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Association of Chlamydia Trachomatis Infection with Tubal Ectopic Pregnancy

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Abstract

Background: Chlamydia trachomatis is a prevalent sexually transmitted bacterium that significantly impacts reproductive health, especially in women. Its infection rate is notably higher than gonorrhea, with over 1.6 million cases reported in 2021. Often asymptomatic, it can lead to severe complications like tubal damage, infertility, and ectopic pregnancy. ***Aim of the study:*** The study aims to identify the risk factors for ectopic pregnancy and explore the potential association between serological evidence of Chlamydia infection with ectopic pregnancy. ***Methods:*** This prospective case-control study analyzed Chlamydia trachomatis infection associated with tubal ectopic pregnancy at the Department of Obstetrics and Gynecology, Community Based Medical College Hospital Bangladesh (CBMCB) from January 2024 to December 2024. Ninety-six participants were equally divided into case (N=48) and control (N=48) groups. The case group included women diagnosed with tubal ectopic pregnancy, confirmed histopathologically, while the control group consisted of women with uncomplicated second-trimester pregnancies. Serological assays measured Chlamydia IgG antibodies using BIOS Chlamydia T. IgG ELISA kits. Data were analyzed with SPSS software. ***Result:*** The age distribution showed significant differences, with more participants aged 20–24 in the control group (50%) than in the case group (29.17%) and more aged 25–34 in the case group (52.08%) than in the control group (27.63%). Marital status was also significant, with all control group participants married and 12.5% of the case group single. The case group had higher IgG titers and chlamydial antibodies. Significant differences were found in parity, history of ectopic pregnancy, PID, and infertility, with higher rates in the case group. No significant differences were found in occupation, residence, smoking, or other factors. ***Conclusion:*** This study found a significant association between Chlamydia trachomatis infection and increased risk of tubal ectopic pregnancy. Women with ectopic pregnancies had higher Chlamydia IgG titers. The findings highlight the importance of early screening and treatment of chlamydial infections to prevent complications like pelvic inflammatory disease and tubal damage.

Keywords: Chlamydia trachomatis infection, pelvic infection and tubal ectopic pregnancy.

INTRODUCTION

Chlamydia trachomatis (C. trachomatis) is one of the most prevalent sexually transmitted bacterial pathogens and is recognized as a significant contributor to reproductive health complications, particularly among women. Its incidence is approximately 2.5 times higher than that of gonorrhea [1,2]. According to the Centers for Disease Control and Prevention (CDC), more than 1.6 million cases of C. trachomatis infections were reported in 2021, with women being disproportionately affected [3]. The prevalence of C. trachomatis infection in sexually active women ranges between 5% and 40%, depending on the population studied [4]. Additionally, 2% to 37% of female services are found to be infected before childbirth [5]. One of the key challenges in managing genital chlamydial infections is their typically asymptomatic nature. The subclinical presentation of these infections in the upper genital tract often leads to delayed diagnosis and treatment, which may result in the progression of acute or persistent infection. This can cause serious reproductive complications, including

