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Original Research Article

Chlamydia Infection as a Risk Factor in Ectopic Pregnancy: A Case Control Study

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Abstract

Background: Due to irreparable tissue damage, Chlamydia trachomatis has been associated to 30-50 percent of all ectopic pregnancies. As a result, it's important to look at the risk factors for Chlamydia infection and ectopic pregnancies.

Aim: The goal is to see if Chlamydia infection is a risk factor for ectopic pregnancy in comparison to early intrauterine pregnancy, as well as look at other ectopic pregnancy risk factors.

Methods and Materials: This was a case-control study that compared patients with ectopic pregnancy to patients with early intrauterine pregnancy as controls in a tertiary care center in Hyderabad. This study was conducted between June to November 2018.

Results: A total of 100 patients, 50 cases and 50 controls were studied. Females over the age of 25 were more likely to have an ectopic pregnancy, with an odds ratio of 2.18, indicating a two-fold increased risk in women over the age of 25. 70% of cases were from upper class socioeconomic status. Thus, it can be confirmed that patients from upper class socioeconomic status were more to develop ectopic pregnancy when compared to subjects from lower socioeconomic status. Total of 40 patients have shown a history of pelvic inflammatory disease. 28 (56%) of them had an ectopic pregnancy, while 12 (24%) of those in the control group had history of pelvic inflammatory disease . A history of pelvic inflammatory illness was shown to have an odd of 3.87 (p value = 0.005). 6 patients had used oral contraceptive pills out of 100 patients in the study group. P value was 0.057. Patients positive for serum chlamydia IgG antibodies were 33 patients in study group and 28 patients in control groups. P value was 0.199.

Conclusion: With the rising prevalence of Chlamydia infection and the possibility of developing irreversible consequences such as ectopic pregnancy, it's more important than ever to detect, treat, and prevent vaginal infection and pelvic inflammatory disease.

Keywords: Ectopic Pregnancy, Chlamydial infection.

Introduction

Ectopic pregnancy is a life-threatening condition that is one of the leading causes of maternal mortality worldwide and in our country, with a prevalence of 1-2 percent in affluent countries and much higher in developing countries. The bacterial sexually transmitted infection Chlamydia trachomatis is the most common in the world.[1] Women, disproportionately, bear the brunt of the problems. Infertility, pelvic inflammatory disease (PID), and ectopic pregnancy are among the consequences. Because of improved awareness, the disease is on the decline in developed countries. Unfortunately, 1.2 billion people still live in locations where endemic diseases are present. According to recent studies from India, Chlamydia trachomatis infection is prevalent in 23 percent of gynaecology outpatient departments and 19.9 percent of STD patients.[2,3] In India, it has been found in 30-60% of instances of salphingitis and pelvic inflammatory disease patients. PID causes 20% of women to become infertile, 18% to experience persistent pelvic pain, and 9% to have a tubal pregnancy. The biggest avoidable cause of pelvic inflammatory disease in young women is Chlamydia trachomatis infection. It's also been connected to 30 to 50% of all ectopic pregnancies.[4] Damage to the fallopian tubes is the direct cause of ectopic pregnancy. Ectopic pregnancy is one of the most dangerous complications of acute salpingitis. The most common cause of acute salpingitis appears to be Chlamydia trachomatis. Chlamydia trachomatis is a potent immunogen that triggers humoral and cell-mediated immune responses. The interplay and balance of cytokines released by activated lymphocytes affects the outcome of Chlamydia infection, in addition to immunogenic antigens. A primary or chronic re-infection of Chlamydia trachomatis can occur. The mucosal cells are infected in series during primary infection. Damaged and infected epithelial cells emit a slew of proinflammatory chemokines and cytokines, which cause vasodilation, increased endothelial permeability, activation and influx of neutrophils, monocytes, and T-lymphocytes, and enhanced adhesion molecule expression. Chronic infection is linked to Chlamydia persistence in host cells, which is more harmful. It causes tissue destruction, fibrosis, and cicatrization in the organs affected. PID can result in irreversible complications such as mechanical infertility, ectopic pregnancy, chronic pelvic discomfort, and chronic urethritis. As a result, it's important to look at the risk factors for Chlamydia infection and ectopic pregnancies. In comparison to early intrauterine pregnancy admitted to a tertiary care centre in Hyderabad, the study's goal was to see if chlamydia infection is a risk factor for ectopic pregnancy. Also look into additional ectopic pregnancy risk factors.

