

Relation of Previous Chlamydial Infection and Ectopic Pregnancy

A Serological Study

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ABSTRACT

Background: Ectopic pregnancy remains a major public health problem especially in developing countries, it is a major contributor to pregnancy related morbidity and mortality. Pelvic inflammatory disease caused by Chlamydia trachomatis infection has been found to be a major risk factor for the development of ectopic pregnancy.

Objectives: To assess whether prior infection with Chlamydia trachomatis is associated with an elevated risk of ectopic pregnancy.

Methods: A case-control study included 100 women; 50 women with ectopic pregnancy (cases) and 50 women with uncomplicated intra-uterine pregnancy (controls) were included in the study at the Department of Obstetrics and Gynecology of Al-Yarmook Teaching Hospital for the period from January 2019 through December 2019.

Both groups were compared in demographic and reproductive characteristics and tested for serological evidence of chlamydia Immunoglobulin G antibodies using enzyme linked immunosorbent assay (ELISA) technique.

Results: It had been noticed that younger ages of marriage make the probability of getting ectopic pregnancy significantly higher than women with older ages of marriage, P value=0.045, OR=2.253, 95% CI=1.521-7.905. And there is significant association between longer duration of marriage and getting ectopic pregnancy, P value=0.003, OR=3.467, 95% CI=1.521-7.905. In addition there is significant association between women who have history suggestive of pelvic inflammatory disease (vaginal discharge, abdominal pain) and getting ectopic pregnancy. P value=0.001, OR=7.433, 95% CI=2.962-18.653. Chlamydia IgG antibodies were found in 80% of women with ectopic and 14% of controls (P value=0.001)

Conclusion: The present study demonstrated that a higher proportion of women with ectopic pregnancy had significant serological evidence of previous infection with chlamydia trachomatis as compared to pregnant women with normal intrauterine pregnancy.

Keywords: Ectopic pregnancy, Chlamydia trachomatis infection, Tubal pregnancy, Chlamydial infection.

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An ectopic or extra-uterine pregnancy is one in which the blastocyst implants anywhere other than the endometrial lining of the uterine cavity⁽¹⁾. It is estimated to be 11 per 1000 pregnancies, with a maternal mortality of 0.2 per 1000 ectopic pregnancies⁽²⁾. Whether it is tubal; the most common type, or non-tubal ectopic pregnancy, there are many risk factors involved in this pathology. Among these risk factors is the pelvic inflammatory disease (PID)⁽³⁾.

It had been recorded that tubal damage -after one episode of PID occurs in 8%, and this percentage increases to 19.5% in the 2nd episode and 40% after three episodes^(4,5).

Chlamydia trachomatis is an obligate intracellular bacterium with a unique quasi-viral 48-hour life cycle⁽⁶⁾. In 2012 it had been estimated 130 million people affected by Chlamydia trachomatis infection worldwide, with a prevalence of 4% among women at reproductive age. Studies indicate that 10-30% of women experience one or more chlamydia episodes, with up to 70% of infections being asymptomatic, many women are left untreated and they are

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prone to chlamydia-related sequela such as pelvic inflammatory disease, ectopic pregnancy and tubal factor infertility⁽⁷⁾. In Iraq the estimated incidence of Chlamydia trachomatis infection among female was 30%⁽⁸⁾.

This study was conducted to assess whether prior infection with Chlamydia trachomatis was associated with an elevated risk of ectopic pregnancy.

Methods

A case-control study including 100 pregnant women attended the Department of Obstetrics and Gynaecology at Al-Yarmook teaching hospital; Baghdad-Iraq, for the period from January 2019 through December 2019. The study protocol was approved by the Scientific Council of Obstetrics and gynaecology Specializations of the Arab Board for Health Specializations. The sample was divided into two groups. Group A "cases" included 50 women with proved diagnosis of ectopic pregnancy, that had been treated surgically. Group B "control" consisted of 50 pregnant women who had a confirmed uncomplicated viable intra-uterine pregnancy. The inclusion criteria include, pregnancy in the first trimester, while the exclusion criteria include missed abortion, in-vitro fertilization pregnancy, women had intrauterine device at the time of conception, blood transfusion in the last 6 months, and previous tubal surgery. An informed consent had been obtained from all women and a detailed routine history and examination conducted. After that, maternal blood samples were obtained from all pregnant women and sent for serological assay to detect chlamydia trachomatis IgG antibodies by enzyme-linked immunosorbent assays (ELISA) technique.

The collected data were introduced into Microsoft Excel sheet 2016 and loaded into SPSS-V26 software statistical program. Descriptive statistics were presented using tables and graphs. Chi-square, Odds ratio (OR), and 95% confidence interval (CI) were used to find out significance of association and odd of getting ectopic

pregnancy in relation to categorical variables, ROC curve and primary logistic regression were used to find out effect of different variables on occurrence of ectopic pregnancy. P-value less than 0.05 was considered as cut off point for discrimination of significance.

