# Clinical findings and chlamydia antibody titre as predictors of tubal factor infertility

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**Citation**

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**Abstract**

Objective:To compare the predictive capacity of clinical scoring system and chlamydia antibody titre in predicting tubal disease.Methods:This study included 70 infertile women with normal ovarian and male factors. All women had detailed history taking, general examination, local examination, and vaginal and cervical swabs for culture and sensitivity. A clinical scoring system based on the following variables was used for prediction of tubal disease; age, infertility duration, previous abortion, previous delivery, dysmenorrhea, dyspareunia, evidence of bacterial vaginosis, and tender adnexa. IgG chlamydia antibody titre (CAT) and mid luteal phase serum progesterone were assessed using enzyme immunoassay (ELISA) technique. Tubal abnormality was assessed by hysterosalpingography (HSG) in the follicular phase. The clinical scoring and the CAT were compared by calculating the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio (+LR), negative likelihood ratio (-LR), the relative risk (RR), and the area under the curve (AUC) of the receiver operator curve.Results:CAT was positive in 20 patients (28.57%) out of the 70 studied women. Evidence of tubal disease identified by HSG was present in 34 patients (48.6%). Seropositive women had significantly higher incidence of tubal abnormality compared to seronegative women (p=0.0001). The CAT was significantly higher in women with tubal disease (11.63 ± 7.27) compared to women with normal tubes (6.76 ± 4.02) (z=3.126, p=0.002). The CAT achieved a low sensitivity of 50% and a high specificity of 91.67%. In comparison, the clinical scoring system achieved a balanced sensitivity and specificity of 82.35% and 86.11% respectively. The AUC of the clinical scoring system (0.891) was found to be significantly higher than that of the CAT (0.717).Conclusion:The clinical scoring system proved to be more accurate than the CAT in predicting tubal disease.

## INTRODUCTION

Tubal factor is considered among the most frequent causes of infertility next to ovulatory disorders and sperm defects. Tubal factors account for 14-38% of causes of female infertility (1, 2). Therefore tubal patency test testing is an integral part of the fertility workup according to several guidelines. The most commonly used tests in this respect are hysterosalpingography (HSG) and diagnostic laparoscopy with chromotubation. HSG is considered painful by some women and may carry a risk of pelvic infection (3). Laparoscopy is considered invasive and requires general anesthesia with its associated risks.

Genital Chlamydia trachomatis infection has a worldwide distribution (4) and is now recognized as the single most common cause of tubal peritoneal damage (5). Several studies suggested that Chlamydia trachomatis antibody testing is accurate in predicting tubal disease (2,6,7).

Several authorities suggested that a careful history taking can identify a specific cause of infertility and thereby help to direct subsequent diagnostic evaluation on the most likely responsible factors. Moreover, guidelines at several countries advocate medical history taking as a tool to select women for tubal testing (8, 9).

The aim of this study is to evaluate several clinical findings and chlamydia antibody titre (CAT) as predictors of tubal disease.

## MATERIALS AND METHODS

This study was carried out during the period from June 2007 to March 2008. 70 women attending the infertility clinic at Kasr El-Aini hospital, Cairo University participated in the study. Local institute approval was taken before starting the study. Informed consents were taken from all participating women. All women had detailed history intake, general examination, and local examination. Vaginal and cervical swabs for culture were also taken from all women. We stressed on the following clinical variables; age, infertility

duration, previous abortion, previous delivery, dysmenorrhea, dyspareunia, evidence of bacterial vaginosis, and tender adnexa. Inclusion criteria included women with regular ovulatory cycles, defined as a cycle length between 23 to 35 days. Ovulation was confirmed by mid luteal phase serum progesterone. Also, women were only included if their partners had normal semen analysis according to the WHO criteria (10). Women with previous pelvic surgery or previous investigation for the tubal factor were excluded.

Tubal patency was assessed by HSG in the early follicular phase. Tubal disease was defined as unilateral or bilateral dye obstruction, abnormal dye pattern suggestive of peritubal adhesions, or hydrosalpinx. A blood sample was taken during performing the HSG to detect Chlamydia trachomatis IgG antibodies. The antibodies were estimated using enzyme immunoassay (ELISA) technique (DRG International Inc., USA). Values were expressed as units, where the cut-off value was 10U. Values more than 11U were considered as positive, values less than 9U were considered as negative, and values between 9-11U were considered equivocal. Equivocal cases were repeated to determine if positive or negative. Mid luteal phase serum progesterone was estimated using enzyme immunoassay for quantitative measurement (DRG International Inc., USA).

