

The Association between Mycoplasma Species Infection and Tubal Obstruction

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Abstract

Objectives: Numerous factors can cause infertility. Tubal factor accounts for approximately 30% of infertility in females. This study was conducted to evaluate the rate of asymptomatic *Mycoplasma hominis* and *Ureaplasma urealyticum* infection in females diagnosed with tubal obstruction. **Methods:** This is a retrospective case-control study conducted at New Life Fertility Centre. We have identified and reviewed the health records of 167 subfertile women that had HSG and an endocervical swab for *Mycoplasma hominis* and *Ureaplasma urealyticum* done. **Results:** We compared the endocervical swab results of ureaplasma and mycoplasma in the patients with tubal obstruction (group 1) to the patients with normal patent tubes (group 2). Diagnosis of tubal patency was based on the HSG results. Our results show that there is a significantly higher rate of *Ureaplasma urealyticum*/*Mycoplasma hominis* infection in group 1 compared to group 2. **Conclusion:** Our data shows that there is a high rate of *U. urealyticum* and *M. hominis* infection in patients diagnosed with tubal factor of infertility and it can be a marker in the prediction of the tubal pathology.

Keywords

Infertility, Tubal Factor, Hysterosalpingogram, *Ureaplasma urealyticum*, *Mycoplasma hominis*

1. Introduction

Infertility is an important subject of reproductive health with a prevalence of 12.5% among women [1]. It has an impact on the quality of life for these patients [2]. Many studies discussed the relationship between infection and tubal factor of infertility [3].

Since *Ureaplasma* was identified as a cause of male urethritis in 1954 [4], it is considered as the most common cause of genital infection in both males and females [5] [6]. Both *Ureaplasma* and *Mycoplasma* are found in genitourinary samples [6].

Ureaplasma has 14 known serotypes [7]. *U. urealyticum* is considered to be the pathogenic organism [8].

Also, it was found that it may be related to unexplained infertility [9].

Not too much is known about its prevalence in pelvic inflammatory disease (PID) [10].

Tubal factor assessment is fundamental in a fertility workup. Many interventions can be used for tubal pathology evaluation [11]. However, Hysterosalpingogram (HSG) has a high sensitivity and specificity for diagnosis of tubal obstruction [12] and is widely used.

The aim of this study is to find out if there is a relationship between endocervical *Mycoplasma*, *Ureaplasma* infection and tubal factor of infertility.

Key Points:

The investigation was to see the correlation between genital mycoplasma/ureaplasma infection and tubal obstruction in sub-fertile women.

2. Materials and Methods

This is a retrospective case-control study conducted at New Life Fertility Centre and Brampton Civic Hospital in Brampton, ON, Canada, in which 167 infertile females who had HSG and an endocervical swab for *Mycoplasma hominis* and *Ureaplasma urealyticum* done.

In between May 2015 to December 2017 were included. The study was approved by the Research Ethics Committee of the Brampton Civic Hospital. Approval number 17-0040.

An endocervical swab was obtained from all of the patients as part of the investigative cycle. Swabs were then immediately placed into a collection tube containing UTM-RT media (*Ureaplasma* and *Mycoplasma* spp.) (Copan ITALIA). All of the samples are stored at 4°C and then transported to the laboratory (Gamma dynacare, Canada) within 24 h of collection. The samples were cultured using A8 *Mycoplasma* Agar.

All of the candidates had HSG done in the luteal phase in Brampton Civic Hospital; Brampton, ON, Canada. We collected and analyzed the clinical data, including demographic information, HSG reports and endocervical swab results. The patients included in the study did not have a previous medical history of PID, chlamydia infection or any other risk factors that increase the risk of tubal disease such as: pelvic/abdominal surgery, previous ectopic pregnancy or a history of endometriosis. Other exclusion criteria included current use of antibiotics. The outcome was the rate of *U. urealyticum*/*M. hominis* infection in patients with tubal obstruction either unilateral or bilateral compared to the rate of infection in patients with open tubes.

Patient and Public Involvement

Since this is a retrospective study, patients were not directly involved. The data was collected from medical records of patients that were already being treated at the clinic with their consent. As a routine, we do cervical swab to test Mycoplasma/Ureaplasma infection. It was noted that most of the patients that had the infection also had tubal obstruction in the HSG. The results were dispersed to study participants by excluding any patient who already had or was at risk of having tubal disease. That ensured accuracy.

Statistical Analysis

Data were collected and analyzed using Microsoft Excel version 7. Data was described in terms of mean and SD. Outcomes were compared using student t test. Statistical software was used for data analysis. P-values < 0.05 were considered statistically significant.

3. Results

A total of 167 patients; either primary or secondary infertility (**Table 1**).

We compared the endocervical swab results of:

Group 1: The patients with tubal obstruction (81 patients) (41 patients with unilateral tubal obstruction and 40 patients with bilateral tubal obstruction) to Group 2: The patients with normal patent tubes (86 patient) (**Table 2**). Diagnosis of tubal patency was based on HSG results. Our results show that there is a significantly higher rate of infection in group 1 than in group 2, (64.19% vs 12.79%, P value < 0.0001) (**Table 2**).

