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Original Research Article

Role of IgG *Chlamydia* antibody in tubal factor infertility

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ABSTRACT

Background: Chlamydial infection is considered to be one of the important causes of tubal factor infertility. This study will help to explore the relationship between positive Chlamydial infection and tubal damage in infertile women assessed by diagnostic laparoscopy. The results will help to determine whether a policy of routine screening for Chlamydia antibody is justifiable in infertile women to suspect tubal factor so that they can be taken up for laparoscopy earlier.
Methods: A prospective study was performed on 158 consecutive patients who underwent laparoscopy as part of infertility evaluation. About 5 mL of venous blood was drawn preoperatively to detect Chlamydia IgG antibody in all the patients by ELISA. The laparoscopic findings were documented and the relationship to Chlamydial antibody evaluated.
Results: Of the 158 patients who underwent laparoscopy, 95 patients had evidence of tubal disease as evidenced by unilateral or bilateral tubal block, peritubal adhesions, hydrosalpinx, beading of the tube and unhealthy shaggy appearance. Of the 95 patients with documented tubal disease at laparoscopy, 14 (14.7%) had antibodies to Chlamydia. Of the 63 patients with normal tubes, 12 (19%) had Chlamydial positivity. The difference is not statistically significant. However of the 26 patients who were positive for Chlamydia antibodies 14 patients (53.8%) had abnormal tubes. Out of the 158 patients who underwent laparoscopy 26 patients were positive for Chlamydia. Hence the prevalence in our study is 16.4% (26/158). The sensitivity is 14.7% and the specificity is 81%.
Conclusions: This study showed no difference in Chlamydial positivity between infertile women with abnormal tubes and those with normal looking tubes in our population. The absence of Chlamydial antibodies cannot be taken as a marker for normal tubes. Hence screening for chlamydial antibody can neither be used as a screening test for tubal factor infertility nor to decide on the need for laparoscopy in the present population.

Keywords: *Chlamydia trachomatis*, *Chlamydia* antibody test, Infertility, Laparoscopy

INTRODUCTION

This study aims to assess the role of *Chlamydia* IgG antibody in patients with tubal factor infertility among women with primary or secondary infertility attending a fertility clinic in a tertiary care hospital in Kerala, India. Tubal disease may be due to various etiologies including pelvic infections, endometriosis and previous pelvic surgery. Pelvic inflammatory disease (PID) can cause damage to the fallopian tubes leading to tubal obstruction or can be the cause of pelvic adhesions which prevent normal tubal movement, ovum pick-up and transport of the fertilized egg into the uterus. Tubal infertility has been estimated to follow in 12 percent, 23 percent, and 54

percent of women following one, two, or three cases of PID, respectively.[1] Nevertheless, a lack of PID history is not overly reassuring, as nearly one half of patients who are found to have tubal damage have no history of antecedent disease.[2] Though data suggests that the etiology of PID is polymicrobial, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are the most common organisms associated with PID. Other microorganisms implicated in PID are *Mycoplasma genitalium*, *Mycoplasma hominis, Ureaplasma spp, Veillonella spp*. and other lower genital tract endogenous anaerobic and facultative bacteria, many of which are associated with bacterial vaginosis.[3-5]

Chlamydial infection is considered an important cause of pelvic inflammatory disease leading to consequent tubal damage and thereby infertility. There are a lot of studies regarding Chlamydial infection and infertility worldwide, but very few from the Indian subcontinent. We still do not know the extent of tubal infertility caused by *Chlamydia* in Indian women. The main challenge is that infection with *Chlamydia* is usually subclinical and asymptomatic and today with the syndromic approach policy it is very difficult to document Chlamydial infection.

This study will help to explore the relationship between positive Chlamydial infection and tubal damage in infertile women assessed by diagnostic laparoscopy. Laparoscopy is considered to be the gold standard for diagnosing tubal pathology. The results will help to determine whether a policy of routine screening of infertile women for Chlamydia IgG antibodies is justifiable and to comment on the role of this infection in tubal damage. Objective of the study was to evaluate the association of *Chlamydia* trachomatis IgG antibody (CAT) with tubal factor infertility.