We built up a clinical scoring system for prediction of tubal disease based on the previously mentioned clinical variables. The broad lines of this scoring system were derived from a large study done by Coppus et al (11), as well as a logistic regression analysis to identify the most significant clinical variables. The predictive capacity of this scoring system was evaluated by calculating the area under the receiver operating characteristic curve (ROC). This scoring system is shown in table 1.

Data were expressed as mean, median, and standard deviation (SD). Fisher's exact and Mann Whitney tests were used for comparison between groups. The clinical variables were entered in a stepwise fashion in a logistic regression model to detect the significant variables. The predictive capacity of the CAT and the scoring system were analyzed by calculating the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio (+LR), negative likelihood ratio (-LR), and the relative risk (RR). Spearman correlation was used to find significant correlation between variables. A p value < 0.05 was considered statistically significant. Microsoft Excell and MedCalc computer programs (MedCalc software, Belgium) were used for analysis.

**Figure 1**

Table 1: Scoring system for prediction of tubal disease

| Variable | Score | | |
|---|---|---|---|
| Age (years) | <30 = 0 | 30-35 = 2 | > 35 =3 |
| Infertility Duration (months) | 12-24 = 1 | 24-36 =2 | >36 =3 |
| Dysmenorrhea | Yes = 3 | No = 0 | |
| Dyspareunia | Yes = 3 | No = 0 | |
| Previous abortion | Yes = 2 | No = 0 | |
| Previous delivery | Yes = 2 | No = 0 | |
| Bacterial Vaginosis | Yes = 2 | No = 0 | |
| Tender adnexa | Yes = 4 | No = 0 | |

## RESULTS

The participating women had a mean age of 25.66 years (SD=6.71) and a mean duration of infertility of 32.40months (SD=21.59). 32 women (45.7%) had secondary infertility and 38 (54.3) had primary infertility.

CAT was positive in 20 patients (28.57%) out of the 70 studied women. Evidence of tubal disease identified by HSG was present in 34 patients (48.6%). Seropositive women had significantly higher incidence of tubal abnormality compared to seronegative women (p=0.0001). This is shown in table 2. The sensitivity, specificity, positive predictive value, negative predictive value, +LR, –LR, and RR for CAT to predict tubal disease were 50%, 91.67%, 85%, 66%, 6, 0.55, and 2.5 (95% confidence interval=1.63-3.83).The CAT was significantly higher in women with tubal disease (11.63 ± 7.27) compared to women with normal tubes (6.76 ± 4.02 ) (z=3.126, p=0.002).

**Figure 2**

Table 2: Validity of CAT in detecting tubal abnormality identified by HSG

| | Tubal disease | Normal tubes | Total |
|---|---|---|---|
| Seropositive | 17 (24.3%) | 3 (4.3%) | 20 (28.6%) |
| Seronegative | 17 (24.3%) | 33 (47.1%) | 50 (71.4) |
| Total | 34 (48.6) | 36 (51.4%) | 70 (100%) |

The most significant clinical variables according to the logistic regression model were dysmenorrhea, dyspareunia, infertility duration, and the presence of tender adnexa. This is shown in table 3.

**Figure 3**

Table 3: Significant clinical variables in logistic regression model

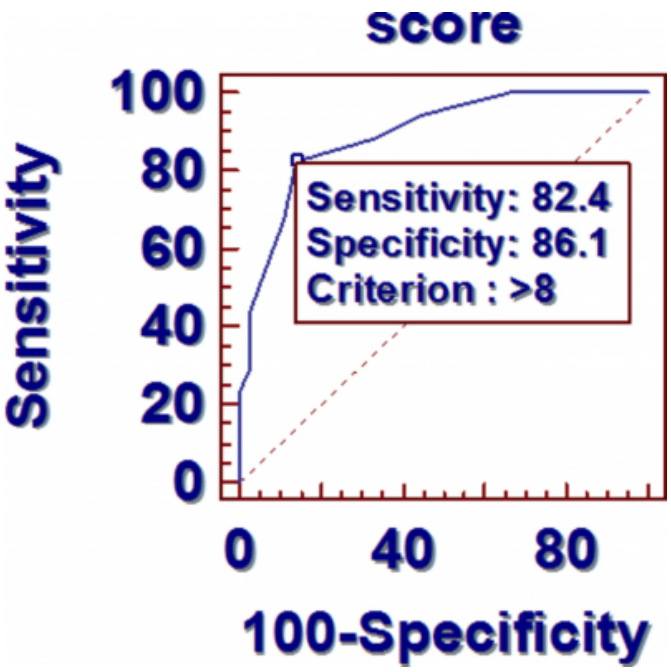
| Variable | Coefficient | SE | OR | P value |
|---|---|---|---|---|
| Dysmenorrhea | 2.76 | 0.88 | 15.79 | 0.001 |
| Dyspareunia | 1.48 | 0.69 | 4.39 | 0.03 |
| Infertility duration | 0.048 | 0.02 | 1.05 | 0.0009 |
| Tender adnexa | 3.45 | 0.93 | 31.44 | 0.0002 |