Rate of *U. urealyticum* infection in group 1: 49.38%.

Rate of *M. hominis* infection in group 1: 8.64%.

Rate of mixed *U. urealyticum* and *M. hominis* co-infection in group 1: 6.17%.

Rate of *U. urealyticum* infection in group 2: 12.79%.

Table 1. Patients' age and type of infertility.

	Group 1	Group 2
Age	38.0 ± 5.04	35.4 ± 4.83
1ry Infertility	25	36
2ry Infertility	56	50

Table 2. Rate of *U. ureaplasma*/*M. hominis* infection in both groups.

Endo-cervical swab result	Group 1 [81 patients]	Group 2 [86 patients]	P value
+ve <i>U. urealyticum</i>	40/81 [49.39%]	11/86 [12.79%]	<0.0001
+ve <i>M. hominis</i>	7/81 [8.64%]	0/86	0.005
Mixed infection	5/81 [6.17%]	0/86	0.025
Total no of infected patients	52/81 [64.19%]	11/86 [12.79%]	<0.0001

Rate of *M. hominis* in group 2: 0%.

Rate of mixed *U. urealyticum* and *M. hominis* co-infection in group 2: 0%.

Odd Ratio: 12.22.

4. Discussion

Although *Neisseria gonorrhoea* and chlamydia are the most common causative organisms for PID, still 70% of cases are of unknown causes [13]. Little data is available regarding the involvement of other organisms within the vaginal micro-environment in the development of PID and tubal pathology [14]. Several studies have described genital *Mycoplasma* and *Ureaplasma* as causative agents of PID [15].

A8 *Mycoplasma* Agar is a sensitive method for detection of genital mycoplasma [16].

In the current study, the rate of *Mycoplasma hominis* and *Ureaplasma urealyticum* genital infections in a group of asymptomatic women was significantly higher in females diagnosed with tubal obstruction compared to those with patent tubes (64.19% vs 12.79%, $P < 0.0001$). The percentage of *Ureaplasma* infection was higher than *Mycoplasma* in the tubal obstruction group (49.38% vs. 8.64%) and 12.79% for *Ureaplasma* with no *Mycoplasma* recorded in the healthy group.

Mycoplasma is a common cause of cervicitis that may be complicated by ascending infection involving the uterine cavity, tubes and ovaries with the subsequent development of PID [17].

Tubal factor accounts for approximately 30% - 35% of cases of female infertility and is a major sequel of PID [18].

In a large study from the Netherlands on 1188 patients screened for STDs, *Mycoplasma* was the second most common organism detected (4.5%) after chlamydia (8.3%) [19]. In vitro studies on mice have detected *Mycoplasma* in the genital tract causing structural changes in the ciliated epithelium of the fallopian tubes [20]. *Mycoplasma* has also been found to be a cause of salpingitis in monkeys [21]. In PEACH study (PID Evaluation and Clinical Health study), Haggerty *et al.* reported a trend towards an increase in the rate of infertility and PID as well as drop in pregnancy and live birth rates in those suffering from *Mycoplasma genitalium* [22]. In another study on 212 infertile couples, an independent association between *Mycoplasma genitalium* and tubal factor infertility has been reported [23]. Tubal occlusion was found in 33% of *Mycoplasma* positive infertile females in a prospective study on 200 Indian women [24]. Clausen *et al.* detected *Mycoplasma genitalium* in 22% of females suffering from tubal factor infertility compared to 6.3% without tubal pathology [25].

On the contrary, IDahl *et al.* reported insignificant association between *Mycoplasma genitalium* serum IgG and female infertility after adjusting to chlamydia trachomatis IgG. This association was not found with subtypes of infertility; however, in this study tubal factor was not excluded by laparoscopy or hystero-

salpingography in some of the studied women [26]. In another Brazilian study, Costaya *et al.* did not detect Mycoplasma species in the fallopian tubes of females with tubo-peritoneal infertility and the organism was only detected in samples free from other organisms. Infertility could not be excluded in this study due to the low number of infected cases [27].

In a current study, the cohort of patients selected was asymptomatic for genital infection and did not give a history suggestive of PID or other risk factors for tubal pathology. Unlike Neisseria gonorrhoea, genital Mycoplasma and chlamydia have less overt inflammatory manifestations [28] and many of those infected with Mycoplasma are asymptomatic carriers resulting in delayed diagnosis and treatment with subsequent deleterious effects on fertility [29] [30]. In addition, Mycoplasma has a high drug resistance to medications commonly used for treatment of PID causing treatment failure and persistent PID eventuates [22].

5. Conclusion

In conclusion, Mycoplasma is an overlooked genital infection that is mostly asymptomatic with high reproductive morbidity. This highlights the importance of including Mycoplasma genitalium in screening programs for STDs and those at high risk for PID.

Limitations

One of the limitations of this study, that we used a retrospective data which didn't include the most recent screening for chlamydia or gonorrhoea infection.

Further studies are needed to include screening for *U. urealyticum* and *M. hominis* and other genital infection at the same time, to identify the best screening methods and treatment options for the organism.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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