Materials and Methods:

This was a case-control study that compared patients with ectopic pregnancy to patients with early intrauterine pregnancy as controls in a tertiary care center in Hyderabad. This study was conducted between June to November 2018. Cases were chosen after trans abdominal and transvaginal sonography confirmed ectopic pregnancy, a positive urine pregnancy test, and high beta human chorionic gonadotrophin hormone levels of over 1500mIU/ml. Controls were those who had a positive urine pregnancy test and trans abdominal and transvaginal sonography that showed early intrauterine gestation, up to 8 weeks gestation. Those having a history of ectopic pregnancy or fallopian tube surgery, as well as those who refused to participate in the trial, were excluded from the control group. A total of 100 patients were taken, including 50 in each group. Following an interview to gather baseline data, each patient had a venous blood sample collected to identify antibodies to Chlamydia trachomatis immunoglobulin G using an Enzyme

Linked Immunosorbent Assay premade kit. Age, socioeconomic status, menstrual cycle regularity, parity, history of more than one sexual partner, history of infertility, history suggestive of pelvic inflammatory disease (chronic pelvic pain, dyspareunia, discharge per vaginum, dysuria), previous history of ectopic pregnancy, use of IUCD, history of tubal surgery/any other abdominal surgery, history of taking combined pills or progesterone only pills, presence of Chlamydia IgG antibodies.

Results:

A total of 100 patients, 50 cases and 50 controls were studied.

Table 1: Distribution based on age.

Age (Years)	Study group (N,%)	Control Group (N,%)	Total (N,%)
>25	29 (58%)	22 (44%)	51 (51%)
≤25	21 (42%)	28 (56%)	49 (49%)

Table 1 shows that females over the age of 25 were more likely to have an ectopic pregnancy, with an odds ratio of 2.18, indicating a two-fold increased risk in women over the age of 25.

Table 2: Distribution based on socioeconomic status.

Socioeconomic	Study group (N,%)	Control Group (N,%)	Total (N,%)
Upper	35 (70%)	27 (54%)	62 (62%)
Lower	15 (30%)	23 (46%)	38 (38%)

Table 2 shows that 70% of cases were from upper class socioeconomic status. Thus, it can be confirmed that patients from upper class socioeconomic status were more to develop ectopic pregnancy when compared to subjects from lower socioeconomic status.

Table 3: Distribution based on number of sexual partners.

Sexual Partners	Study group (N,%)	Control Group (N,%)	Total (N,%)
One	45 (90%)	46 (92%)	91 (91%)
Two	5 (10%)	4 (8%)	9 (9%)

Table 3 shows that the highest number of sexual partners were 2. In the study group, 5 (10%) had two sexual partners and in the control group, 4 (8%) had two sexual partners. P value was observed to be 0.425 which was not significant when compared to control group.

Table 4: Distribution based on pelvic inflammatory disease history.

Pelvic Inflammatory Disease	Study group (N,%)	Control Group (N,%)	Total (N,%)
Yes	28 (56%)	12 (24%)	40 (40%)
No	22 (44%)	38 (76%)	60 (60%)

Table 4 shows that a total of 40 patients have shown a history of pelvic inflammatory disease. 28 (56%) of them had an ectopic pregnancy, while 12 (24%) of those in the control group had history of pelvic inflammatory disease . A history of pelvic inflammatory illness was shown to have an odd of 3.87 (p value = 0.005).

