Section: Obstetrics and Gynaecology

Original Research Article

A STUDY ON ROLE OF CHLAMYDIA INFECTION IN PRIMARY AND SECONDARY INFERTILITY

Akansha Singh[1], Somya Singh[2], Priya Sharma[3], Neeti Singh[1]

[1]Assistant Professor, Mayo Institute of Medical Sciences, Gadia, Uttar Pradesh, India
[2]Associate Professor, Mayo Institute of Medical Sciences, Gadia, Uttar Pradesh, India
[3]Professor, Mayo Institute of Medical Sciences, Gadia, Uttar Pradesh, India

Received : 11/11/2023
Received in revised form : 22/12/2023
Accepted : 04/01/2024

Keywords:
Infertility, C. trachomatis, Hysterosalpingography, STD.

Corresponding Author:
Dr. Somya Singh,
Email: somyadr5@gmail.com

DOI: 10.47009/jamp.2024.6.1.40

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (1); 206-210

Abstract

Background: Primary infertility is defined as the inability of a couple to conceive after a year or two of unprotected and appropriately timed sexual intercourse. Chlamydial trachomatis infections are one of the most prevalent sexually transmitted pathogen throughout the world. The objective is to study the prevalence of Chlamydia Trachomatis infection in women with infertility and to study the pathology associated with Chlamydia Trachomatis infection in women with infertility. **Materials and Methods:** The proposed study was conducted in the Department of Obstetrics and Gynaecology in association with Radiology and Microbiology Department at Dr Rajendra Prasad Government Medical College Kangra at Tanda, HP over a period of one year from Jan 2018 to Dec 2018. The sample size consisted of 100 respondents having 50 patients in each group. SPSS was used for analysis. **Result:** Mean age of the patients was 27.18±4.11 years. Mean age of control was 26.22±2.22 years. In 98% of the cases, the time was between 21-30 minutes while in only 2% case, the time was between 10 and 20 minutes. 84% of the patients and 12% of the controls had Chlamydia positivity for IgG and 46% of the patients had Chlamydia positivity while 2% of the controls had Chlamydia positivity for IgM antibodies. Hysterosalpingography findings were abnormal in 54% patients. Out of the 42 patients who were chlamydia IgG positive, 76.2% had abnormal HSG findings. **Conclusion:** It may be concluded that there is significant association between C. trachomatis infection and infertility. Screening of infertile women for C. trachomatis may be recommended for early therapeutic options.

INTRODUCTION

A World Health Organization (WHO) study documented that 18%–20% of infertile women are infected with C. trachomatis worldwide and in India, 28%–30% of infertile women were reported to be C. trachomatis infected, which is quite high in terms of world scenario.[1-3]

Chlamydia trachomatis is one of the leading causes of tubal infertility in women and is likely to be responsible for up to 45% of tubal infertility cases.[4] The infection progresses to pelvic inflammatory disease in approximately 9.5% of cases.[5] While it is less clear how many infections progress to tubal infertility or ectopic pregnancy, the infection is clearly responsible for substantial reproductive morbidity worldwide.[6]

The reproductive morbidity in women results from fallopian tube tissue damage, such as tubal adhesions, tubal occlusion and/or salpingitis. These disorders may be the results of destruction of cilia layer of the fallopian tube and closure of fallopian tube.[7] Therefore, detection and control of C. trachomatisinfection prevalence is necessary to prevent its related sequels. This tissue damage is generally detectable by investigations such as hysterosalpingography or laparoscopy.[8]

Chlamydial pelvic inflammatory disease (PID) is the most important preventable cause of infertility and adverse pregnancy outcomes.

In many developing countries, little is known about the prevalence of genital C. trachomatis infections and its complications, such as infertility, thus preventing any policy from being formulated regarding screening of patients at risk for infertility. Many studies have been conducted to determine the prevalence or frequency of urogenital C. trachomatis in fertile and infertile individuals. Screening tests are useful in establishing the risk for tubal pathology in an individual patient. For preventive as well as therapeutic measures, it is highly desirable to have sensitive screening markers for chlamydial infection. Therefore, it is important to understand the diagnostic value of serological testing in different clinical conditions. There is paucity of studies on infertility related to Chlamydia infection in India, hence we have planned a study to study the role of C.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

trachomatis infection in women presenting with infertility in our hospital.