early or late miscarriage, post-abortion pelvic inflammatory disease (PID), stillbirth, postpartum salpingitis, tubal damage leading to tubal factor infertility, and ectopic pregnancy (EP) [6]. Tubal ectopic pregnancy, in which the fertilized egg implants outside the uterine cavity, most commonly in the ampullary region of the fallopian tube, is one of the most severe consequences of acute salpingitis and C. trachomatis infection [7,8]. While the precise mechanisms through which C. trachomatis leads to tubal damage remain incompletely understood, two primary pathways have been proposed. The first, and perhaps most critical, involves chronic infection triggering a low-grade immune response that damages the epithelial cells of the fallopian tubes, distorting the luminal architecture and impairing the normal transport of the embryo to the uterine cavity, thus increasing the risk of ectopic pregnancy [9]. The second mechanism involves direct damage to the tubal epithelium by C. trachomatis itself. As the bacterium completes its replication cycle, elementary bodies are released through cytolysis of the host epithelial cells, further contributing to tubal pathology [10,11]. Following C. trachomatis infection in the upper genital tract, anti-Chlamydia trachomatis IgG antibodies are produced and may persist in the serum for an extended period, even after antibiotic treatment [7,10,12]. The presence of these antibodies has been closely linked to poor reproductive outcomes, including tubal ectopic pregnancy and tubal factor infertility [13,14]. Therefore, undiagnosed and untreated C. trachomatis infections pose significant epidemiological, social, and economic challenges. Current diagnostic approaches for C. trachomatis infections primarily rely on nucleic acid amplification techniques, such as polymerase chain reaction (PCR) and ligase chain reaction (LCR), which have largely replaced traditional cell culture methods and other tests for Chlamydia trachomatis are direct fluorescent antibody and enzyme immunoassay. [15,16]. Recent research has yielded conflicting findings regarding the association between Chlamydia infection and the risk of ectopic pregnancy. Some studies have reported a decreased risk of ectopic pregnancy following Chlamydia trachomatis infection [17], while others have found no significant correlation [18,19]. These inconsistencies highlight the necessity for further investigation into the relationship between Chlamydia trachomatis infection and ectopic pregnancy risk. Our study aims to identify the risk factors for ectopic pregnancy and explore the potential association between serological evidence of Chlamydia infection and ectopic pregnancy.

METHODOLOGY & MATERIALS

This prospective case-control study was conducted at the Department of Obstetrics and Gynecology, Community Based Medical College Hospital Bangladesh (CBMCB) from January 2024 to December 2024. The research aimed to analyze cases of Chlamydia trachomatis infection associated with tubal ectopic pregnancy treated at this tertiary care hospital during the specified timeframe. A total of 96 participants were selected for inclusion, with equal representation in the case and control groups.

Participants were divided into two groups:

- **Case Group (N=48):** Comprised of 48 women diagnosed with tubal ectopic pregnancy, confirmed through histopathological examination.
- **Control Group (N=48):** Comprised of 48 women with uncomplicated second-trimester pregnancies.

Detailed information regarding the study's objectives, goals, and procedures was thoroughly explained to all participants, and written informed consent was obtained before their enrollment. Baseline demographic data were collected for each participant, ensuring strict adherence to confidentiality protocols. The study was conducted in full compliance with ethical standards, receiving approval from the institutional ethics committee.

Inclusion Criteria

- Women diagnosed with tubal ectopic pregnancy confirmed through laparotomy and histological evaluation.
- Uncomplicated second-trimester pregnant women attending antenatal clinics.

Exclusion Criteria

- Blood transfusion received within the last six months.
- Use of antibiotics within the past three months.
- Use of hormonal contraception at the time of conception.
- History of tubal ectopic pregnancy, infertility, miscarriage, tubal surgery, and primigravida in controls.

Serological Assay

The sera were subsequently extracted from the venous blood (5 mL) was collected from each participant's antecubital fossa. The sera were then frozen at -20°C until batch analysis for Chlamydia IgG antibodies was performed by a consultant chemical pathologist. The assay was conducted using BIOS Chlamydia T. IgG ELISA kits (Chlam-T-G-326, Chemux BioScience, INC., USA), an indirect solid-phase enzyme immunoassay (EIA) designed to measure IgG antibodies to Chlamydia trachomatis in human serum quantitatively. Reagent test strips were equilibrated to room temperature, and 10 microliters of serum were pipetted into the assay with control reagents following the manufacturer's protocol. The absorbance value of the calibrator was used to calculate sample results (titer levels) as follows: (Sample absorbance value/Calibrator absorbance value) ×10. A *positive result* was defined as a titer level ≥11, representing a value ≥10% higher than the calibrator (titer = 10), while values <11 were classified as negative.

Statistical Analysis

Data were entered and analyzed using SPSS software (version 26). Categorical variables were reported as frequencies and percentages, whereas continuous variables were presented as means with standard deviations. Chi-square tests were employed to assess associations between categorical variables, and t-tests were used for continuous variables. *Statistical significance* was defined as a p-value < 0.05.