Table 5: Distribution based on IUCD duration.

Years of IUCD	Study group (N,%)	Control Group (N,%)	Total (N,%)
<5 years	3 (60%)	4 (100%)	7 (77.8%)
5-10 years	2 (40%)	0	2 (22.2%)

Table 5 shows that 3 patients had IUCD duration of less than 5 years in study group. 4 patients had IUCD duration of less than 5 years. 2 patients had IUCD duration of 5-10 years in study group.

Table 6: Distribution based on history of using oral contraceptive pills.

Oral Contraceptive Pills	Study group (N,%)	Control Group (N,%)	Total (N,%)
Yes	6 (12%)	0	6 (6%)
No	44 (88%)	50	94 (94%)

Table 6 shows that 6 patients had used oral contraceptive pills out of 100 patients in the study group. P value was 0.057.

Table 7: Distribution based on serum chlamydia IgG antibodies.

chlamydia IgG	Study group (N,%)	Control Group (N,%)	Total (N,%)
Positive	33 (66%)	28 (56%)	61 (61%)
Negative	17 (34%)	22 (44%)	39 (39%)

Table 7 shows that patients positive for serum chlamydia IgG antibodies were 33 patients in study group and 28 patients in control groups. P value was 0.199.

Discussion:

The current study was a case-control study that aimed to see if Chlamydia trachomatis infection is linked to ectopic pregnancy. Women above the age of 25 were found to have a 2.18 chance of having an ectopic pregnancy, according to this study. As a result, when compared to women between the ages of 15 and 25, older women of reproductive age have a higher chance of ectopic pregnancy. Similar results were observed in Angela George et al study[5]. Mridula AB et al.[6] conducted a study in Brunei and found that 123 of the total 123 ectopics were between the ages of 26 and 35. However, contrary to the findings of this study, there was no significant difference in age between the two groups (cases and controls). These findings were also in line with those of Ashihi et al[7], who found that women between the ages of 26 and 38 were more likely to have an ectopic pregnancy, whereas women between the ages of 20 and 30 were more likely. When the individuals' socioeconomic statuses were analysed, it was discovered that the Upper Socioeconomic Class more likely than the Lower Socioeconomic Class to experience ectopic pregnancy. This was in contrast to a study conducted in Lagos, Nigeria, by Adewunmi AA et al[8], which found that women from lower socioeconomic classes are more likely to suffer ectopic pregnancy (p= 0.001, level of education p= 0.001). When the parity of the two groups was compared, it was discovered that nulliparas outnumbered multiparas in ectopic pregnancies. However, there was no discernible difference between the two groups (p value-0.979). Nulliparas are more likely to develop ectopic pregnancy, according to a study conducted in Shanghai by Cheng Li et al[9], however there was no significant difference between the ectopic and intrauterine pregnancy groups. In contrast to the findings of this study, Adewunmi AA et al[8] found that