The area under the curve (AUC) of the ROC was calculated for the clinical score to predict tubal abnormality. The AUC of the clinical score was 0.891 (z=9.64, p=0.0001) when the

cut off value was > 8. This is shown in figure 1.

**Figure 4**

Figure 1: the ROC of the clinical scoring system




The predictive capacity of the CAT and the clinical scoring were assessed by calculating the sensitivity, specificity, positive predictive value, negative predictive value, +LR, and –LR, and RR. This is shown in table 4.

**Figure 5**

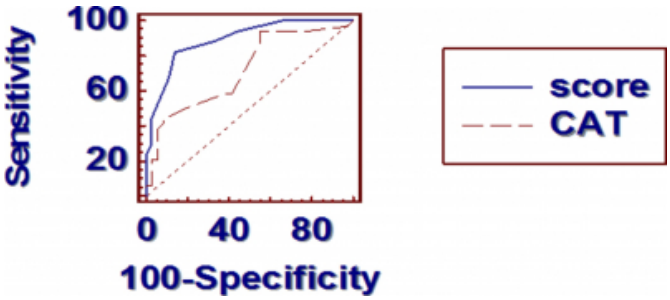
Table 4: Comparison of predictive capacity of the CAT and Clinical Scoring

| | CAT | Clinical Scoring |
|---|---|---|
| Sensitivity | 50% | 82.35% |
| Specificity | 91.67% | 86.11% |
| + Predictive Value | 85% | 84.85% |
| - Predictive Value | 66% | 83.78% |
| + LR | 6 | 5.93 |
| - LR | 0.55 | 0.20 |
| RR | 2.50 | 5.23 |

The AUC of the ROC of the CAT used to predict tubal block was 0.717. The AUC of the clinical scoring system (0.891) was significantly more than that of the CAT (z=2.422, p=0.015).This is shown in figure2.

**Figure 6**

Figure 2: The AUC of the clinical scoring system and the CAT




There was no significant correlation between the CAT and the patient's age or infertility duration. There was significant correlation between the CAT and the clinical scoring system (p=0.035).

## DISCUSSION

In this study we evaluated 70 infertile women regarding their CAT and regarding 8 clinical variables to predict the probability of having tubal disease assessed by HSG. The studied women were chosen to have normal ovulation and male partners. The aim was to find whether CAT or the clinical history scheme has more predictive value in detecting tubal disease. This would be very important for early selection of women for tubal testing either by HSG or laparoscopy. At the same time, it will avoid the inconvenience which many women face if they are advised for tubal testing in their early evaluation visits. Moreover, this may reduce many laparoscopies which are done early and prove to be normal.

We developed a clinical scoring system composed of 8 clinical variables to predict the probability of tubal disease. The choice of these variables was based upon previous studies as well as a stepwise logistic regression model. We used the clinical variables which most suite our population. We ignored the variables which have very low prevalence in our population. We tried not to use variables which depend on recall like “Did you have previous episode of PID or STD” because we felt that this will not be accurate in our patients. Finally, we give a higher score for the variables which proved to be significant in our logistic regression model.

Our study showed that 48.6% of patients had evidence of tubal disease according to HSG. The CAT seropositive patients were 20 out of 70 (28.57%). The CAT achieved a low sensitivity of 50% and a high specificity of 91.67%. In comparison, the clinical scoring system achieved a balanced

sensitivity and specificity of 82.35% and 86.11% respectively. The AUC of the clinical scoring system was found to be significantly higher than that of the CAT. Consequently, the clinical scoring system, according to our study, was found to be more accurate in predicting tubal disease.

The limited performance of the CAT in predicting tubal disease in our study could be due to the low prevalence of the seropositive patients in our population. It appears that the Chlamydia trachomatis is not the primary pathogen responsible for PID and tubal disease in our population. Several studies found a higher incidence of Chlamydia ranging from 40-65% among infertile women (12,13). Others suggested that tubal factor infertility not associated with C. trachomatis infection is found in up to 25-50% of cases which limits the use of CAT on its own (14).

