Chlamydial infection in asymptomatic infertile women

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Summary

Thirty-six asymptomatic infertile women undergoing laparoscopic examination as part of their infertility investigations, were included in this study on chlamydial infection. Patients were tested for chlamydial antigen in the cervix and peritoneal fluid. The serum of twenty-five of these patients was titrated for evidence of chlamydial antibodies. Fifty women attending a family planning clinic were used as a control group. The study showed a strong relationship between chlamydial infection and infertility due to tubal pathology. The incidence of chlamydial infection in asymptomatic infertile women was 33.3%. The results indicate that *Chlamydia trachomatis* should be sought in patients presenting with infertility and, if detected, appropriate medical treatment be given.

Introduction

Infertility is an increasingly significant health problem in many areas of the world. About 15–20% of couples are involuntarily infertile and various factors have been implicated.[1] Amongst them tubal factors contribute to the problem in 15–30% and infection of the fallopian tubes[2] in 50% of these cases.

Infertility due to tubal disease has increased over the past decade, presumably due to the continuing epidemic of salpingitis. The incidence of infertility increases with repeated episodes of pelvic inflammatory disease in a logarithmic manner.[3] Surveys done in the Western world over the years have implicated a whole range of organisms and *Chlamydia trachomatis* has been shown to be among the common offending organisms.[4–7]

In recent years newer and simpler techniques to detect chlamydial antigen and antibody have been made available. This study is among the first to be initiated in this region, with the aim of finding out the prevalence of chlamydial infection in Malaysian women – namely among asymptomatic women with infertility. The effects of chromotubation in disseminating infection to the upper genital tract was also looked at and the data analysed to see if there was any correlation between chlamydial infection and tubal damage.

Materials and methods

This is a preliminary report of 36 patients in a prospective ongoing study being carried out at the

University Hospital, Kuala Lumpur, since January 1986. All of them presented to our gynaecological clinic with the problem of either primary or secondary infertility.

A full history was taken at the initial visit. A thorough physical examination was carried out on the couple; a complete infertility work up included basal body temperature, seminal analysis, postcoital test and a laparoscopic examination timed in the luteal phase of the menstrual cycle. Blood tests to estimate various reproductive hormones were done as and when indicated.

During laparoscopy, three specimens were taken for detection of chlamydial antigen. The first was a high endocervical swab, followed by aspirates from the pelvic peritoneal fluid, before and after chromotubation. In cases where initially there was no peritoneal fluid available, 10ml of sterile normal saline was introduced into the pelvic cavity via the laparoscope. The saline was then aspirated and sent for detection of chlamydial antigen. Detailed laparoscopic findings were noted. Five millilitres of blood was also sent for detection of chlamydial antibody. Patients were diagnosed as having had chlamydial infection if either the antigen, antibody or both were detected.

Results

A total of 36 patients participated in this study. Table 1 shows that 25 patients (69.5%) who participated in the study were in the upper social class. Twenty-one patients (58.3%) were in the older age group between 31–40 years of age, as shown in Table 2. None of the patients were above 40 years of age.

As shown in Table 3, 31 patients (86.1%) were infertile for a duration of more than two years. The duration of infertility in the study group ranged between one and 13 years.

Twelve patients (33.3%) in this study were found to have chlamydial infection. Four patients had a significantly raised chlamydial antibody titre of one in 64 which was suggestive of past infection. The other eight patients had chlamydial antigen in one or more of the specimens taken, indicating active infection. No chlamydial antibody was detected in these patients. In the control

Table 1
Social class

	Class*	Frequency	Percentage
I	Professional	10	27.8
II	Teacher/Civil Service	15	41.7
III	Clerical/Skilled Worker	3	8.3
IV	Skilled Labour	5	13.9
V	Unskilled Labour	3	8.3
	Total	36	100.0

* According to husband's occupation – WHO classification

Table 2
Age distribution

Age (years)	Frequency	Percentage
20 – 30	15	41.7
31 – 40	21	58.3
Total	36	100.0

Table 3
Duration of infertility

Duration (years)	Frequency	Percentage
< 2	5	13.9
2 – 5	23	63.9
> 5	8	22.2
Total	36	100.0

group chlamydial antigen was detected in one patient and antibody detected in four patients as shown in Table 4.

Table 5 shows the state of the fallopian tubes and other associated abnormalities noted at laparoscopy, in patients who showed evidence of active and past infection. More than one pathology was noted in some patients. One patient in the 'past infection' group who had a bilateral cornual block was also found to have pelvic tuberculosis.

Table 4
Detection of chlamydial antigen and antibody among women attending infertility and family planning clinics

Patient	Test	No. Tested	No. positive (%)
Infertility	antigen	36	8 (22.2)
	* antibody	25	4 (16)
Family planning	antigen	50	1 (2)
	* antibody	50	4 (8)

* a positive titre is $\geqslant$ 1:64
(X^2 value = 7.18; $p < 0.01$)

In the 24 patients without chlamydial infection, 11 patients were found to have normal pelvis with patent tubes while 10 other patients were found to have varying degrees of endometriosis with peritubal adhesions. Three other patients were found to have bilateral tubal block with gross pelvic adhesions. It was concluded that these patients could have had pelvic inflammatory disease caused by other pathogenic organism. No causal agent was identified in these patients.

