Research Article

Role of maternal serum *Chlamydia trachomatis* IgG antibodies and serum C- reactive protein in preterm labour

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ABSTRACT

Background: The objective was to find the role of maternal serum C- reactive protein and *Chlamydia trachomatis* IgG antibodies as predictors of preterm delivery.
Methods: This prospective study was conducted in UISEMH, Department of Obstetrics and Gynecology, GSVM Medical College, Kanpur from September 2011 to September 2013. The present study comprised of a total of 100 cases, out of which 50 were in study group and 50 in control group. Cases were compared with respect to presence of *Chlamydia trachomatis* antibodies and maternal C- reactive protein levels.
Results: CRP levels were higher and *C. trachomatis* immunoglobulin G levels were more often present in the women with preterm deliveries. A total of 20 cases (40%) were found to be seropositive for IgG antibodies to *C. trachomatis*. The seropositive women were significantly more likely to have a preterm birth (75% [15/20] v. 40% [12/30]; p = 0.0182, odds ratio 4.50, 95% CI 1.29 to 15.67). In study group 21 cases were CRP positive (42%). The CRP positive women were significantly more likely to have a preterm birth (76.2% [16/21] v. 37.93 % [11/29]; p = 0.009, odds ratio 5.24, 95% CI 1.49 to 18.34). Thus risk of preterm delivery was greater in seropositive women and in CRP positive women.
Conclusion: The detection of maternal serum C- reactive protein and antichlamydial antibodies are valuable, non-invasive diagnostic procedure for prediction of preterm delivery and can be used as predictors of preterm delivery.

Keywords: Preterm labor, *Chlamydia trachomatis*, Antibody

INTRODUCTION

Preterm labour is a syndrome causing approximately 30% of all preterm births. Globally, the rate of preterm birth ranges from 5% to 18% of babies born. India accounts for the greatest number of preterm births.[1] Methods to detect preterm labour at early stage include ultrasound examination of the cervix and detection of biochemical markers of preterm labour in blood, saliva and cervicovaginal secretions. In majority of cases the precise causes of labour before term are not known. Intrauterine infections may contribute to 40-50 percent of all preterm births.[2] *Chlamydia trachomatis* is an important cause of sexually transmitted infections (STIs) in women, which may lead to pelvic inflammatory disease, tubal infertility, ectopic pregnancy, and chronic abdominal pain.[2]

The literature regarding the detrimental effects of *C. trachomatis* infection on pregnancy outcome, however, yields conflicting results that seem primarily due to differences in study design, population and microbiological tests employed. Various changes in pregnancy have been proposed to influence *C. trachomatis* infection. First, cervical ectopy (related to estrogen levels) has been associated with *C. trachomatis* infection and with pregnancy, and is supposed to increase shedding of *C. trachomatis* and/or increase the risk of chlamydial infection. Second, pregnancy is physiologically immunosuppressive and alters the immune responses progressively with advancing gestation to a nadir at 32 weeks gestation, which may affect replication and shedding of *C. trachomatis*. Third, maternal antichlamydial antibodies cross the placenta

after 5-6 weeks gestation and are found in breast milk, which may be protective for neonates.[2]

It has been hypothesized that inflammation of decidual tissue or chorioamnion leads to prostaglandin production, cervical ripening, and subsequent uterine contractions. It is not known exactly when this inflammatory process begins, or how long a latency period is required for symptoms to manifest.[2]

C- reactive protein (CRP) is a sensitive marker of systemic inflammation and is primarily synthesized in hepatocytes in response to infection and tissue injury. Maternal concentration of CRP have been studied as an aid to diagnosing subclinical infection in pregnant women who experience preterm labour and premature rupture of membranes.[3] A significant association of elevated serum CRP levels with a nearly twofold increased risk of delivery before 37 weeks gestation. As adiposity, pre- eclampsia, and intrauterine growth retardation are linked to increased CRP levels therefore these patients were be excluded from the study group.[3]

In India, there are a very few studies on the association of *C. trachomatis* antibodies and CRP levels with spontaneous preterm delivery and their results are conflicting. Therefore we have conducted this prospective study to find the role of maternal serum CRP levels and C. trachomatis antibodies as predictors of preterm delivery.