Results

In this case-control study, involving 100 pregnant women divided into two groups, 50 women with ectopic pregnancy considered as (group A) and 50 women with normal intrauterine pregnancy considered as (group B). There was no age difference between the two groups with a P value of 0.191. Regarding the reproductive characteristics, there was no significant association between gravidity, parity, and abortion and getting ectopic pregnancy (P value=0.523, 0.874 and 0.834, respectively).

The present study noticed that younger ages of marriage made the probability of getting ectopic pregnancy significantly higher than women with older ages of marriage, P value=0.045, OR=2.253, 95% CI=1.521-7.905. There was significant association between longer duration of marriage and getting ectopic pregnancy, P value=0.003, OR=3.467, 95% CI=1.521-7.905.

There was no significant association between use of different types of contraception and getting ectopic pregnancy, P value=0.324. And no significant association between exposure to previous pelvic surgeries (apart from tubal surgery) and getting ectopic pregnancy, P value=0.131. While there was significant association between women who have history suggestive of pelvic inflammatory disease (vaginal discharge, abdominal pain) and getting ectopic pregnancy. P value=0.001, OR=7.433, 95% CI=2.962-18.653, (Table 1).

According to detection of Chlamydia trachomatis IgG antibodies by ELISA technique, it had been noticed that there was a strong association between Chlamydia infection and ectopic pregnancy

with a significant P value=0.001, OR=24.571, 95%CI=8.53-70.75, (Table 2 and Figure 1).

In table 3, logistic regression shows that chlamydia infection was a significant risk factor that may cause ectopic pregnancy, P value=0.001, OR=45.83, 95% CI=5.22-

401.74, while other factors show low risk (not significant) in causing ectopic pregnancy, P value more than 0.05 in all conditions.

ROC curve can detect 0.879 (area under the curve) of cases according to IgG level more than 0.320, (Figure 2).

Table 1: Demographic and reproductive variables of the two groups.

Variables		Group A No. (%)	Group B No. (%)	OR	95% CI		P value
					Lower limit	Upper limit	
Age groups in years	<20	1 (2)	1 (2)				0.191
	20-24	4 (8)	10 (20)				
	25-29	21 (42)	21 (42)				
	30-34	14 (28)	16 (32)				
	≥35	10 (20)	2 (4)				
Gravidity	<5	32 (64)	35 (70)				0.523
	≥5	18 (36)	15 (30)				
Parity	Zero	9 (18)	11 (22)				0.874
	1-3	30 (60)	28 (56)				
	>3	11 (22)	11 (22)				
Abortion	Abortion	17 (34)	18 (38)				0.834
	No Abortion	33 (66)	32 (64)				
Age at Marriage (years)	< 20	31 (62)	21 (42)	2.253	1.011	5.019	0.045
	≥20	19 (38)	29 (58)				
Duration of Marriage (years)	≥10	31 (62)	31 (62)	3.467	1.521	7.950	0.003
	<10	19 (38)	34 (68)				
Types of Contraception	No	32 (64)	29 (58)				0.324
	Pills	11 (22)	17 (34)				
	Others	7 (14)	4 (8)				
History of previous PID	Yes	31 (62)	9 (18)	7.433	2.962	18.65	0.001
	No	19 (38)	41 (82)				
History of abdominal-pelvic surgery	Yes	19 (38)	12 (24)				0.131
	No	31 (62)	38 (76)				

Table 2: Chlamydia infection in both groups.

Chlamydia Infection	Group A No. (%)	Group B No. (%)	OR	95%CI		P value
				Lower limit	Upper limit	
yes	40 (80)	7 (14)	24.571	8.53	70.75	0.001
No	10 (20)	43 (86)				

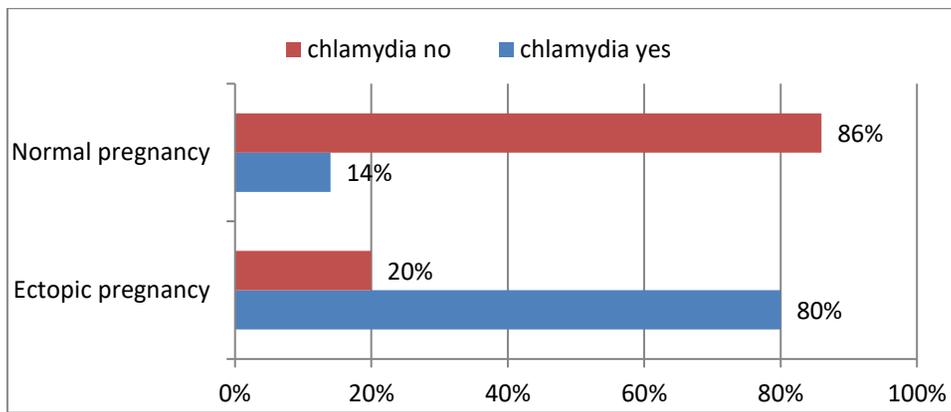


Figure 1: Association between Chlamydia infection and type of pregnancy.