multiparas were more susceptible to ectopic pregnancy, with a significant difference between ectopic and intrauterine pregnancy (p-value=0.005). A study conducted by Shraddha Shetty et al[10] in Mangalore, Karnataka, indicated that multiparas were more likely to experience ectopic pregnancy. When it came to the number of sexual partners, neither group had more than two. 5 (10%) of the study participants had two sexual partners, while 4 (8%) of the control participants had two sexual partners. When comparing the two groups, the P value was found to be 0.425, indicating that there was no significant difference. Multiple sexual partners, on the other hand, are known to increase the risk of having ectopic pregnancy by predisposing to sexually transmitted infections. Adewunmi AA et al[8] study found a substantial risk associated with several sexual partners (p-value=0.0009). Menarche occurred at an average age of 14 years. In this investigation, no substantial risk relationship between menarche and menstrual cycle, as well as ectopic pregnancy, was discovered. This finding is consistent with prior research that found no link between the two variables and the chance of ectopic pregnancy. After that, participants with a history of infertility were compared to those without, and it was discovered that those with a history of infertility had a 4.28 higher chance of developing an ectopic pregnancy than those without. This finding is consistent with Cheng Li et al[9] findings, which demonstrated a substantial link between past infertility history and ectopic pregnancy in both tubal (OR-8.81, 5.09) and non-tubal infertility (OR-8.81, 5.09) cases (OR-5.51, 2.83). Tubal factor infertility is one of the most common causes of ectopic pregnancy. Shraddha Shetty et al[10] evoked a similar finding of a substantial risk relationship between infertility and ectopic pregnancy. Pelvic inflammatory illness is one of the key risk factors for ectopic pregnancy. Patients having a history of pelvic inflammatory disease were found to have a higher risk of ectopic pregnancy. There was a history of pelvic inflammatory illness in 40 of the patients. A total of 28 (56%) of them experienced an ectopic pregnancy, while 12 (24%) of the control group had a history of pelvic inflammatory illness. The odds of having a history of pelvic inflammatory sickness were found to be 3.87 (p value = 0.005). As a result, It can be concurred that the logic that past pelvic inflammatory disease can damage the fallopian tubes, increasing the chance of an ectopic pregnancy. Dyuria and chronic pelvic discomfort were reported to be the most common symptoms in both groups, with P values of 0.055 and 0.044, respectively, for prior history of pelvic inflammatory disease. Discharge PV (p=0.119) and dyspareunia (p=0.115) were less prevalent. These findings are in line with other studies such as Ashishi AM et al7, Shetty SK et al[10], Cheng Li et al9, Rekart ML et al[11] studies that show that women with a history of pelvic inflammatory illness are more likely to have an ectopic pregnancy. Porwal Sanjay et al[12] colleagues found that nearly half of the cases had a positive history of pelvic inflammatory illness. A p value of 0.003 was found in Adewunmi AA et al[8] study, indicating a substantial risk relationship between ectopic pregnancy and pelvic inflammatory illness. In present study, 6 patients had used oral contraceptive pills out of 100 patients in the study group. P value was 0.057. In a study of 61,448 IUD users by Heinemann K et al[13], 118 contraceptive failures were identified, 21 of which were ectopic. Cheng Li et al[9] discovered a link between IUCD use and ectopic pregnancy, with the risk increasing as the duration of the IUCD increases. Prior abdominal surgery had no significant connection with ectopic pregnancy in this study. This was in line with the findings of Adewunmi AA et al[8] investigation, which found no significant link. Past abdominal surgery, particularly