There is controversy regarding the value and accuracy of medical history in predicting tubal disease. Some authors suggested that clinical decision rule based on medical history can accurately express women probability of tubal disease at couple's first consultation (11, 15). Others suggested that history taking related to past genital infection appears to be of little use in evaluation of infertile women (16, 17).

Our model is characterized by being simple and easily applied. The items were carefully chosen to suite our population. The items depended on clinical history and clinical examination not on history alone.

In our study, we had some weak points. We used HSG to verify tubal disease. HSG is not the gold standard test and suffers from possible false results in comparison to laparoscopy. We considered unilateral or bilateral tubal disease as abnormal, however, in practice women with unilateral tubal disease can still get pregnant. We proposed that because women with bilateral tubal abnormality were limited in number. Moreover, our interest was to prove tubo-peritoneal disease related to clinical items or past chlamydial infection rather than occurrence of pregnancy. Finally, the study would have more applicability if the number of patients was larger.

The present study suggests that clinical evaluation is an important step to choose women who could benefit from early tubal testing. Further larger studies are needed to confirm this.

## References

1. Evers JL. Female subfertility. Lancet 2002; 360: 151-159.
2. Dabekausen YAJM, Evers JLH, Land JA, Stals FS. Chlamydia trachomatis antibody testing is more accurate than hysterosalpingography in predicting tubal factor infertility. Fertil Steril 1994; 61: 833-837.
3. Forsey JP, Caul EO, Paul ID, Hull MG. Chlamydia trachomatis, tubal disease and the incidence of symptomatic and asymptomatic infection following hysterosalpingography. Hum Reprod 1990; 5: 444-447.
4. Stamm WE. Chlamydia trachomatis infections of the adults 1999. In
5. McGraw-Hill, New York, pp. 407-432.
6. WHO task force on the prevention and management of infertility. Tubal
7. Sex. Transm Dis 1995; 22: 71-77.
8. Veenemans LMW, Van der Linden PJQ. The value of Chlamydia trachomatis antibody testing in predicting tubal factor infertility. Hum Reprod 2002; 17(3): 695-698.
9. .Akande VA, Hunt LP, Cahill DJ, Caul EO, Ford WCL, Jenkins JM. Tubal damage in infertile women: prediction using chlamydia serology. Hum Reprod 2003; 18(9): 1841-1847.
10. American Society for Reproductive Medicine. Optimal evaluation of the infertile female. A committee opinion 2000. http://www.asrm.org
11. National Institute for Clinical Excellence. Guideline CG11: Fertility: Assessment and Treatment for People with Fertility problems, 2004.
12. WHO (1992). WHO laboratory manual for the examination of human semen and
13. Cambridge University Press, Cambridge, 1-107.
14. Coppus SFPJ, Verhoeve HR, Opmeer BC, van der Steeg JW, Steures P, Eijkemans MJC, Hompes PGA, Boussuyt PMM, van der Veen F, Mol BWJ. Identifying subfertile ovulatory women for timely tubal patency testing: a clinical decision rule based on medical history. Hum Reprord 2007; 22 (10): 2685-2692.
15. Thomas K, Coughlin L, Mannion PT, Haddad NG. The value of Chlamydia trachomatis antibody testing as part of routine infertility investigations. Hum Reprod 2000; 15: 1079-1082.
16. Kelver ME, Nagamani M. Chlamydial serology in women with tubal infertility. Int J Fertil 1989; 34 (1):42-45.
17. Rice PA, Schachter J. Pathogenesis of pelvic inflammatory disease. What are the questions? J Am Med Assoc 1991; 266: 2587-2593.
18. Coppus SF, Opmeer BC, Logan S, van der Veen F, Bhattacharya S, Mol BW. The predictive value of medical history taking and Chlamydia IgG ELISA antibody testing (CAT) in the selection of subfertile women for diagnostic laparoscopy: a clinical prediction model approach. Hum Reprod 2007; 22: 1353-1358.
19. Hubacher D, Grimes D, Lara-Ricalde R, Jara J, Garcia-Luna A. The limited clinical usefulness of taking a history in the evaluation of women with tubal factor infertility. Fertil Steril 2004; 81: 6-10.
20. Logan S, Gazvani R, McKenzie H, Templeton A, Bhattacharya S. Can history, ultrasound, or ELISA chlamydial antibodies, alone or in combination, predict tubal factor infertility in subfertile women? Hum Reprod 2003;18(11): 2350-2356.

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