

Poor Correlation of Positive *Chlamydia Trachomatis* Antibody Tests and Infertility in Middle Class Women

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Abstract

Previous exposure to infection by *Chlamydia trachomatis* is thought to be a significant contributing factor to tubal disease and subsequent infertility. For this reason, levels of *Chlamydia trachomatis* antibody (CTA) are measured rather routinely during investigation of the infertile couple. To determine how the results should influence the subsequent management of the infertile woman, we studied 283 middle class patients who were seen for infertility of at least 1.5 years duration. The patients were treated for a variety of infertility factors for six months without performing tubal studies in order to determine if a positive CTA reduced the pregnancy rate during conservative nonsurgical therapy. Furthermore, we evaluated whether fecundity would be inversely proportional to the CTA index.

Our findings suggest that with progressively higher CTA levels, the risk of ectopic pregnancy and more serious tubal disease increases. However, the majority of patients with positive CTA were not adversely affected by previous infec-

tion, since the pregnancy rates in the CTA-positive patients were as good as, if not better than, the pregnancy rates in the CTA-negative patients. It is therefore just as valid to correct other infertility factors and to defer laparoscopy in CTA-positive patients as in CTA-negative patients.

Introduction

Many investigators have suggested that there is a higher prevalence of positive *Chlamydia trachomatis* antibody (CTA) in infertile women than in fertile control patients and also a higher prevalence of positive CTA tests in infertile women with tubal disease than in infertile women with normal tubes.¹⁻⁵

Over the last two decades, *Chlamydia trachomatis* (CT) has been implicated as a cause of pelvic inflammatory disease (PID), fallopian tube disease, pelvic adhesions and infertility. In the late seventies, Mardh *et al* first noted that CT infection was involved with PID.⁶ They noted that 30% of women with documented PID had CT infections of the Fallopian tubes. Further studies by this group in Scandinavia revealed that up to 58% of all PID in a group of Swedish women involved CT.⁷

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Table 1
Incidence of Chlamydia Antibody Levels in Infertile Middle Class Patients

CTA Levels	N	%
Negative	139	49
Positive	144	51
low ^a	55	19
mid ^b	58	20
high ^c	31	11

^a low positive, 1.00-1.49

^b mid positive, 1.50-3.19

^c high positive, ≥ 3.20

The use of the chlamydia serologic test as a diagnostic tool in the work-up of the infertile couple remains controversial. In the late 1970s, studies in Seattle showed that 20% of women with PID had positive chlamydia antibodies.⁸ Later studies found that 73% of women with distal tubal disease had positive *Chlamydia trachomatis* antibody (CTA).⁹ It has been concluded that CT antibodies have a high predictive value for the presence of hydrosalpinx and peritubal disease. Studies showed that 50% of patients with tubal occlusion had positive titers, while only 6% without positive titers had tubal occlusion. Although these results showed a low false-positive rate, the false-negative rate was 50%, thus placing into question the usefulness of this test. The present study was undertaken to evaluate whether infertile middle class women with positive CTA levels who were seen in private practice had a higher frequency of tubal disease and whether they had a more recalcitrant infertility problem.

Materials and Methods

Two hundred eighty-three middle class patients with infertility of at least 1.5 years duration, who had no previous tubal studies or previous CTA testing, were studied. Patients

Table 2
Correlation of Chlamydia Antibody Levels in Infertile Middle Class Patients with Pregnancy Rates Within Six Months of Therapy

Intrauterine Pregnancies*		
CTA Levels	N	%
Negative	41/139	30
Positive	62/144	43
low ^a	26/55	47
mid ^b	28/58	48
high ^c	8/31	26

* No significant differences

^a low positive, 1.00-1.49

^b mid positive, 1.50-3.19

^c high positive, ≥ 3.20

with known severe male factor infertility were excluded from the study. Chlamydia antibody levels were assayed utilizing a quantitative ELISA method (Whittaker M.A. Bioproducts, Walkersville, MD). The positive CTA patients were subdivided into three groups based on manufacturer-established ranges: low-positive (1.00-1.49), mid-positive (1.50-3.19), and high-positive (≥ 3.20). Those patients who were CTA negative were used as the control group.

A complete infertility work-up was undertaken at this time. Immediate laparoscopy and hysterosalpingography were offered to the patients; however, most opted to delay these tests. All abnormalities found in the work-up were aggressively treated. Six months after the initial work-up, laparoscopy and hysterosalpingography were strongly suggested to define the status of tubal disease in all patients who were still not pregnant.

