

The value of negative chlamydia trachomatis antibody in prediction of normal tubes in infertile women

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Summary

Objective: To evaluate the value of Chlamydia trachomatis antibody testing in prediction of at least one normal tube in infertile women. **Materials and Methods:** Eighty infertile women without any history of abdominal or pelvic surgery, pelvic inflammatory disease, and endometriosis were recruited in this cross-sectional study from 2009 to 2010. The patients underwent hysterosalpingography, laparoscopy, and anti Chlamydia trachomatis IgG antibody (CAT) testing. We compared laparoscopy findings and CAT regarding sensitivity, specificity, accuracy, and predicting value of tubal conditions. **Results:** The CAT was positive in 50 patients (62.5%) and laparoscopy was positive in 32 patients (40%). The CAT was significantly higher in women with tubal disease (1.88 ± 0.34) versus in women with normal tubes (1.21 ± 0.28) ($p = 0.003$). Five out of 30 sero-negative women had unilateral tubal abnormality and none of them had bilateral tubal obstruction or severe pelvic adhesion. The sensitivity, specificity, positive and negative predictive value, and accuracy of the CAT in prediction of one normal tube were 100%, 42.25%, 18%, 100%, and 48.75%, respectively. **Conclusion:** The negative predictive value of CAT to predict at least one normal tube in infertile women without history of abdominal or pelvic surgery, pelvic inflammatory disease, and endometriosis was 100%.

Key words: Chlamydia trachomatis antibody; Fallopian tube evaluation; Female infertility; Predictive value.

Introduction

Tubal factor is one of the most important factors in the diagnosis and treatment of infertile women. The evaluation of tubal factor requires invasive techniques such as hysterosalpingography (HSG) and laparoscopy. Laparoscopy is the gold standard for evaluation of tubal abnormalities but it is expensive, invasive, and requires general anesthesia. Thus, using a noninvasive and cost benefit technique to evaluate tubal factor may reduce unnecessary laparoscopy.

Genital Chlamydia trachomatis infection has a worldwide distribution [1] and is recognized as the single most common cause of tubal peritoneal damage [2, 3]. Previous studies have confirmed a strong correlation between positive Chlamydia serologic results and salpingitis, which results in infertility [4, 5] and the other study revealed that the severity of tubal disease correlates with an increase in antibody titer [6]. Keltz showed that Chlamydia serology as a screen test for tubal infertility is an inexpensive, noninvasive test that matches the predictive value of most standard infertility tests [7]. Because pregnancy is possible with one normal tube, the aim of this study is to evaluate the value of the Chlamydia IgG antibody (CAT) in prediction of at least one normal tube in infertile women.

Material and Methods

In this cross-sectional study we enrolled 80 infertile women referred to the Gynecology clinic in Akbarabadi and Raso-

lakram hospitals, Tehran University of Medical Sciences from April to December 2010. This study was approved by the ethical committee of Tehran University of Medical Sciences. Informed consents were given by all participants. Exclusion criteria were history of four previous abdominal or pelvic surgeries, history of pelvic inflammatory disease, history of tuberculosis in patient or her family, history compatible with endometriosis (premenstrual spotting, progressive pelvic pain, dysmenorrhea, dyspareunia and pain in defecation), and male factor infertility.

After history taking and general physical examination, infertility workups such as semen analysis, HSG, and hormonal assay were carried out on all patients. Venous blood (5 cc) was drawn for laboratory measurement of the serum CAT. CAT was measured by the Elisa technique (trinity USA). According to the kite brochure, the positive titer was ≥ 1.1 and the negative titer was ≤ 0.9 . A titer of 0.91-1.09 was considered suspicious. If the patient's CAT was in this range the test was repeated three weeks later. Laparoscopy was performed for all patients because of history of abnormal HSG, unexplained infertility, and demand for ovarian cauterization. Laparoscopic findings were categorized as normal, unilateral tubal obstruction or abnormality, bilateral tubal obstruction, and frozen pelvis. All data were analyzed using SPSS. Statistical evaluation was performed using Student's t-test and chi square tests. Statistical significance was defined as $p < 0.05$ and the results were expressed as means \pm SD and percentage. CAT data were compared to laparoscopy findings regarding sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) and accuracy.

Results

We studied 80 infertile women with a mean age of 26.7 ± 3.8 years and mean duration of infertility of 4.8 ± 2.1 years. Sixty-eight out of the 80 patients (85%) had been treated for at least one cycle for infertility.

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CAT was positive in 50 out of 80 patients (62.5%). Evidence of tubal disease which identified by laparoscopy was present in 32 patients (40%) (Table 1).

Seropositive woman had a significantly higher incidence of tubal abnormality in comparison with seronegative women ($p = 0.002$). CAT sensitivity, specificity, PPV, NPV, and accuracy to predict tubal abnormality were 84%, 52%, 54%, 83% and 65%, respectively. CAT levels were significantly higher in women with tubal disease (1.88 ± 0.34) in comparison with the normal tube group (1.21 ± 0.28), ($p = 0.003$) (Table 2).