METHODS

This prospective case control study was conducted in Upper India Sugar Exchange Maternity Hospital, Department of Obstetrics and Gynaecology, GSVM Medical College, Kanpur from September 2011 to September 2013. The present study comprised of a total of 100 cases, out of which 50 were in study group and 50 were in control group. Study group consisted of pregnant women with singleton foetus with symptoms of preterm labour. A similar number of matched controls were randomly selected from a similar female cohort with no symptoms of preterm labour and had term singleton delivery.

Following were the exclusion criteria of present study

1. Multiple gestation
2. A plan to move out of the area before delivery
3. Gestational age greater than 28 completed weeks at the initial prenatal visit
4. History of associated infection and inflammation
5. Hormone use
6. Obese females
7. Metabolic syndrome
8. Cardiovascular disease
9. Medication use (particularly statins, fibrates, and niacin)

Maternal non-fasting blood sample was collected in 10 ml vacutainer tubes for all routine investigations; ABO & Rh grouping, CBC, RBS, VDRL, PPTCT, HBsAg, urine for routine and microscopic examination. Serum CRP samples were also taken and sent to laboratory for estimation. CRP levels in maternal blood were measured in both study and control group by latex agglutination method. In this study CRP level <0.9 mg/dl was taken normal and patients were compared on the basis of CRP level in to two groups; with normal and with increased CRP levels (≥0.9 mg/dl).

Serum *C. trachomatis* specific immunoglobulin G (IgG) antibodies were estimated by the ELISA (Enzyme linked Immunosorbent Assay) technique. Absorbance at 450 nm is read using an ELISA microwell plate reader. Samples are considered positive if the absorbance value is higher than 10% over the cut-off. Samples are considered negative if the absorbance value is lower than 10% below the cut-off.

Medcalc 12.7.4.0 and SPSS version 22 software were used in the present study for statistical analysis.

RESULTS

In our study, the mean age of the study group was 25.06±3.45 while of control group was 24.60±3.00. Among the cases, mean gestational age was 24.46±2.01 and 22.6±2.34 in control group. In study group only 8% cases had positive history of smoking while in control group none of the case had positive history of smoking (Table 1). The two groups did not differ significantly with respect to mean maternal age, parity, history of preterm birth, presence of illness or obstetric complications known to lead to preterm birth, smoking status and educational status. In the present study a total of 20 cases were *C. trachomatis* antibody positive, out of them 85% cases were multigravida while in CRP positive cases 71.4 % were multigravida. (Table 2)

Table 1: Demographic Profile.

Characteristics		Study Group	Control Group
Mean Age		25.06±3.45	24.60±3.00
Mean Gestational Age		24.46±2.01	22.6±2.34
Parity	P0	48 %	38%
	P1	26%	46%
	P2	20%	14%
	P≥3	06%	02%
Mean BMI		21.63±1.69	21.63±1.63
History of Smoking		4 (8.0%)	Nil

Table 2: Relation of CRP level and *Chlamydia trachomatis* antibodies with gravida in study group.

Gravida	CRP Positive		*Chlamydia trachomatis* antibody positive	
	No.	%	No.	%
Primigravida	6	28.6	3	15
Multigravida	15	71.4	17	85
Total	21	100	20	100

Table 3 shows distribution of CRP level and *Chlamydia trachomatis* antibody positivity in study group according to gestational age on admission. On admission in 20-22 weeks group CRP level was higher as compared to other two groups while *Chlamydia trachomatis* antibody positive cases were almost same in all groups.

Table 3: Distribution of CRP level and *Chlamydia trachomatis* antibody positivity in study group according to gestational age on admission.