METHODS

A prospective study was done in women undergoing laparoscopy at the Reproductive Medicine unit in SAT Hospital, Government Medical College Trivandrum, India for 1 year in 2015.158 consecutive women who underwent laparoscopy were included in the study. Women with obvious evidence of endometriosis on ultrasound were excluded from the study. Clearance was obtained from the Institutional Review Board and Ethics Committee. Written informed consent was obtained from all the subjects.

A detailed history was taken from all the subjects and demographic details, type and duration of infertility and previous pregnancy loss recorded. The symptomatology was also noted. Infertility was defined as failure to conceive after one year of unprotected intercourse. Laparoscopy was performed for all patients with suspicion of tubal infertility like abnormal findings on hysterosalpingogram or ultrasound. Other indications were suspected endometriosis, myomectomy, laparoscopic ovarian drilling and unexplained infertility. Laparoscopy was performed in the proliferative phase by two surgeons and the pelvis was examined in detail with special reference to the appearance of the tubes.

Chromotubation was also done. Meticulous documentation of the laparoscopic findings was done. About 5 mL of venous blood was drawn preoperatively to detect Chlamydia IgG antibody in all the patients. The serum samples were stored in the deep freezer in the department of Microbiology, Government Medical College Trivandrum. Chlamydia IgG antibodies were detected using readymade ELISA kit (CT054G-Calbiotech Inc). Antibody Index interpretation was as follows (<0.9-no detectable antibody; 0.9-1.1- borderline positive; >1.1- detectable antibody).

Data was expressed in frequency distribution and data analysis was performed using SPSS Version 22.0. Between group comparisons of qualitative variables were analysed by Chi Square Test. A p value of 0.005 was taken as the level of significance.

RESULTS

Of the 158 patients who underwent laparoscopy, 95 patients had evidence of tubal disease as evidenced by unilateral or bilateral tubal block, peritubal adhesions, hydrosalpinx, beading of the tube and unhealthy shaggy appearance. Out of the 158 patients who underwent laparoscopy 26 patients were positive for Chlamydia antibody. Hence the prevalence in our study is 16.4% (26/158). Of the 95 patients with documented tubal disease at laparoscopy, 14 (14.7%) had antibodies to Chlamydia (Table 1).

Table 1: Tubal disease and chlamydial sero positivity.

E/O tubal disease	Chlamydia				Total		$\chi 2$	df	p-value
	Positive		Negative						
	N	%	N	%	N	%			
Present	14	14.7	81	85.3	95	100	0.512	1	0.474
Absent	12	19	51	81	63	100			
Total	26	16.5	132	83.5	158	100			

Of the 63 patients with normal tubes, 12 (19%) had Chlamydial positivity. The difference is not statistically significant. The sensitivity is 14.7% and specificity is 81%.

Tubal disease was predominant in the age group 26-35 years (almost 75%). Similarly Chlamydial antibodies were also more common after 26. 73% of *Chlamydia* antibody positive patients were in the age group 26-35. Of the 95 patients with tubal disease, 61 patients (64%) had primary infertility. Of those 26 patients who were Chlamydia positive, 22 patients (84.6%) had primary infertility which is significant. Miscarriages were not commonly seen in patients with tubal disease or those with Chlamydia antibodies. Ectopic pregnancy had occurred in only16.8% of the patients with tubal disease. Similarly, only one patient of the 26 Chlamydia positive patients (3.8%) had ectopic pregnancy. In the patients with tubal disease the significant signs and symptoms were chronic pelvic pain (p=0.018), tenderness in fornices during pelvic examination (p=0.009), presence of adnexal mass (p=0.027) and restricted mobility of the uterus (p<0.001).

Of the patients with tubal disease 46.3% had adnexal mass in ultrasonogram and of the Chlamydia positive patients 50% had adnexal mass. Of the patients with tubal disease 64% had block in one or both tubes, 70% had peritubal adhesions, 13.7% had hydrosalpinx and 62.1% had unhealthy looking tubes. The association of abnormal tubes (one or both) with *Chlamydia* is shown in Table 2. There is no statistical significance.

Table 2: Tubal disease seen at laparoscopy and chlamydial seropositivity.