Table 5
Laparoscopic findings

	Active infection		Past infection	
	Freq.	Percent	Freq.	Percent
Peritubal Adhesions	3	37.5	–	–
Fimbrial Block	3	37.5	–	–
Cornual Block	–	–	3	75.0
Hydrosalpinx	1	12.5	–	–
Endometriosis	4	50.0	1	25.0
Normal	2	25.0	1	25.0

(More than one pathology was noted in some patients)

The pregnancy rate in patients with chlamydial infection in this series was 33.3% (two patients with active infection and two patients with past infection).

One patient with active infection and tubal block conceived after a course of doxycycline therapy, followed by surgical treatment i.e. salpingostomy and salpingolysis procedures. The other patient had mild endometriosis and the tubes were normal at laparoscopy. She too conceived after a course of doxycycline.

In the two patients who had past chlamydial infection, one had normal laparoscopic findings and was treated with a course of doxycycline. The other patient had bilateral cornual block with pelvic tuberculosis as evidenced by a positive culture on endometrial biopsy. She was treated with a course of antituberculous drugs and doxycycline. She conceived spontaneously and was in her second pregnancy at the time of this write up.

None of the patients gave a history of sexually transmitted disease in their male counterparts while one patient with a positive endocervical swab had cervical intraepithelial neoplasia detected on Papanicolaou smear.

Discussion

The pioneering studies on chlamydial genital tract infection were performed in 1911 by Lindner, an ophthalmologist who traced the microbiologic origin of neonatal chlamydial conjunctivitis back to its source in the infected lower genital tracts of the infants' parents.

Chlamydia trachomatis on obligate intra-cellular bacteria is believed to be the most prevalent sexually transmitted micro-organism in the world today. There are many serotypes, but the ones which are sexually transmitted are serotypes D through to K. The baseline cervical carrier rate is about 5%, whereas in selected population, (for example those attending venereal disease clinics, or those presenting with vaginal discharge) the cervical isolation rate ranges from 15% to as high as 60%. In those with laparoscopically proven acute salpingitis, the cervical isolation rate is between 5–37%.[4] Despite being common, its presence often goes undetected until the ultimate consequence of infection, infertility, become apparent. The consequences of this silent epidemic are particularly tragic because they are preventable.

The overall prevalence of chlamydial infection in this study i.e. among asymptomatic infertile women was 33.3%. Sixteen percent had a significant level of antibody to *Chlamydia trachomatis* as compared to only 8% in those women attending our family planning clinic. The corresponding antigen detection rates were 22.2% and 2% respectively. This was statistically significant ($P < 0.01$).

As can be seen from the data a high percentage of patients with positive chlamydial antigen and/or antibody were found to have tubal pathology viz. peritubal adhesions, fimbrial block, cornual block and hydrosalpinx. Analysis of data revealed that fifty percent had tubal factor as the sole or contributing cause to their infertility. This result is consistent with those obtained by several other workers.[6,8,9]

All the patients in this study did not give any history suggestive of past or recent pelvic inflammatory disease. This fact has been observed by many other workers, thus suggesting that subclinical tubal infection is a common antecedent to infertility.[5,6,10,11]

Whether *Chlamydia trachomatis* produces fibrosis and tubal occlusion due to a host-determined response to past infection is at present still unknown. We could not detect chlamydia trachomatis antigen in all the three specimens taken from the four patients with past infection. Brunham et al[8] and Gump et al[10] did not recover *Chlamydia trachomatis* in any of the patients in their studies. In contrast, Henry-Suchet et al[9] recovered *Chlamydia trachomatis* from fallopian tubes or pelvic peritoneum cultures in 18% of women with tubal blockage, thus suggesting that persistent chlamydial infection could be the underlying factor.

The majority of patients (69.5%) evaluated in this study were among social class I & II (upper, middle socio-economic group). Similar findings were noted by Jones et al.[6] However, in the study by Brunham et al,[8] no significant difference in age, marital status, educational level or occupation were noted in their patients.

The study by Moller et al[12] emphasised the increased risk of chlamydia positive women in developing upper genital tract infection subsequent to gynaecological procedures which penetrate the cervical barrier. However, the effect of chromotubation in disseminating chlamydial infection to the upper genital tract was not clearly shown in this study. This could be due to several factors:–

1. small sample studied
2. sampling error
3. initial inexperience of the microscopist who had difficulty in differentiating between elementary bodies and artifacts

Paavonen et al[13] in their preliminary results showed that cervical intra-epithelial neoplasia (CIN) was more common in chlamydial than in non-chlamydial cervicitis. We had only one patient with CIN in the study. She had positive endocervical swab for chlamydial antigen.

The high pregnancy rate in this study (33.3%) may be attributed to the small number of patients studied. The finding of chlamydial antibodies in high titres in infertile women does not necessarily prove the presence of damaged tubes, but such damage can be expected in many cases and chlamydia is likely to be the cause.[14]

Our preliminary results, in conjunction with that available in the literature suggest that subclinical chlamydial infection is a major cause of tubal infertility in asymptomatic infertile women. As such chlamydia antigen and antibody detection should be routinely offered as part of infertility investigations. Eacly detection and aggresive treatment in these women would decrease the incidence of serious complications which include endometritis, salpingitis and perihepatitis.[15]

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