Gestational age on admission (weeks)	No. of cases	Range of CRP	Mean of CRP	*Chlamydia trachomatis* antibody positive cases
20-22	10	0.31-2.13	1.13±0.67	7
23-25	22	0.32-1.6	0.80±0.32	7
26-28	18	0.30-1.9	0.83±0.39	6

In study group 36% cases had positive history of previous abortion and 22% cases had positive history of previous preterm delivery (Table 4). In study group a total of 20 cases were *Chlamydia trachomatis* antibody positive and 21 cases were CRP positive. Out of the 20 seropositive cases for *Chlamydia trachomatis*, 15 (75%) cases were delivered prematurely, while 12 (40%) cases were delivered prematurely out of 30 cases who were negative (75% [15/20] v. 40% [12/30]; p = 0.0182, odds ratio 4.50, 95% CI 1.29 to 15.67). Out of the 21 CRP positive cases 16 cases were delivered prematurely, while 11 cases were delivered prematurely out of 29 CRP negative ones. (76.2% [16/21] v. 37.93 % [11/29]; p = 0.009, odds ratio 5.24, 95% CI 1.49 to 18.34). There was statistically significant association of maternal serum CRP and *C. trachomatis* antibodies with preterm delivery (Table 5).

Table 4: Previous obstetric History.

Positive History	Study Group	Control Group
Previous Abortion	36%	26%
Previous Preterm Delivery	22%	16%

Table 5: Association of CRP and *Chlamydia trachomatis* antibodies with preterm and term delivery.

	CRP		*C. trachomatis* antibodies	
	Positive	Negative	Positive	Negative
Preterm delivery	16	11	15	12
Term delivery	05	18	05	18
Total	21	29	20	30
	p = 0.009, odds ratio 5.24, 95% CI1.49 to 18.34		p = 0.0182, odds ratio 4.50, 95% CI1.29 to 15.67	

DISCUSSION

Preterm birth is one of the most important problems in modern obstetrics and the leading cause of neonatal mortality and morbidity. Approximately 5−10% of all births are preterm, and the frequency has not decreased over the past 20–30 years.[4] IgG antibodies against *C. trachomatis* were more often, although not nominally significantly, present in the mothers with preterm delivery.[4]

In our study age distribution of sample was compared in the study and control groups. Mean age of study group was 25.06 and of control group was 24.60 years. There was no significant difference in mean age in two groups (p: 0.454). Age groups were matched. In study group 18 cases (36%) had history of previous abortion while in control group 13 cases (26%) had positive history of previous abortion. Statistically there is no significant difference in both the groups (p = NS). Karinen et al[3] found that 6.7% cases in study group and 9.2% in control group had history of previous abortions. Statistically there was no significant difference in both groups; this finding is similar to our study. In our study only 4 patients had history of smoking and all of them were present in study group while in Hollegaard S et al[5] study 39.5%, in Blass MM et al[6] study 29.5% patients had positive history of smoking. Probably the reason behind this finding is that in this part of world smoking is not common in females.

Our study demonstrated a statistically significant association between maternal blood CRP levels and preterm delivery. Out of the 21 CRP positive cases 16 cases were delivered prematurely, while 11 cases were delivered prematurely out of 29 CRP negative ones (76.2% [16/21] v. 37.93 % [11/29]; p = 0.009, odds ratio 5.24, 95% CI 1.49 to 18.34). Similar findings were reported by Hvilsom et al[7] and Moghaddam et al.[8] They found statistically significant association of CRP with preterm delivery. However, Ghezzi et al[9] found no relationship between midterm maternal blood highly sensitive CRP levels and preterm delivery.