RESULT

Age distribution revealed a significant difference (p=0.021), with a higher percentage of participants aged 20–24 in the control group (50%) compared to the case group (29.17%). Conversely, more participants aged 25–34 were observed in the case group (52.08%) than in the control group (27.63%). Regarding education level, although no significant difference was found (p=0.401), the case group had a higher percentage of participants with secondary (31.25%) and higher secondary (25%) education compared to the control group (18.75% and 14.58%, respectively) (Table 1). Marital status showed a significant association (p=0.00), with all participants in the control group being married, while 12.5% of the case group were single. Occupation and residence type did not show significant differences between the groups, with the majority of both groups being housewives (p=1.000) and residing in rural areas (p=0.863) (Table 1). A larger proportion of the control group (85.42%) had IgG titers in the range of 0-10.9, while this was observed in only 54.17% of the case group. In contrast, a significantly higher percentage of the case group (37.50%) had IgG titers ≥13 compared to just 6.25% in the control group. 45.83% of participants in the case group tested positive for chlamydial antibodies, which was notably higher than the 14.58% found in the control group (p=0.002). The mean IgG titer was also elevated in the case group (12.07±1.82) compared to the control group (9.65±2.65) (Table 2). Table 3 shows that a significant difference (p=0.000) was observed in parity, with 35.42% of the case group having no children and none in the control group. History of ectopic pregnancy (EP) was more common in the case group (14.58%) than in the control group (p=0.021). Additionally, a significantly higher percentage of the case group reported a history of pelvic inflammatory disease (PID) (58.33%, p=0.001) and infertility (58.33%, p=0.001), in comparison of none in the control group. While there were no significant differences in factors such as pelvic surgery, puerperal/postabortal sepsis, dysuria, and prior use of IUCD, the case group had more participants with irregular menstrual cycles (18.20%) than the control group. Moreover, a larger proportion of the case group reported having more than one sexual partner (66.67%) compared to the control group (43.75%, p=0.027). Smoking was absent in both groups, and no significant differences were found in the prevalence of abdominal or pelvic pain with fever (Table 3).

Table 1: Socio-demographic characteristics of study participants based on case and control group

Variables	Case Group (N=48)		Control Group (N=48)		p-value
	N	%	N	%	
Age range (in years)					
16–19	4	8.33	6	15.79	0.021
20–24	14	29.17	24	50.00	
25–34	25	52.08	13	27.63	
≥35	5	10.42	5	6.58	
Mean ±SD					
Level of education					
Illiterate	3	6.25	10	20.83	0.401
Primary	8	16.67	15	31.25	
SSC	15	31.25	9	18.75	
HSC	12	25.00	7	14.58	
Graduate and above	10	20.83	7	14.58	
Marital status					
Married	42	87.5	48	100.00	0.00
Single	6	12.5	0	0.00	
Occupation					
Housewife	33	68.75	41	85.42	1.000
Other occupations	15	31.25	7	14.58	
Residence type					
Rural	30	62.50	24	50.00	0.863
Urban	18	37.50	24	50.00	

Table 2: Chlamydia IgG titer in cases and control group

IgG titer levels	Case Group (N=45)		Control Group (N=45)		p-value
	N	%	N	%	
0-10.9	26	54.17	41	85.42	0.006
11-11.9	3	6.25	4	8.33	
12-12.9	1	2.08	0	0.00	
≥13	18	37.50	3	6.25	
Positive chlamydial antibody					
Yes	22	45.83	7	14.58	0.002
No	26	54.17	41	85.42	
Mean±SD	12.07±1.82		9.65±2.65		

Table 3: Relationship between clinical/risk factors for pelvic infection and chlamydia trachomatis among study participants