MATERIALS AND METHODS

The proposed study was conducted in the Department of Obstetrics and Gynaecology in association with Radiology and Microbiology Department at Dr Rajendra Prasad Government Medical College Kangra at Tanda, HP over a period of one year from Jan 2018 to Dec 2018. The sample size consisted of 100 respondents having 50 patients in each group.

Inclusion Criteria

All women between 18 to 37years of age with complaints of primary and secondary infertility with Regular menstrual cycles.
Normal TSH and Prolactin levels.
Normospermic male partner as per WHO guidelines
Normal results on ovulatory tests
Normal Mantoux test
Normal chest X-ray examination results
No specific findings on endometrial biopsy

Exclusion Criteria

Women witha positive history of tuberculosis
Women with endocrinological disorders in the form of untreated thyroid dysfunction, hyperproclactinemia and Cushing syndrome.
Patient not willing to participate in the study.

Methodology

After obtaining the approval of the institutional "Protocol Review Committee" and "Ethics Committee" of the institution. All the couples attending OPD with complaints of infertility were screened, investigated and exclusion criteria applied. Those who fulfilled for the criteria was enrolled in the study after taking their informed consent. The demographic and infertility characteristics of sampled women recorded. Clinical details regarding the age, chief complaints with duration, history of chief obstetric complaints, obstetrical history, menstrual history and personal history recorded. Clinical examination included per abdominal, per speculum and vaginal examination in all women was done. Investigation included semen analysis, hormonal evaluation, baseline ultrasound of pelvis and hysterosalpingogram and if needed hysteroscopy and laparoscopy was done. After getting informed consent, subjects were randomly assigned to one of two groups based on lot method.

Group 1: In this group, 50 women of similar age composition as inclusion criteria coming with complaints of primary or secondary infertility were considered as case. In such women all the relevant investigations were done. Hysterosalpingography (HSG) was done in all cases subsequent to enrollment. If the patient had symptoms, that is, had evidence of PID or mucopurulent discharge or had tender adnexa, she was given antibiotic treatment, and HSG was performed only after the symptoms improved. Tubal infertility was present if bilateral tubal occlusion with or without hydrosalpinx was seen on HSG.

Group 2: In this group, 50 healthy women of similar age composition and free of all signs and symptoms attending the OPD with no history of infertility were considered as control. In this group only Chlamydia antibody testing was done.

Determination of IgG and IgM antibodies to C. trachomatis

Serum samples were collected in clean dry vials and stored at -20°C. The IgGand IgMantibodies to C. trachomatiswere detected by VIR-ELISA anti-chlamydiaIgG Kit and IgM kit. According to the manufacturer's documentation, titers of more than 1:320 was considered significant.

Statistical Analysis

Data were presented as frequency, percentages, mean, and SD. Diagnostic values was calculated using SPSS v21. P value <0.05 was considered significant.

RESULTS

[Table 1] shows general characteristics of the patients. Mean age of the patients was 27.18±4.11 years. Mean age of control was 26.22±2.22 years. Mean age of the patients' husband was 30.0±3.78 years. Mean age of the controls' husband was 28.84±2.36 years. 72% of the patients were from rural areas while 76% of the controls belonged to rural areas. 74% of the patients never conceived while 10% each had pre-term and term pregnancy. 6% of the patients had abortion. 60% of the patients were from lower socio-economic class while 38% of the patients were from middle socio-economic class. Only 2% patients belonged to higher socio-economic class.

As per [Table 2] our study observed that in all cases, serum LH, FSH, estradiol, TSH, and prolactin levels were normal.