Table 3: SPSS output of logistic regression analysis where the dependent variable is ectopic pregnancy.

	P value	Odd ratio OR	95% C.I. for OR	
			Lower limit	Upper limit
Marriage age	0.502	1.482	0.471	4.668
Marriage duration	0.412	1.893	0.412	8.703
PID	0.355	2.824	0.313	25.436
Chlamydia	0.001	45.830	5.228	401.737
Constant	0.016	0.004		

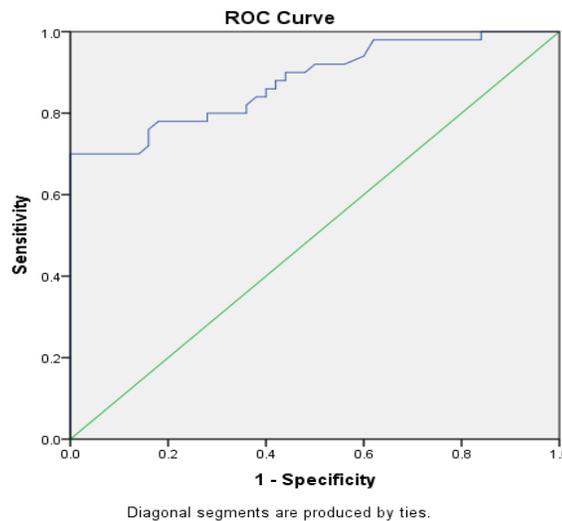


Figure 2: ROC curve of chlamydia IgG level and its sensitivity to detect ectopic pregnancy. (Area under the curve =0.879, SE=0.034, p value=0.001, 95%CI=0.812-0.946).

Discussion

Tubal ectopic pregnancies are a leading cause of global maternal morbidity and mortality in the first trimester of pregnancy. Epidemiological studies indicate that previous pelvic *C. trachomatis* infection is a major risk factor for ectopic pregnancy,

through alteration of tubal epithelial cells phenotype predisposing to ectopic embryo attachment and implantation later in a woman's reproductive life^(7,9).

In the current study, the results reveal no significant difference between study groups regarding women age (p value 0.191), but there is significant difference between the

two groups in relation to the younger age at marriage and duration of marriage (p value 0.45 and 0.003 respectively, table 1). In an unmatched case–control study performed by Kwaku et al including 104 women with ectopic pregnancy in comparison with 208 women with normal intrauterine pregnancy there were no statistically significant difference between the two groups regarding the age groups, but it was significant in sexual debut at younger than 15 years⁽¹⁰⁾.

Women who have history suggestive of pelvic inflammatory disease have significant association with ectopic pregnancy (P value=0.001), this agree with a retrospective matched-cohort study design done by Chun-Chung Huang et al 2019; which includes 30,450 patients with PID and 91,350 controls. During the follow-up period, patients in the PID group were more likely to develop ectopic pregnancy than patients in the control group (P-value=0.050)⁽¹¹⁾.

In the present study, there is no significant association between previous exposure to pelvic surgeries and getting ectopic pregnancy (P-value=0.131). In a study conducted by Louis Jacob et al 2017; on 3003 women with ectopic pregnancy in comparison with 97194 women without ectopic pregnancy found prior genital surgery positively associated with ectopic pregnancy (P value=0.001), (Odd ratio “OR” =2.67)⁽¹²⁾, the present study disagrees with Jacob et al study. This could be explained by the small number of participants in this study who had a history of abdomino-pelvic surgeries.

The prevalence of chlamydial IgG antibodies was significantly higher in women with ectopic pregnancy than in women with intrauterine pregnancy, due to its association with endosalpingeal damage and ectopic pregnancy resulting from pelvic inflammatory disease (P-value=0.001). On logistic regression analysis, chlamydial infection remains the most significant risk factor associated with ectopic pregnancy with a (P=0.001), and the area under the curve of 0.879. These observations were in

accordance with a study done by Rantsi et al, a total of 800 women with ectopic pregnancy, 800 women with miscarriage, and 1350 women with preterm birth anti-chlamydial IgG antibodies were associated with ectopic pregnancy. Positive antibody levels were found in 21.0% of cases and 14.6% of controls (P = 0.001), previous exposure to *C. trachomatis*, doubled the risk of ectopic pregnancy⁽⁹⁾. Another study done by Hoenderboom et al, which revealed no association between chlamydia IgG positivity and ectopic pregnancy. Although differences in risk between chlamydia-positive and chlamydia-negative women were considerable and highly significant, the cumulative incidence for the sequela studied was low (<5%)⁽¹³⁾.

In conclusions; this study demonstrated that a higher proportion of women with ectopic pregnancy had serological evidence of prior *Chlamydia trachomatis* infection as compared to women with confirmed intrauterine pregnancy, therefore presence of *Chlamydia trachomatis* antibodies predict presence of tubal pathology in high accuracy but doesn't define its impact on fecundity.

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