In the present study *C. trachomatis* IgG antibodies were associated with preterm delivery. In the study group a total of 20 (40%) cases were seropositive for *Chlamydia* antibodies, out of them 15 (75%) were delivered before term. This is statistically significant (p value = 0.0182). In *Chlamydia trachomatis* antibodies positive cases the chances of preterm delivery increases to 4.5 times (odds ratio - 4.50). Our findings are similar to a study by Paul Claman et al (1995),[10] they reported that seropositive women were significantly more likely than the seronegative women to have a preterm birth (24% vs. 7%; p = 0.029). Results of our study are very similar to the previous studies by Andrews WW et al,[3] Rastogi S et al[11] and Odendaal HJ et al.[12] Andrews WW et al (2000)[3] concluded that *C. trachomatis* infection at 24 weeks' gestation was associated with a 2-fold to 3-fold increased risk of subsequent spontaneous preterm birth. Similarly Rastogi S et al (1999)[11] reported that there was an increased incidence of still-birth, prematurity and low birth-weight in the *C. trachomatis*-positive women. In a prospective South-African study by Odendaal HJ et al (2006),[12] *Chlamydia*-positive cases had a relative risk of 2.20 for preterm delivery.

CONCLUSION

In present study there is a statistically significant association of preterm delivery with maternal serum CRP and *Chlamydia trachomatis* antibodies (IgG). The detection of specific antichlamydial antibodies and serum CRP are valuable, noninvasive diagnostic procedure for prediction of preterm delivery and they can be used as predictors of preterm delivery and further study is required to determine whether serologic testing for *C. trachomatis* and CRP levels should be a routine part of prenatal care.

REFERENCES

1. Blencowe H, Cousens S, Oestergaard M, Chou D, Moller AB, Narwal R, Adler A, Garcia CV, Rohde S, Say L, Lawn JE. National, regional and worldwide estimates of preterm birth. Lancet 2012;379(9832):2162-72.
2. Klein LL, Gibbs RS. Infection and Preterm Birth. Obstet Gynecol Clin N Am 2005;32:397-410.
3. Karinen L, Pouta A, Bloigu A, Koskela P, Paldanius M, Leinonen M et al. Serum C-reactive Protein and Chlamydia trachomatis Antibodies in Preterm Delivery. Obstet & Gynecol. 2005;106:73-80.
4. Andrews WW, Goldenberg RL, Mercer B, Iams J, Meis P, Moawad A, et al. The preterm prediction study: association of second-trimester genitourinary chlamydia infection with subsequent spontaneous preterm birth. Am J Obstet Gynecol. 2000;183:662-8.
5. Hollegaard S, Vogel I, Thorsen P, Jensen IP, Mordhorst CH, Jeune B. Chlamydia trachomatis C-complex serovars are a risk factor for preterm birth. In Vivo 2007;21:107-12.
6. Blas MM, Canchihuaman FA, Alva IE, Hawes SE. Pregnancy outcomes in women infected with Chlamydia trachomatis: a population-based cohort study in Washington State. Sex Transm Infect. 2007;83:314–8.
7. Hvilsom G, Thorsen P, Jeune B, Bakketeig L. C-reactive protein: a serological marker for preterm delivery. Acta Obstet Gynecol Scand 2002;81:424–9.
8. Moghaddam Banaem L, Mohamadi B, Asghari Jaafarabadi M, Aliyan Moghadam N. Maternal serum C-reactive protein in early pregnancy and occurrence of preterm premature rupture of membranes and preterm birth. J Obstet Gynaecol Res. 2012 May;38(5):780-6.
9. Ghezzi F, Massimo F, Raio L, Di Naro E, Bossi G, D'Eril G, et al. Elevated amniotic fluid C-reactive protein at the time of genetic amniocentesis is a marker for preterm delivery. Am J Obstet Gynecol 2002;186:268–73.
10. Claman P, Toye B, Peeling RW, Jessamine P, Belcher J. Serologic evidence of Chlamydia trachomatis infection and risk of preterm birth. CMAJ. 1995;153:259–62.
11. Rastogi S, Kapur S, Salhan S, Mittal A. Chlamydia trachomatis infection in pregnancy: risk factor for an adverse outcome. Br J Biomed Sci. 1999;56:94-8.
12. Odendaal HJ, Schoeman J. The association between Chlamydia trachomatis genital infection and spontaneous preterm labour. S Afr J Obstet Gynaecol. 2006;12:146-9.