As per [Table 3] liquefaction time was defined as the time taken for the semen to liquefy. In 98% of the cases, the time was between 21-30 minutes while in only 2% case, the time was between 10 and 20 minutes. In 56% cases, sperm count was more than 20 million/ml while in 34% of the cases, the sperm count was between 1.5 to 5 million. In 98% cases, sperm motility was more than 32% while in 2% of the cases, the sperm motility was up to 32%.In all cases, sperm morphology was more than 4% of normal. In all cases, semen WBC count was <1 million/ml.

As per [Table 4] our study observed that 84% of the patients and 12% of the controls had Chlamydia positivity for IgG and 46% of the patients had Chlamydia positivity while 2% of the controls had Chlamydia positivity for IgM antibodies. We also observed that incidence of positivity of both IgG and IgM was significantly higher in the patients in comparison to controls.

As per [Table 5] our study observed that hysterosalpingography findings were abnormal in

ISSN (O): 2687-5365; ISSN (P): 2753-6556

54% patients. Out of the 42 patients who were chlamydia IgG positive, 76.2% had abnormal HSG findings. We also observed that the patients who were Chlamydia positive for IgG had had significant higher number of patients who were higher on HGG abnormality (P=0.029).

As per [Table 6] our study observed that sensitivity of chlamydial IgG antibodies as a diagnostic marker for infertility was 84% and specificity was 88% for IgG antibodies while for IgM antibodies, sensitivity and specificity was 46% and 98% respectively.

Table 1: General characteristics

	Patients (n=50)	Controls (n=50)
Subjects' age (Years)	27.18±4.11	26.22±2.22
Subjects' husband age (Years)	30.0±3.78	28.84±2.36
Residence; n, [Rural:Urban]	36:14	38:12

Data were expressed as mean±SD otherwise indicated

Table 2: Biochemical analysis

	n	%
Normal Serum LH	50	100
Normal Serum TSH	50	100
Normal Serum Estradiol	50	100
Normal Serum FSH	50	100
Normal Serum Prolactin	50	100

Table 3: Semen analysis

		n	%
Liquefaction Time	10-20 Minutes	1	2
	21-30 Minutes	49	98
Sperm count	1.5-5.0 million/ml	17	34.0
	5.5-20 million/ml	5	10.0
	>20 million/ml	28	56.0
Sperm Motility	<32%	1	2.0
	>32%	49	98.0
Sperm Morphology	<4%	0	0
	>4%	50	100.0
Semen WBC	<1 million/ml	50	100.0
	>1 million/ml	0	0

Table 4: Chlamydia infection (IgG and IgM)

	IgG			IgM		
	Patients (n=50)	Controls (n=50)	P Value	Patients (n=50)	Controls (n=50)	P Value
Positive	42 (84%)	6 (12%)	<0.0001	23 (46%)	1 (2%)	0.0001
Negative	8 (16%)	44 (88%)		27 (54%)	49 (98%)	

Data were expressed as frequency and percentages.

Table 5: Hysterosalpingography findings

	Positive	Negative	P Value
Abnormal	40	5	0.029
Normal	2	3	

Data were expressed as frequency and percentages

Table 6: Diagnostic value

	IgG	IgM
Sensitivity	84.0% (70.89-92.83)	46.0% (31.81-60.68)
Specificity	88.0% (75.69-95.47)	98.0% (89.35-99.95)
Positive Predictive Value	87.5% (76.60-93.74)	95.83% (76.35-99.39)
Negative Predictive Value	84.62% (74.30-91.28)	64.47% (58.35-70.16)
Accuracy	86% (77.63-92.13)	72% (62.13-80.52)

Data were expressed as value (95% Confidence Interval)

DISCUSSION

In our study, C. trachomatis infection was found in 84 per cent of the infertile females which is quite high. WHO taskforce in 1995 have reported the chlamydial infection in infertile women to be 18-20 per cent in India. Malik et al in 2006 reported the Chlamydia infection in 28% infertile women.[3] In 2009, the same group reported that in women with secondary infertility past C. trachomatis infection was found in 55% and current infection was observed in 45.4% of cases.[9]

The incidence of C. trachomatis infection is more common in women with secondary infertility. This increased susceptibility could be due to their longer period of active sexual life thus enhancing their

ISSN (O): 2687-5365; ISSN (P): 2753-6556

exposure to chlamydial infection. Secondary infertility associated with higher rates of chlamydial infection have been reported earlier.[10,11]

Prevalence of C. trachomatis also varies with the population under study and the sensitivity of the laboratory method used. Our study suggests that all infertile women should be screened for C. trachomatis. The index of suspicion should be higher in asymptomatic women in whom our study revealed a larger chlamydial positivity.

