



Prevalence of antichlamydial antibodies in women with infertility and its association with tubal factors

Gynaecology

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ABSTRACT

Introduction: The tubal and peritoneal pathology due to PID are the foremost cause of infertility in developing countries and Chlamydia Trachomatis is an important causative agent. Due to asymptomatic nature, there is delay in diagnosis; hence better understanding of its role in infertility is imperative.

Method: 50 infertile women were subjected to anti chlamydial IgG and IgA antibodies by ELISA, and the relationship to tubal damage was analysed.

Results: 21 (42%) of infertile women were sero positive. A significant correlation of sero-positivity with secondary infertility, tubal factors and adhesions was observed. The sensitivity, specificity, positive predictive value and negative predictive value of anti Chlamydial antibodies in prediction of tubal infertility were 85.71%, 68.97%, 66.67%, and 86.96%.

Conclusion: The timely diagnosis of Chlamydia infection by detection of specific anti-Chlamydial antibodies by ELISA is a simple, valuable, non-invasive, diagnostic procedure and hence it should become an integral part of infertility work up.

KEYWORDS:

Chlamydia Trachomatis anti bodies, Tubal Factors, Infertility

Introduction:

On infertility, "What comes so naturally for many can be a hardship for millions of others". The challenges in reproductive medicine today require improvement in the investigations and management of infertile patients. The tubal and peritoneal pathology have been seen to be the foremost cause of infertility especially in developing countries. Infertility is a consequence of tubal damage which occurs when acute Pelvic Inflammatory Disease progresses into chronic form leading to fibrosis and scarification of tubes¹. Of various organisms causing sexually transmitted infections, genital Chlamydia trachomatis has emerged as the most important causative agent². The organism has been recovered from about 30 to 60% cases of salpingitis in India³. Due to the asymptomatic nature of disease, there is delay in diagnosis leading to harmful after effects in women like infertility and tubal pregnancy. Better understanding of the role of persistent Chlamydia trachomatis infection in infertility is imperative.

Traditional method of diagnosis of Chlamydia is isolation of the organism in culture and antigen detection tests by various methods, but these test are costly and require expertise. In chronic Chlamydia infection, organism may not be detectable and a positive serology may be the only indication of Chlamydia involvement. Data on the importance of this infection, burden of disease in the community, morbidity in terms of sequel is limited. So, this study has been conducted as an attempt to address these lacunae.

Methods:

50 patients of infertility, between ages of 18 to 40 years, attending gynaecology OPD at Kasturba Hospital, Delhi were taken including both primary and secondary infertility. Any patient who has been diagnosed as a case of tuberculosis or having a past history of tuberculosis has been excluded from the study. A detailed history was obtained from these patients including age, marital status, occupation, duration and type of infertility, investigations and treatment received before.

Detection of specific anti chlamydial IgG and IgA antibodies in single serum samples of all patients was done by ELISA technique. The presence of only IgG antibody in serum signifies a past infection with Chlamydia Trachomatis. The presence of both IgG and IgA signifies chronic or persistent infection. The presence of only IgA signifies recent active infection.

Tubal patency was checked by Hysterosalpingography and diagnostic laparoscopy. Pelvic findings such as congestion, appearance of tubes, site of blockage, adhesion especially in peritubal region, presence of hydrosalpinx (unilateral or bilateral), adhesion between pelvic structures, adhesion between diaphragm and liver, endometritis, and ovarian cysts etc were observed on laparoscopy. The data collected during the study was analysed and evaluated using appropriate statistical tests.

Observations and Results:

The mean age of presentation was 29.74 ± 3.1 years. The main symptoms of infertile women were discharge per vagina (74%), pain abdomen (56%), dysuria (38%), frequency of micturition (46%), dysmenorrhea (42%) and dyspareunia (32%). 19 (38%) patients had a history of STI/PID in the past.

38 (76%) patients presented with primary infertility and 12 (24%) patients presented with secondary infertility. 24 (48%) infertile patients were diagnosed to have tubal block by HSG. 4 women diagnosed to have tubal block on HSG were false positive as they had patent tubes on laparoscopy and only 20 (40%) of infertile patients were diagnosed to have tubal blockage. 23 (46%) patients had peritubal adhesions seen during laparoscopy. Adhesions were more commonly encountered in the secondary infertility patients (66.67%) than primary infertility patients (39.47%).

21 (42%) of infertile women were seropositive (presence of either IgG and/or IgA). 18% were positive for only IgG, 2% were positive for only IgA, 22% for both IgG and IgA. There was no difference in demographic profile of sero-positive and sero-negative women (Table No. 1). However history of abortion and PID, genitourinary symptoms in partner, menstrual symptoms and abnormal clinical features on P/S and P/V examination correlated well with sero-positivity. (Table 2) In the present study, seropositivity i.e. presence of IgG, IgA or both was seen in 26% primary infertility patients in comparison to 92% of secondary infertility patients. p value < 0.0005 showed a correlation of seropositivity with secondary infertility. (Table 1)

Table 1: Clinical features of sero-positive and sero-negative infertile patients

Chlamydia Trachomatis Antibodies	Sero positive 21(%)	Sero negative 29(%)	p value
Primary Infertility (n=38)	10 (26)	28(74)	<0.0005
Secondary Infertility (n=12)	11(92)	1(8)	
Menstrual symptoms	9(43)	1(3.5)	0.009
Genitourinary symptoms in husband	9(43)	5(17)	0.043
History of abortion	7(33)	0	0.004
History of PID	13(62)	6(21)	0.003
Cervical pathology on P/S	11(52)	3(10)	0.007
Abnormal P/V findings	9(43)	4(14)	0.027