Variables	Case Group (N=45)		Control Group (N=45)		p-value
	N	%	N	%	
Gravida					
1	20	41.67	17	35.42	0.182
2-3	18	37.50	24	50.00	
4-5	10	20.83	7	14.58	
Parity					
0	17	35.42	0	0.00	0.000
1-4	29	60.42	40	83.33	
≥5	2	4.17	8	16.67	
History of EP					
Yes	7	14.58	0	0.00	0.021
No	41	85.42	48	100.00	
History of PID					
Yes	28	58.33	0	0.00	0.001
No	20	41.67	48	100.00	
History of pelvic surgery					
Yes	25	52.08	4	8.33	0.964
No	23	47.92	44	91.67	
History of smoking					
Yes	0	0.00	0	0.00	0.717
No	48	100.00	48	100.00	
History of infertility					
Yes	28	58.33	0	100.00	0.001
No	20	41.67	48	100.00	
History of puerperal/postabortal sepsis					
Yes	2	4.17	1	2.08	0.409
No	46	95.83	47	97.92	
Age at coitarche (years)					
<18	24	50	22	45.83	0.578
≥18	24	50	26	54.17	
Menstrual cycle					
Regular	39	81.80	48	100.00	0.112
Irregular	9	18.20	0	0.00	
Sexual partners					
One partner	16	33.33	27	56.25	0.027
More than one	32	66.67	21	43.75	
Dysuria					
Yes	2	4.17	5	10.42	0.569
No	46	95.83	43	89.58	
Prior use of IUCD					
Yes	2	4.17	1	2.08	0.675
No	46	95.83	47	97.92	

Purulent per vaginal discharge					
Yes	6	12.50	3	6.25	0.159
No	42	87.50	45	93.75	
Abdominal pain with fever					
Yes	4	8.33	1	2.08	0.652
No	44	91.67	47	97.92	
Pelvic pain with fever					
Yes	1	2.08	0	0	1
No	47	97.92	48	100	

DISCUSSION

Chlamydia trachomatis is a globally prevalent pathogen and is recognized as one of the most common sexually transmitted infections. In women, it is known to cause a range of infections, including cervicitis, endometritis, acute urethral syndrome, and salpingitis [20]. The association between *Chlamydia trachomatis* infection and tubal ectopic pregnancy (TEP) has been a focal point of reproductive health research due to its significant clinical implications. This present research was a case-control study tailored to determine whether *Chlamydia trachomatis* infection is associated with ectopic pregnancy. The socio-demographic characteristics of this study's participants (Table 1) showed that the majority of cases were between 25 and 34 years of age, with a statistically significant difference in the age distribution between the case and control groups (p=0.021). This finding aligns with a study conducted by Mridula AB *et al.*, in Brunei, which reported that among 123 ectopic pregnancies, the majority of patients fell within the 26-35 age range [21]. Furthermore, our results are consistent with those of Ashihi *et al.*, who identified a susceptibility to ectopic pregnancy in women aged 26 to 38 years [22]. The educational level showed no significant differences between groups (p=0.401), suggesting that education may not be a direct risk factor for EP in this population, which contrasts with findings from other studies where lower educational attainment was associated with higher rates of EP. The findings regarding Chlamydia trachomatis IgG titers (Table 2) indicate a strong correlation between previous chlamydial infections and the onset of ectopic pregnancy (EP). Notably, women in the case group exhibited significantly elevated IgG titers (p=0.006), with 45.83% testing positive for Chlamydia trachomatis antibodies, compared to just 14.58% in the control group (p=0.002). This prevalence aligns with rates observed in the UK (30.0%) and Zaria, Nigeria (38.5%) [23,24]. The elevated chlamydial antibody titers in patients with EP suggest chronic infection and an associated immune response. These findings are consistent with studies by Adewumi *et al.*, in Lagos (62.4% vs. 29.0%), Agholor *et al.*, in Benin (48.0% vs. 16.3%), and Ibe *et al.*, in Port Harcourt (53.1% vs. 28.1%) [10,25,26]. The analysis of clinical risk factors (Table 3) further supports the association between chlamydial infection and tubal ectopic pregnancy (TEP). In our study, nulliparity was significantly associated with ectopic pregnancy; 35.42% of the case group reported no previous childbirth, while none in the control group had this history (p < 0.000). This finding aligns with research conducted by Cheng Li *et al.*, in Shanghai, which indicated that nulliparous women are at higher risk for ectopic pregnancy. However, no significant differences were noted between the ectopic and intrauterine pregnancy groups [27]. Conversely, Adewunmi AA *et al.*, reported a greater susceptibility to ectopic pregnancy among multiparous women, with a significant distinction between ectopic and intrauterine pregnancies (p = 0.005) [25]. In this study, a history of ectopic pregnancy (EP) was observed in 14.58% of cases (p=0.021), reinforcing evidence from several studies that indicate a prior EP increases the risk of recurrence. Consistent with Petrini A. *et al.*, (2020), this study found that a previous ectopic pregnancy elevates the likelihood of future episodes, likely due to existing tubal damage. Additionally, a notable prevalence of pelvic inflammatory disease (PID) was identified in the case group (58.33%), while none were reported in the control group (p=0.001). This significant association between PID and EP has been well-documented, with Chlamydia trachomatis recognized as a leading cause of PID. The heightened incidence of tubal damage in women with a history of chlamydial infections emphasizes the critical need for early diagnosis and intervention to mitigate long-term reproductive complications. These findings are corroborated by various studies indicating that women with a prior history of PID are at a greater risk for ectopic pregnancies. For instance, nearly half of the cases analyzed by Porwal Sanjay *et al.*, reported a positive history of PID, and Adewunmi AA's study demonstrated a significant association (p=0.003) between ectopic pregnancy and PID [25,29,30]. The results also suggest an association between reproductive behaviors and increased risk of EP. Specifically, women in the case group reported a higher number of sexual partners (66.67%) compared to the control group (43.75%) (p=0.027). This finding is congruent with research indicating that increased sexual exposure is a risk factor for sexually transmitted infections (STIs) such as *Chlamydia trachomatis*, which are linked to tubal pathology [29,31]. A significant risk association with respect to multiple sexual partners was seen in the study done by Adewunmi AA [25]. Furthermore, the incidence of infertility was markedly higher among women in the case group (58.33%) compared to the control group (0%) (p=0.001). This finding is consistent with the studies done by Cheng Li *et al.*, where a significant association