	Chlamydia				Total (N=158)		$\chi 2$	df	p- value
	Positive (N=26)		Absent (N=132)						
	N	%	N	%	N	%			
Absent spill	6	23.1	55	41.7	61	38.6	3.167	1	0.075
Peritubal adhesions	12	46.2	58	43.9	70	44.3	0.043	1	0.835
Hydrosalpinx	2	7.7	11	8.3	13	8.2	0.012	1	0.913
Un healthy appearance	6	23.1	53	40.2	59	37.3	2.707	1	0.100

Chi-square test was used to analyse the variables. A p value of 0.005 was taken as the level of significance.

Even though obvious endometriosis on ultrasound was taken as an exclusion criterion, of the 95 patients with tubal disease 48.4% (n=46) had evidence of endometriosis at laparoscopy like endometriotic deposits, adhesions and partial obliteration of the pouch of Douglas. Among the 46 patients with evidence of endometriosis, 7 (15%) had antibodies to *Chlamydia* (Table 3).

Table 3: Evidence of endometriosis and chlamydial sero positivity.

Chlamydia	Tubal disease with evidence of endometriosis			
	Present		Absent	
	N	%	N	%
Positive	7	15.2	7	14.3
Negative	39	84.8	42	85.7
Total	46	100.0	49	100.0

DISCUSSION

The present study sought to determine the association between *Chlamydia trachomatis* IgG antibodies and tubal factor infertility among infertile women with primary or secondary infertility attending the Fertility Clinic of a tertiary care hospital in Kerala, India. In the present study, the prevalence of *Chlamydia* IgG antibodies among women with primary or secondary infertility was found to be 16.4% (26/158). This result is consistent with various studies across the world as well as studies in India. In a study conducted at the Reproductive and Gynaecology departments of Aurobindo Medical college Indore in 2015 by Swapnil Singh et al; 10 out of 200 patients tested positive for *Chlamydia* (5%).[6]

In the present study 73% of patients who tested positive for *Chlamydia* belonged to the age group 26-35. 26.9% patients were above 35 years of age. Tubal disease was also predominant in the age group 26-35 years. Almost 73% of the patients with *Chlamydia* positivity had been married for a period of less than 10 yrs. Similarly, 78% of patients with tubal disease were married for a period of less than 10 years.

In a study of the prevalence of *Chlamydia* infection in Samoan women by Walsh et al participants who had a previous pregnancy were less likely to be positive (OR 0.49; 95% CI 0.27–0.87).[7] Primiparous and multiparous women were less likely to be positive than nulliparous women (OR 0.54; 95% CI 0.30–0.99 and OR 0.46; 95% CI 0.24–0.89, respectively).[7] These findings were consistent with our results as 84% of patients in our study with antibodies against *Chlamydia* were being treated for

primary infertility. Similarly, 64% patients with tubal disease had primary infertility.

In the present study, of the 95 patients with abnormal tubes in laparoscopy determined by presence of tubal block, peritubal adhesions, hydrosalpinx and unhealthy appearance, only 14.7% (n=14) had antibodies to *Chlamydia*, showing a sensitivity of 14.7% and specificity of 81.0%. Of the patients with tubal disease in our study, 64% had block in one or both tubes, 70% had peritubal adhesions, 13.7% had hydrosalpinx and 62.1% had unhealthy looking tubes. In two studies by Land et al and by the WHO task force, it was found that among women with tubal pathology at laparoscopy, 60–70% were *Chlamydia* antibody positive.[8,9]

In the present study, the sensitivity is 14.7% and specificity is 81%. This is similar to another Indian study by Swapnil et al, where the sensitivity was 20% and the specificity was 100%.[6]

Of the 26 patients in the present study with *Chlamydia* positivity 53.8% (n=14) had tubal disease. This was consistent with results from various other studies showing tubal pathology at laparoscopy in 30-65% of *Chlamydia* antibody positive women. In another study by Shrikhande et al in Nagpur it was found that *Chlamydia* was responsible for 33% of cases with pelvic inflammatory disease.[10]

In the present study, of the 63 patients with normal tubes 12 patients (19%) had *Chlamydia* positivity. The difference was not significant. In the Swapnil Singh study, however, it was negative in all 150 patients with normal tubes, giving a specificity of 100%. One hypothesis to explain subfertility in patients with normal tubes but positive *Chlamydia* antibodies is that intratubal microdamage may have resulted from a previous *Chlamydia* infection that cannot be detected with conventional patency tests such as hysterosalpingogram or laparoscopy. In addition, these tests have interobserver variability, but it is unlikely that this would explain the substantially lower pregnancy rates in *Chlamydia* positive women.