In the absence of requisite infrastructure and skills for culture and for direct fluorescent assay, ELISA can play a significant role in screening for C. trachomatis in infertile women. Our study observed that sensitivity and specificity of chlamydial IgG antibodies as a diagnostic marker for infertility was 82.16% and 85.19% respectively. A study from Saudi Arabia reported that the rate of chlamydia infection detected by ELISA was 9.84%.[12] Dabekausen et al reported that the positive likelihood ratio for C. trachomatis antibody testing was 9.1, indicating a patient with tubal factor infertility to be 9.1 times more likely to have abnormal serology results than a patient without tubal factor infertility. This was superior to HSG, which had a positive likelihood ratio of 2.6.[13] In Contrast, Veenerman and Linden suggested that C. trachomatis antibody testing and HSG have a poor predictive value.[14] However, C. trachomatis antibody testing causes minimal inconvenience to the patient, in contrast to HSG, and therefore should be maintained in infertility examinations. This finding also supports that in a resource-poor country such as India ELISA for chlamydial IgG antibodies can easilybe substituted for HSG.

In our study, 34% patients and 12% controls were positive for IgG and 46% patients and 2% controls were positive for IgM. A recent Iranian study showed that 6% infertile and 1.6% fertile women were positive for IgM. They did not find any seropositive immunoglobulin G in both groups.[15] High titers of IgG in our patients may be due to the presence of previous exposure with C. trachomatis. According to results of Malik et al, it seems that IgG detection and past chlamydial infections have a strong role in women with secondary infertility rather than primary infertility.[9] In their study, IgG antibodies were present in 55% of women with secondary infertility compare to 5.5% in health women. Rashidi et al in their study reported that IgG was positive in 9.0% of the infertile and 5.0% in the fertile group while IgM assays identified that 0.9% of the infertile and 1.8% of the fertile women were positive for the micro-organism.[16]

In our study, mean age of the infertile women were 27.18 years. Direct comparison on chlamydia prevalence cannot be made precisely with western studies that include younger women (aged 15–19 years).[17] Also, due to local cultural and social constraints, our study excluded women aged less than 18 years. Moreover, unmarried women were also excluded from the present study, as the management of any positive cases would create both legal and social problems. Furthermore, routine inquiries about number of sexual partners are not realistic in our community.

Women's preconception and pregnancy diet and nutritional status are associated with maternal and neonatal outcomes. A higher "fertility diet" score was characterized by a lower intake of trans fat with a greater intake of monounsaturated fat; a lower intake of animal protein with greater vegetable protein intake; a higher intake of high-fiber, low-glycemic carbohydrates; greater preference for high-fat dairy products; higher plant-based iron intake; and higher frequency of multivitamin use.[18] In our study, 20% of the women were consuming vegetarian diet.

CONCLUSION

It may be concluded that there is significant association between C. trachomatis infection and infertility. Absence of signs and symptoms associated with this infection highlights the need for its investigation in women with a history of infertility for their better management. Even though, IgM antibodies to Chlamydia infections are higher in cases; it cannot be used a marker as sometimes, it takes a month to increase in IgM antibodies. Chlamydial IgG antibodies can be taken as a diagnostic marker as it has high sensitivity. IgG antibody detection is an effective and noninvasive tool for the detection of Chlamydia and a more viable option than any other techniques in India due to better sensitivity and specificity. C. trachomatis should be preferred as a routine baseline investigation for infertility. Screening of infertile women for C. trachomatis may be recommended for early therapeutic options. However, studies with a large sample size may be needed for validation for our findings.