was found between previous infertility history and ectopic pregnancy [27]. In terms of clinical symptoms, there were no significant between the groups in the reporting of dysuria, abdominal pain with fever, or purulent vaginal discharge. The absence of these differences may suggest that CT infection often remains asymptomatic or manifests with subtle symptoms, which aligns with previous literature suggesting that the asymptomatic nature of CT contributes to delayed diagnosis and treatment. This was consistent with the findings in Adewunmi AA's study, in which no significant association was seen [25,29]. In this study, no significant correlation was observed between prior intrauterine contraceptive device (IUCD) use and the occurrence of ectopic pregnancy (p=0.675). A related investigation involving 61,448 IUD users identified 118 cases of contraceptive failure, 21 of which resulted in ectopic pregnancies [32]. The findings underscore the need for comprehensive sexual health education and screening programs for *Chlamydia trachomatis*, especially among high-risk groups such as young women and those with multiple sexual partners. Early detection and treatment of *Chlamydia trachomatis* infection could significantly reduce the incidence of PID, tubal factor infertility, and, ultimately, ectopic pregnancy.

Limitations of the study: This hospital-based study has several limitations that may impact the generalizability of the results. The study was conducted over a short period, restricting the ability to assess long-term complications and mortality rates. Additionally, selection bias may have been introduced as the participants were drawn from a single tertiary care hospital, and their socio-demographic characteristics might not represent the broader population. Thus, the findings may not be applicable to the entire country or globally.

CONCLUSION AND RECOMMENDATIONS

This study confirms a significant association between Chlamydia trachomatis infection and an increased risk of tubal ectopic pregnancy. Women with tubal ectopic pregnancies demonstrated higher Chlamydia IgG titers, indicating prior chlamydial infection, compared to the control group. The findings emphasize the necessity for early screening and treatment of chlamydial infections to prevent reproductive complications such as pelvic inflammatory disease and tubal damage. Comprehensive sexual health education and targeted screening for high-risk groups are crucial.

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