C Reactive Protein (CRP) is a marker of ongoing low grade inflammation, and together with Chlamydia antibody testing, it can help in diagnosis of tubal pathology, as 8 patients had a positive C reactive protein, and 7 of them were sero-positive for Chlamydia. (Table 2)

Table 2: Special investigations of sero-positive and sero-negative infertile patients

Chlamydia Trachomatis Antibodies	Sero positive 21(%)	Sero negative 29(%)	p value
C Reactive Protein	7(33)	1(3.4)	0.007
Tubal Block on HSG	16(76)	8(27.5)	0.0003
Tubal Block on Laparoscopy	15(72)	5(17)	0.001
Tubal Adhesions on Laparoscopy	17(80)	9(31)	0.001
Hydro-salpinx	9(43)	1(3.5)	0.001
Presence of any tubal abnormality	18(86)	9(31)	0.0002

A statistically significant correlation of sero-positivity with tubal factors, like tubal block, hydro-salpinx and peritoneal adhesions was observed. In the sero positive group, 10 patients had dense adhesions and 7 had flimsy adhesions. The adhesions were peritubal, peri fimbrial and peri ovarian in location. 2 of the patients had typical peri hepatic adhesions (adhesions between the liver and diaphragm). (Table 2)

Table 3: Chlamydia antibodies as a predictor of Tubal Pathology

Sero-positivity	Tubal factor of infertility	95% class interval
Sensitivity	85.71%	63.66% to 96.95%
Specificity	68.97%	49.17% to 84.72%
PPV	66.67%	46.04% to 83.48%
NPV	86.96%	66.41% to 97.22%

The sensitivity, specificity, positive predictive value and negative predictive value of serum anti Chlamydial antibodies in prediction of tubal infertility are 85.71%, 68.97%, 66.67%, and 86.96% respectively. (Table 3)

Discussion:

Our study has reaffirmed that infection with Chlamydia Trachomatis in past plays an important role in tubal factors of infertility as 42% of infertile women were tested positive for Chlamydia antibodies and 85.71% of all sero positive women had tubal factor infertility. The prevalence of seropositivity was higher in the secondary infertility group (92%) as compared to primary infertility (26%).

The symptoms of genitourinary infection, menstrual irregularities, and signs of pelvic inflammation were more commonly associated with seropositive women in the present study, however in a study conducted by Joyee et al, no significant association between clinical presentation and seropositivity to Chlamydia could be established and they recommended that Chlamydia infection cannot be predicted on the basis of clinical grounds⁴.

According to Westorm classical studies, the symptoms and signs of salpingitis are variable. Many patients with tubal infections are afebrile and have a benign clinical course. Some patients with tubal infection are asymptomatic¹. Therefore they neither present with any complaint suggestive of genital infection; nor present with non specific complaints. Up to 70 to 80 % of PID due to Chlamydia are asymptomatic and remain unrecognized and untreated (Rahm et al)⁵. The frequent occurrence of unsuspected silent chronic PID in infertile patients stresses the need to evaluate these patients based on more than only history and clinical criteria. These patients should be screened for

Chlamydia infection.

All 7 women in the study with history of abortion were sero positive, and hence it correlates positively to subfertility along with infertility.

Based on Hystero-salpingography findings, 24 women (48%) were diagnosed to have tubal block. 76 % of sero positive women had tubal block and 72.5% sero negative women had patent tubes on HSG.

Dabekausen et al tested for antichlamydial antibodies in 211 infertility patients, results were compared with the results of HSG with respect to their predictive values. Likelihood ratio calculations were used⁶. The positive likelihood ratio of serology was 9.1, indicating that a patient with tubal infertility is 9.1 times more likely to have abnormal serology than a patient without tubal infertility. It was superior to that of HSG which had a positive likelihood of 2.6.

In the present study 8 patients had a positive C reactive protein, and 7 of them were sero positive for Chlamydia.

J.E.den Hartog, S.A.Morre and J.A Land assessed the risk of tubal pathology in sub fertile women, using IgG antibody and C reactive protein. It was observed that a positive IgG against Chlamydia is an indicative of a past infection with Chlamydia. But patients with persistent infection are at highest risk of tubal infertility. It was observed that C reactive protein is a promising serological marker of persistent infection by Chlamydia⁷.

On laparoscopy tubal block, peritoneal adhesions, hydrosalpinx were all more prevalent in seropositive women. Peritoneal adhesions associated with Chlamydia infection interfere with ovum transport and tubal peristalsis and contributes significantly to infertility.

The sensitivity, specificity, positive predictive value and negative predictive value of serum anti chlamydial antibodies in prediction of tubal infertility were 85.71%, 68.97%, 66.67%, and 86.96% respectively.

In a study by Malik et al the sensitivity, specificity of antichlamydial antibodies as an indicator for tubal infertility was reported to be 72.7% and 77.7%⁸.

According to M.Tanikawa et al, patients with low or negative chlamydia antibody titre have lower risks of tubal factor infertility⁹.

Keltz MD et al conducted a prospective study of 210 infertile patients investigating the role of Chlamydia serology as a screening test and reported the sensitivity, specificity and positive predictive value of Chlamydia serology to be 74%, 93% and 94% respectively¹⁰.

In a study by E. Mboloko, the sensitivity, specificity, positive and negative predictive values for Chlamydia antibody test as a predictor of tubal infertility was 72.7%, 93.3%, 84.2% and 87.5%.¹¹

Conclusion:

The timely diagnosis of Chlamydia infection by detection of specific anti-Chlamydial antibodies by ELISA is a simple, valuable, non-invasive, cost effective, diagnostic procedure and hence it should become an integral part of infertility work up in resource poor country like India. Early screening even in asymptomatic women and timely treatment will prevent of development of deleterious sequelae of Chlamydia infection.

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