</td>
<td>50</td>
<td>27.16 ± 4.73</td>
<td>28 (56%)</td>
<td>22</td>
<td>4 (8%)</td>
<td>46</td>
</tr>
<tr>
<td>Control group</td>
<td>46</td>
<td>31.57 ± 5.44</td>
<td>18 (39%)</td>
<td>28</td>
<td>0 (0%)</td>
<td>46</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>0.35</td>
<td>0.265</td>
<td></td>
<td>0.49</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05: Statistically significant
per genital tract of sexually active women [11, 18, 20, 29]. But it was not suggestive for a direct relationship between *U. urealyticum* and tubal disease, except *M. hominis* [30]. Tyagi established that the presence of antibodies to *M. hominis* was more common in infertile women with tubal disorder [31].

*U. urealyticum* not only reduces the success rate of the modern infertility treatments, but also causes a marked reduction in very early embryonic development after IVF [18-21]. If patients testing positive for *M. hominis* and *U. urealyticum* were treated by suitable antibiotics, favourable outcomes in highly specialized infertility treatments might be achieved [8, 32].

**CONCLUSION**

In this study we found no statistically significant differences between the groups for both agents, but the higher prevalence of *U. urealyticum* in infertile women suggests the wisdom of evaluating these agents in patients that have no other etiological factor for infertility. Randomized placebo-controlled studies are needed to elucidate the role of *M. hominis* and *U. urealyticum* in infertile women who have no other concomitant reasons for infertility.

*Key Words:* U. urealyticum, M. hominis, Women Infertility.

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**RIASSUNTO**

*Ureaplasma urealyticum* e *Mycoplasma hominis* sono noti come agenti eziologici di malattie a trasmissione sessuale. Se il loro ruolo quale fattore di rischio di infertilità maschile è ben definito, non ancora risulta chiarito il loro ruolo patogenetico quali responsabili della infertilità femminile. Il presente studio prospettico controllato è stato condotto al fine di valutare la prevalenza delle infezioni sostenute da tali agenti patogeni in pazienti giunte alla nostra osservazione presso il nostro centro di infertilità e verificare se *U. urealyticum* e *M. hominis* possano rappresentare dei fattori di rischio per la fertilità femminile.

Nello studio sono state arruolate complessivamente 96 donne coniugate suddivise in due gruppi: gruppo di studio costituito da 50 donne non fertili e gruppo di controllo composto da 46 donne fertili. L’isolamento di *U. urealyticum* e *M. hominis* è stato effettuato con un micrometodo in fase liquida. I campioni sono stati raccolti dalla regione endocervicale con tamponi in dacron. L’esame colturale per *U. urealyticum* è risultato positivo in 28/50 (56%) pazienti nel gruppo di studio e in 18/46 (39%) nel gruppo di controllo. *M. hominis* è stato isolato in 4 delle 50 donne del gruppo di studio (8%); nessun isolamento nel gruppo di controllo. Le differenze di isolamento osservate tra i due gruppi sia per *U. urealyticum* che per *M. hominis* non sono risultate statisticamente significative (*p* > 0.05), ma la più elevata incidenza di *U. urealyticum* nelle donne non fertili suggerisce che nelle pazienti senza ulteriori fattori di rischio anche questi agenti vengano presi in considerazione quali causa di infertilità.

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**SUMMARY**

*Ureaplasma urealyticum* and *Mycoplasma hominis* are known as sexually transmitted agents. *U. urealyticum* and *M. hominis* jeopardize male fertility. However, it is unclear whether these infections significantly contribute to female infertility. In this controlled study we aimed to establish whether *M. hominis* and *U. urealyticum* are risk factors for female fertility and the prevalence of infection from these agents in patients attending our infertility clinic. A total of 96 married women were enrolled in this prospective study; the infertile (study) group consisted of 50 women and the fertile (control) group comprised 46 women. The patients were searched for the presence of *U. urealyticum* and *M. hominis* by a micro-liquid culture method. The samples were collected from the endocervical area with a dacron swab. In the study and control groups 28 of 50 (56%) and 18 of 46 (39%) women were evaluated, respectively, as positive for *U. urealyticum* culture. *M. hominis* was cultured from 4 of 50 (8%) women in the study group while none of those in the control proved positive. There were no statistically significant differences between the groups for either agent (*p* > 0.05), but the higher prevalence of *U. urealyticum* in infertile women suggests that these agents should be evaluated in patients that have no other etiological factor for infertility.