Eighty-nine of the 139 CTA-negative patients had a hysterosalpingography and/or laparoscopy (37 had a laparoscopy only) compared to 72 of the 144 CTA-positive patients who had tubal assessment (46 of these had a

Table 3
Correlation of Tubal Disease and Chlamydia Antibody Levels
in Infertile Middle Class Patients

CTA Levels	Bilateral Tubal Occlusion*		Unilateral Tubal Occlusion**		Adhesions†	
	N	%	N	%	N	%
Negative	1/89 ^d	1.1	5/89 ^d	5.6	1/37 ^e	2.7
Positive	8/72 ^d	11.0	8/72 ^d	11.0	10/46 ^e	21.7
low ^a	2/28	7.1	1/28	3.9	6/18	33.0
mid ^b	3/25	12.0	2/25	8.0	4/19	21.0
high ^c	3/19	15.7	5/19	26.0	0/9	0.0

* Negative vs total positive, $P=.001$; negative vs high positive, $P=.002$

** No significant differences

† Negative vs total positive, $P=.001$

^a low positive, 1.00-1.49

^b mid positive, 1.50-3.19

^c high positive, ≥ 3.20

^d represents no. of patients having hysterosalpingography and/or laparoscopy

^e represents no. of patients having a laparoscopy

laparoscopy only). This was a heterogeneous group of infertility patients with anovulatory disorders, cervical factor disorders, unexplained infertility and tubal disease. Fisher's exact test was used to analyze the data.

Results

Positive CTA levels were found in 51% of the patients studied. As can be seen in Table 1, 19% had low-positive, 20% had mid-positive and 11% had high-positive CTA levels. Table 2 shows that 30% of patients with negative CTA levels achieved intrauterine pregnancies, while 43% of patients with positive levels achieved intrauterine pregnancies (no significant difference).

The intrauterine pregnancy rates in all four groups were: 41 of 139 patients who were CTA negative (30%); 26 of 55 patients who were low-positive (47%); 28 of 58 patients who were mid-positive (48%) and 8 of 31 patients who were high-positive (26%).

Though the 26% pregnancy rate in patients with high-positive levels was not statistically lower than the 47.5% rate in patients with low-positive and mid-positive levels, one could agree that statistical significance may be demonstrated in a larger series. However, only 30% of the patients in the control group achieved a pregnancy.

Table 3 demonstrates that 1.1% of patients with negative CTA levels had bilateral tubal occlusions (BTO), while 11% of patients with positive levels had BTO ($P = .001$). Bilateral tubal occlusions occurred in only 1 of 89 patients who were CTA negative (1.1%) compared to 3 of 19 patients who were high-positive (15.7%) ($P = 0.01$); 3 of 25 patients who were mid-positive (12%); and 2 of 28 patients who were low-positive (7.1%).

Unilateral tubal occlusion occurred in 5 of 89 CTA-negative patients (5.6%); 5 of 19 CTA high-positive patients (26%); 2 of 25 mid-positive patients (8%); and one of 28 low-positive patients (3.9%). When patients with negative

CTA levels who had unilateral occlusion (5.6%) were compared to patients with positive titers (11%), the difference was not statistically significant.

Adhesions were found in 2.7% of the laparoscopy-only patients with negative titers, while 21.7% of laparoscopy-only patients with positive titers had adhesions ($P = .001$). Adhesions were found in only 1 of 89 CTA-negative patients (1.11%) compared to 10 of 72 CTA-positive patients (13.9%) ($P = .001$).

Ectopic pregnancies occurred in one of 42 CTA-negative patients (2.3%) versus 10 of 62 CTA-positive patients (16.1%). Tubal pregnancies were found in one of 27 women with low-positive levels (3.7%), 5 of 33 women with mid-positive levels (15.1%) and 4 of 12 women with high-positive tests (33.3%). Fisher's exact test comparing negative and low-positive to mid-positive and high-positive patients was significant ($P < .002$).

Discussion

In our study of 283 middle class infertile couples, over 50% of the patients who were tested with the highly sensitive ELISA assay showed serologic evidence of previous CT infection. Infertile middle class American couples are showing a high prevalence of previous CT infection. Despite these findings, intrauterine pregnancy rates after six months follow-up showed no correlation to chlamydia antibody levels. Patients with high-positive, mid-positive and low-positive CT titers became pregnant at the same rate as those patients with no evidence of previous CT infection.

It is of note that although 50% of patients showed serologic evidence of previous CT infection, less than 25% of these patients showed evidence of any tubal disease, and only 11% of those with a positive titer showed BTO. It is possible that not all CT infections are particularly damaging to the Fallopian tubes.

Bilateral tubal occlusion, the presence of adhesions and the number of ectopic pregnancies did show some correlation with elevated CTA levels. In particular, patients with high-positive CTA titers were at a 15-times greater risk for BTO than CTA-negative patients and at a 13-times greater risk for ectopic pregnancy when compared to patients with negative results. However, even with high-positive CTA levels, the large majority of patients had normal tubal patency, absence of pelvic adhesions, and no history of an ectopic pregnancy. The presence of CTA in the serum should not alter a patient's infertility management. In a setting where CTA are present in a majority of middle class patients who are seen for infertility without apparent tubal disease, the finding of CTA should not necessarily prompt immediate tubal investigation. Patients should be provided with these data and can then make the choice to initiate or delay invasive diagnostic procedures.

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