prior adnexal surgery, surgery for ectopic pregnancy, and surgery for tubal infertility, increases the risk of developing ectopic pregnancy, according to Cheng Li et al et al[9] research. When looking at other ectopic pregnancy risk factors, history of oral contraceptive use was found in six participants, all of whom were from the cases group and none from the control group. As a result, no odds ratio was calculated. The risk of ectopic pregnancy associated with prior use of oral contraceptives was found to be very significant in this study, with a p=0.057. These findings were in line with those of other investigations. The physiology of tubal ciliary and myoelectrical activity had been described by Pulkkinen and Talo et al study[14]. Because patients with congenital inactivity of all cilia (Kartagener's condition) are able to have intrauterine pregnancies, the static force of the cilia causes fluid flow into the uterus, which the spermatozoa normally overcome, demonstrating that cilia are not required for normal implantation. Tubal propulsion is dependent on myoelectrical activity. Progesterone reduces tubal myoelectrical activity while estrogens stimulate it in Hodgson BJ et al[15] study. The mechanisms of levonorgestrel's contraceptive activity are thought to be complex. Among these mechanisms, changes in tubal motility may contribute to a delayed entry of the egg in the endometrial cavity, resulting in ectopic pregnancy in Morre SA et al[16] study. The mechanisms of levonorgestrel's contraceptive activity are thought to be complex. Among these mechanisms, changes in tubal motility may contribute to a delayed entry of the egg in the endometrial cavity, resulting in ectopic pregnancy in Liukko P et al[17] study. Furthermore, pharmaceutical progesterone levels may relax tubal myoelectric activity to the point where transfer via the isthmus is not possible. Similar findings were reported in a multi-center case control research undertaken by Cheng Li et al[9] in Shanghai, China, which indicated a three-fold increase in the incidence of ectopic pregnancy with the use of oral contraceptive tablets (AOR=3.02, 95 percent CI, 1.16-7.86). Patients positive for serum chlamydia IgG antibodies were 33 patients in study group and 28 patients in control groups. P value was 0.199. According to Adewunmi AA et al[8] study in Lagos, Nigeria, there were 91 occurrences of ectopic pregnancy out of 2468 deliveries, giving an incidence of 3.68 percent, or one in every 27 deliveries. The results showed that seropositivity for Chlamydia IgG (62.4%) was considerably greater in the patients than in the controls (p <0.0001). In addition, Cheng Li et al[9] colleagues in Shanghai, China, discovered a three-fold increase among the probability of ectopic pregnancy in women who had previously been infected with Chlamydia trachomatis. Rekart et al.[11] conducted a descriptive analysis of trends in Chlamydia cases, PID, and ectopic pregnancy in British Columbia, Canada, from 1992 to 2009. Between 1992 and 2009, there was a significant increase in Chlamydia cases. From 1992 to 2003, the number of inpatient, outpatient, and total diagnoses of pelvic inflammatory illness and ectopic pregnancy decreased. PID rates continued to decline after 2003, however there was a recent increase in Chlamydia infection from 1996 to 2009 as male Chlamydial urethritis rates increased, producing re-infection and increased incidence, which may contribute to the significant increase in ectopic pregnancy rates. In a prospective case-control study conducted in Saudi Arabia by AshishiA M et al[7], 31.8 percent of 135 participants had sexually transmitted illness, with the frequency of ectopic pregnancy being higher. In comparison to other sexually transmitted diseases, Chlamydia trachomatis infection had a greater rate of ectopic pregnancy, with a frequency of 27.4 percent. However, NAAT, multiplex PCR was employed to

test for Chlamydia infection in this study, which is the leading diagnostic and screening test for Chlamydia trachomatis genital infection. Despite its high sensitivity and specificity rates, its usage in our setting has been limited due to the high cost and scarcity of these tests. However, the peptide-based assays, such as ELISA kits, that were used to detect Chlamydia IgG are well-standardized, less expensive, and widely available, with a sensitivity of 73 percent to 83 percent and a specificity of 97 percent to 99 percent. To summarise, 61 percent of the subjects in this study (61 out of 100) tested positive for Chlamydia IgG, indicating that we must be more vigilant in diagnosing, treating, and, most importantly, preventing Chlamydia infection and other causes of pelvic inflammatory disease to avoid long-term consequences such as ectopic pregnancy.

Conclusion:

Infection with Chlamydia trachomatis is one of the most frequent sexually transmitted diseases in the world. This condition has been linked to a number of negative outcomes, the most prevalent of which are pelvic inflammatory disease, infertility, and ectopic pregnancy. In this study, we focused on the risk linked with chlamydia and ectopic pregnancy, which causes irreparable tissue damage in the fallopian tubes at the molecular level. As shown in this study, our population has a higher rate of Chlamydia infection. To avoid these complications, early diagnosis, treatment, particularly using a syndromic approach, and prevention of vaginal infections and pelvic inflammatory disease are critical. In the previous decade, there has been an increase in ectopic pregnancy, which can be attributed to a number of variables, including a history of pelvic inflammatory illness, infertility, and oral contraceptive use. Other risk factors include being over 25 years old, being from a higher socioeconomic class, having used IUCD for more than 5 years, and having had a previous ectopic pregnancy.