REFERENCES

1. Joyee AG, Thyagarajan SP, Sowmya B, Venkatesan C, Ganapathy M. Need for specific and routine strategy for the diagnosis of genital chlamydial infection among patient with sexually transmitted disease in India. India J Med Res. 2003;118:152-7
2. WHO Task Force Tubal infertility: serologic relationship to past chlamydial and gonococcal infection. Sex Transm Dis. 1995;29:71–7.
3. Malik A, Jain S, Hakim S, Shukla I, Rizvi M: Chlamydia trachomatis infection & female infertility. Indian J Med Res. 2006;123:770–7.
4. Singh V, Salhan S, Das BC, Mittal A: Predominance of Chlamydia trachomatis serovars associated with urogenital infections in females in New Delhi, India. J Clin Microb 2003; 41:2700–702.
5. Singh V, Rastogi S, Garg S, Kapur S, Kumar A, Salhan S, et al. Polymerase chain reaction for detection of endocervical C. trachomatis infection in women attending a gynecology outpatient department in India. Acta Cytol. 2002;46:540–44.
6. Mittal A, Kapur S, Gupta S: Chlamydial cervicitis: role of culture, enzyme immunoassay, and Giemsa cytology in diagnosis. Acta Pathol Microbiol Immunol Scand. 1993;101:37–40.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

7. Mittal A, Kapur S, Gupta S. Screening for genital chlamydial infection in symptomatic woman, Indian. J Med Res. 1993;98:119–23.
8. Swart P, Mol BW, Van der Veen F, Van Beurden M, Redekop W K, Bossuyt PM. The accuracy of hysterosalpingography in the diagnosis of tubal pathology: a meta-analysis. Fertil Steril. 1995;64:486–91.
9. Malik A, Jain S, Rizvi M, Shukla I, Hakim S. Chlamydia trachomatis infection in women with secondary infertility. Fertility and Sterility. 2009;91:91-5.
10. Cengiz L, Kiyan M, Cengiz AT, Aksoy AM, Kara F, Seçkin L, Kiliç H. [Chlamydia trachomatis antigens in endocervical samples and serum IgG antibodies in sterile-infertile women using ELISA]. Mikrobiyol Bul. 1992;26:203-13
11. Shi XB, Liu FY, Zhang HW. Study of Chlamydia trachomatis infection on cervical secretion of women with early pregnancy and secondary infertility. Hunan Yi Ke Da Xue Xue Bao) 2001; 26 : 169-70
12. Kamel RM. Screening for Chlamydia trachomatis infection among infertile women in Saudi Arabia. Int J Womens Health. 2013;5:277–84.
13. Dabekausen YA, Evers JL, Land JA, Stals FS. Chlamydia trachomatis antibody testing is more accurate than hysterosalpingography in predicting tubal factor infertility. Fertil Steril. 1994;61:833–7.
14. Veenemans LM, van der Linden PJ. The value of Chlamydia trachomatis antibodytesting in predicting tubal factor infertility. Hum Reprod. 2002;17:695-8
15. Joolayi F, Navidifar T, Mohammad Jaafari R, Amin M. Comparison of Chlamydia trachomatis infection among infertile and fertile women in Ahvaz, Iran: A case-control study. Int J Reprod Biomed (Yazd). 2017;15(11):713–718.
16. Rashidi BH, Chamani-Tabriz L, Haghollahi F, Jeddi-Tehrani M, Naghizadeh MM, Shariat M, et al. Effects of Chlamydia trachomatis Infection on Fertility; A Case-Control Study. J Reprod Infertil. 2013;14:67-72.
17. Centers for Disease Control and Prevention (CDCP) Sexually transmitted disease surveillance 2004 supplement, Chlamydia Prevalence Monitoring Project. Atlanta, US: Department of Health and Human Services; 2005. http://www.cdc.gov/std/chlamydia2004.
18. Chavarro JE, Rich-Edwards JW, Rosner BA, Willett WC. Diet and lifestyle in the prevention of ovulatory disorder infertility.Obstet Gynecol. 2007;110:1050-8.

ISSN (O): 2687-5365; ISSN (P): 2753-6556