Twenty-three patients in our study had at least one normal tube with unilateral tubal pathology (28.75%) and nine patients had at least two-sided tubal pathology (11.25%). CAT levels were significantly higher in women with bilateral tubal pathology compared to unilateral (2.37 ± 0.42 vs 1.39 ± 0.27) ($p < 0.0001$). Three out of nine patients with bilateral tubal damage had frozen pelvis. The mean of CAT in this group was 2.8 ± 0.54 and in women with bilateral tubal pathology without frozen pelvis it was 2.2 ± 0.89 ($p = 0.001$).

One normal tube was identified by laparoscopy in all patients with a negative CAT (Table 3). The CAT sensitivity, specificity, PPV, NPV, and accuracy for prediction of at least one normal tube were 100, 42.25, 18, 100, and 48.75, respectively.

We also compared the HSG findings to laparoscopic findings (Table 4) and the predictive values of HSG in comparison with CAT are shown in Table 5.

Discussion

The most common sexually transmitted disease is Chlamydia trachomatis and CAT, as an inexpensive and non-invasive screening test for tubal factor infertility, has been presented in the fertility work-up. However, laparoscopy is considered the gold standard for the evaluation of tubal function which is an invasive and expensive procedure requiring general anesthesia.

In this study we evaluated the value of the negative CAT in prediction of at least one normal tube in infertile women. Our study showed CAT has a sensitivity and NPV of about 100% to predict at least one normal tube. This could be important for the inconvenience which many women face for tubal testing such as laparoscopy. CAT was negative in five patients who had tubal abnormalities in laparoscopy (17% false negative rate). All of these five women had unilateral tubal abnormalities and one normal tube, indicating that CAT can predict at least one normal tube with sensitivity and NPV of 100%.

Pregnancy is possible with one normal tube. So we can offer measurement of antichlamydia antibody as screening test at starting of evaluation of infertile couples that leads to prevention of invasive techniques as laparoscopy. However, there are challenges in our conclusion about negative CAT. The first one is the other pathologic micro organisms which would be responsible for tubal disease. According to Vlasak study, PID with organisms such as anaerobes or facultative aerobes may be initiated by gon-

Table 1. — Results of CAT in comparison with the laparoscopic findings.

CAT	Laparoscopic finding		Total
	Abnormal tube	Normal tube	
Positive	27	23	50
Negative	5	25	30
Total	32	48	80

Table 2. — CAT in women with tubal disease in comparison with normal tubes.

Tubal condition	CAT (average \pm SD)	<i>p</i> value
Abnormal tube	1.88 ± 0.34	0.003
Normal tube	1.21 ± 0.28	

Table 3. — Results of CAT in comparison with the laparoscopic findings in regards to at least one normal tube.

CAT	Laparoscopy		Total
	ALONT*	BTD**	
Positive	41	9	50
Negative	30	0	30
Total	71	9	80

* At least one normal tube; ** Bilateral tubal damage.

Table 4. — HSG findings in comparison with laparoscopic findings.

HSG finding	Laparoscopy finding		Total
	Abnormal tube	Normal tube	
Abnormal tube	18	4	22
Normal tube	14	44	58
Total	32	48	80

Table 5. — Comparison of the diagnostic value of CAT and HSG in prediction of tubal abnormality.

Diagnostic value	Chlamydia trachomatis antibody (CAT) (%)	Histerosalpingography (HSG) (%)
Sensitivity	84.3	56.2
Specificity	52	91.6
PPV*	54	81.8
NPP**	83/3	75.8
Accuracy	65	77.5

* Positive predictive value; ** Negative predictive value.

orrhea, Chlamydia or both [8] and the second one is this fact that not all women develop Chlamydia trachomatis antibody after a Chlamydia infection [9, 10]. Time-related antibody titer decline is also a possible reason for false negative results.

In these cases, some studies have suggested a chronological decline in titer [11, 12] but Gijzen *et al.* in their study revealed C. trachomatis IgG antibodies never became undetectable [13]. Rodgers *et al.* also showed that there is a novel link of tubal factor infertility with Chlamydial anti-clpp. (caseinolytic protease protein) antibody [14].

HSG is a less invasive test, as well to assessment of tubal patency is associated with a post procedure pregnancy rate from 12% to 33% [15]. In our study HSG

showed a high specificity and low sensitivity. Thus if HSG and CAT are combined, it can be suggested that laparoscopy can be omitted in a normal CAT and also in a very high level of CAT. In high titers of IgG (at least two times greater than normal), it can predict bilateral tubal occlusions and thus it may reduce many unnecessary laparoscopy procedures). In our study high titers of CAT were seen in the nine patients who had frozen pelvis or bilateral tubal obstructions. There were no false positive results in these nine patients. Thus laparoscopy can be avoided and assisted reproductive technique can be directly offered to these infertile women.

The limitations of the current study were small sample size, lack of a control group, and infection because of other microorganisms. In this case, to achieve better and comparable results, we suggest a case control study with large sample size and close attention to other infections in infertile women.

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