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References:

1. World Health Organization. Global incidence and prevalence of selected curable sexually transmitted infections-2008. Geneva: World Health Organization,2012:1-20.
2. Patel AL, Sachdev D, Nagpal P, Chaudhry U, Sonkar SC, Mendiratta SL et al. Prevalence of Chlamydia infection among women visiting a gynaecology outpatient department: evaluation of an in-house PCR assay for detection of Chlamydia trachomatis. Ann Clinic Microbiol Antimicrob. 2010;9(1):24.
3. Malhotra M, Bala M, Muralidhar S, Khunger N, Puri P. Prevalence of sexually transmitted infections in patients attending a tertiary care hospital in North India -a retrospective Study. Indian J Sex Transm Dis. 2008,29(2):82-5.
4. Akande V, Turner C, Horner P, et al. British Fertility Society Impact of Chlamydia trachomatis in the reproductive setting. British Fertility Society Guidelines for practice. Hum Fertil. 2010, 13(3):115-25.
5. Angela George, Shaila S ; Chlamydia infection as a risk factor in ectopic pregnancy: a case control study; International Journal of Reproduction, Contraception, Obstetrics and Gynecology; *2018 Oct;7(10):4254-4260*.
6. Mridula AB, Roselina Y, Mary P, Jaleha MY, Osmali O. Role of chlamydial infection in ectopic pregnancy, Brunei Int Med J. 2013; 9(2):97-101.

7. Ashihi AM, Batwa SA; Prevelance of 7 sexually transmitted organisms by multiplex real time PCR in fallopian tube specimens from Saudi women with and without ectopic pregnancy. BMC Infect Dis. 2015; 15 (1):569.
8. Adewunmi AA, Orekoya OO, Rabiu KSA, OttunTA. The Association between Chlamydia trachomatisand Ectopic Pregnancy in Lagos, Nigeria—A Case Control Study. Open J Obstet Gynecol. 2015,5(2):115-22.
9. Li C, Zhao WH, Zhu Q, Cao SJ, Ping H, Xi X et al. Risk factors for ectopic pregnancy: a multicenter case- control study. BMC Preg Childbirth. 2015,15:187.
10. Shetty SK, Shetty AK. A Clinical Study of Ectopic Pregnancies in a Tertiary Care Hospitalof Mangalore, India. Innovat J Med Health Sci. 2014;4(1):305-9.
11. Rekart ML, Gilbert M, Rafael M, Paul HK, Chang M, Money DM, et al. Chlamydia Public Health Programs and the Epidemiology of Pelvic Inflammatory Disease and Ectopic Pregnancy. JID. 2013:207(1):30-8.
12. Gupta R, Porwal S, Swarnkar M, Sharma N, Maheshwari P. Incidence, trends and risk factors for Ectopic Pregnancies in a tertiary care hospital of Rajasthan. JPBMS 2012;16(07):1-3.
13. Heinemann K, Reed S, Moehner S, Do Minh T. Comparative contraceptive effectiveness of levonorgestrel-releasing and copper intrauterine devices: the European Active Surveillance Study or Intrauterine Devices. Contracep. 2015;91(4):280-3.
14. Pulkkinen MO, Talo A. Tubal physiologic consideration in ectopic pregnancy. Clin Obstet Gynecol. 1987;30(1):164-9.
15. Hodgson BJ, Talo AN. Spike bursts in rabbit oviduct. II. Effects of estrogen and progesterone. Am J Physiol Endocrinol Metabol. 1978;234(4): E439.
16. Morré SA, Munk C, Persson K. Comparison of three commercially available peptide-based IgG and IgA Assays to Micro-immunofluorescence Assay for Detection of Chlamydia trachomatis antibodies. J Clin Microbiol.2002;40(2):584-7.
17. Liukko P, Erkkola R, Laakso L. Ectopic pregnancies during use of low-dose progestogens for oral contraception. Contracep. 1977;16(6): 575-80.