Another hypothesis is that persistent *Chlamydia* infections also elicits an autoimmune response to human heat shock proteins (HSPs) due to their structural similarity with *Chlamydia* HSP. Human HSPs play an important role in early pregnancy. Animal as well as human research indicate that autoimmunity to human HSP exerts a negative influence on embryo development and implantation.[11-14]

Limitation of the study

As the study was conducted at a tertiary centre where most of these patients were referred, it is likely that many had already received syndromic treatment for various complaints.

CONCLUSION

This study showed no difference in Chlamydial antibody positivity between women with tubal factor infertility and those without. Patients with normal tubes in laparoscopy had Chlamydial antibodies in similar proportion to those with abnormal tubes. The absence of Chlamydial antibodies cannot be taken as a marker for normal tubes. Hence screening for Chlamydial antibody can neither be used as a screening test for tubal factor infertility nor to decide the need for laparoscopy in our population.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Lalos O. Risk factors for tubal infertility among infertile and fertile women. Eur J Obstet Gynecol Reprod Biol. 1988;29:129.
2. Rosenfeld DL, Seidman SM, Bronson RA, Scholl GM. Unsuspected chronic pelvic inflammatory disease in the infertile female. Fertil Steril. 1983;39:44.
3. Ljubin-Sternak S, Meštrović T. Chlamydia trachomatis and Genital Mycoplasmas: Pathogens with an Impact on Human Reproductive Health. J Pathog. 2014;2014:183167.
4. Sharma H, Tal R, Clark NA, Segars JH. Microbiota and Pelvic Inflammatory Disease. Semin Reprod Med. 2014;32(1):43-9.
5. Lis R, Rowhani-Rahbar A, Manhart LE. Mycoplasma genitalium infection and female reproductive tract disease: a meta-analysis. Clin Infect Dis. 2015;61(3):418-26.
6. Singh S, Bhandari S, Agarwal P, Chittawar P, Thakur R. *Chlamydia* antibody testing helps in identifying females with possible tubal factor infertility. Int J Reprod Biomed (Yazd). 2016;14(3):187-92.
7. Walsh MS, Hope E, Isaia L, Righarts A, Niupulusu T, Temese SV, et al. Prevalence of *Chlamydia trachomatis* infection in Samoan women aged 18 to 29 and assessment of possible risk factors: a community- community-based study. Trans R Soc Trop Med Hyg. 2015;109:245-51.
8. Land JA, Gijsen AP, Kessels AGH, Slobbe MEP, Bruggeman CA. Performance of five serological *chlamydia* antibody tests in subfertile women. Hum Reprod. 2003;18:2621-7.
9. WHO Task Force on the Prevention and Management of Infertility. Tubal infertility: serologic relationship to past chlamydial and gonococcal infection. Sex Transm Dis. 1995;22:71-7.
10. Shrikhande SN, Joshi SG, Zodpey SP, Saoji AM. *Chlamydia trachomatis* in pelvic inflammatory disease. Indian J Pathol Microbiol. 1995;38:181-4.

11. Neuer A, Spandorfer SD, Giraldo P, Dieterle S, Rosenwaks Z, Witkin SS. The role of heat shock proteins in reproduction. Hum Reprod Update. 2000;6:149-59.
12. Witkin SS. Immunity to heat shock proteins and pregnancy outcome. Infect Dis Obstet Gynecol. 1999;7:35–38.
13. Witkin SS. Immunological aspects of genital clamydia infections. Best Pract Res Clin Obstet Gynaecol. 2002;16:865-74.
14. Witkin SS, Sultan KM, Neal GS, Jeremias J, Grifo JA, Rosenwaks Z. Unsuspected *Chlamydia* trachomatis infection and in vivo fertilization outcome. Am J Obstet Gynecol 1994;171:1208-14.

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