

Association between Chlamydia Trachomatis Cervicitis and Preterm Labor

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ABSTRACT

Background: Preterm labor (PTL) is a major determinant of neonatal morbimortality with adverse consequences for health. The causes are multifactorial, with intrauterine infection probably explaining most of these outcomes. It is believed that infection with Chlamydia trachomatis (CT) is also involved in PTL.

Objective: To compare the prevalence of chlamydia trachomatis cervicitis in women with preterm labor and control at term. **Methods:** This was a case-control study conducted at Ain Shams University Maternity Hospital. This study included 70 pregnant women with singleton fetus who attended the causality and were selected to participate in the study. They were divided into two groups, cases and control group each 35 patients. Swab was taken from endocervix and chlamydia trachomatis DNA was examined by real time polymerase chain reaction (PCR). Data were analyzed by Chi-square test.

Results: The prevalence of chlamydia trachomatis cervicitis in women with preterm labor is higher than in women at term; 8 cases out of 35 (22.9%) as compared to the women in the control group which was 2 cases out of 35 (5.7%) and this difference was statistically significant using ($p=0.04$).

Conclusion: This study proved that there is an association between chlamydia trachomatis cervicitis and preterm labor. Screening and treatment of Chlamydia trachomatis infection are recommended to decrease cases of preterm labor.

Keywords: Chlamydia Trachomatis, Preterm labor, polymerase chain reaction.

INTRODUCTION

The etiology of preterm labor remains unknown, prediction lacks specificity, prophylaxis is helpless, diagnosis is difficult and the benefits and risks of tocolytic therapy are still debatable. The above quote testifies to the complexity of preterm labor, a process that ultimately results in considerable neonatal morbidity and mortality. It is difficult to quantify the incidence of spontaneous preterm labor, as many studies related to preterm birth do not discriminate between spontaneous preterm labor and iatrogenic/therapeutic preterm delivery⁽¹⁾. However, it has been estimated that the incidence of preterm labor varies from 5% to 10% of all births in developed countries⁽²⁾.

The pathogenesis of preterm labor is not well understood, and it is often not clear whether preterm labor represents early idiopathic activation of the normal labor process or results from a pathogenic mechanism⁽³⁾. So, preterm labor probably represents a syndrome rather than a specific diagnosis, since the causes are varied⁽⁴⁾. Recent studies of the epidemiology and pathophysiology of preterm birth have identified four pathways leading to preterm labor and delivery:

- 1) Inflammation.
- 2) Decidual hemorrhage.
- 3) Uterine over-distension.
- 4) Premature activation of the normal physiologic initiation of labor⁽⁵⁾.

A history of a preterm delivery is one of the most significant risk factors. The recurrence risk factor of preterm birth in women with a history of preterm delivery ranges from 17% to 40% and appears to depend on the number of prior preterm deliveries⁽³⁾. Multiple gestations carry one of the highest risks of preterm delivery. Approximately 50% of twins and nearly all higher multiple gestations end before 37 completed weeks. The average length of gestation is significantly shorter for twins (36 weeks), triple (33 weeks), and quadruplets (31 weeks) than it is for singletons (39 weeks)⁽⁶⁾.

Vaginal infections, such as bacterial vaginosis⁽⁷⁾ and those due to Neisseria gonorrhoea, Chlamydia trachomatis, group B streptococcus, Ureaplasma urealyticum and Trichomonas vaginalis have been associated with preterm delivery⁽⁸⁾.

Infections play a major role in the genesis of preterm birth and may account for 25-40% of events. The frequency of infection in preterm birth is inversely related to the gestational age. Endotoxins released by microorganisms and cytokines stimulate uterine contractions. Further the decidual response may include release of matrix-degrading enzymes that weaken fetal membranes leading to premature rupture⁽⁹⁾.

Trials of prevention of spontaneous preterm labor received greater interest to prevent associated complications and allow trials to enhance fetal lung maturity⁽¹⁰⁾.

The first step in prevention of preterm labor is early identification of women at risk for preterm birth⁽¹⁰⁾.

Proper management of threatened preterm labor significantly reduces neonatal morbidity and mortality, neonatal complications of prematurity which include respiratory distress syndrome, intracranial hemorrhage, retinopathy, enterocolitias, brain disorders and increased liability to infection⁽¹¹⁾.

The therapeutic interventions in the setting of preterm labor aim to inhibit or reduce the strength and frequency of contractions, which delays the time of delivery and to optimize fetal status before preterm delivery⁽¹²⁾.

Chlamydia trachomatis is an obligate intracellular Gram-negative bacterium, which has a unique biphasic developmental cycle. C. trachomatis is the most common bacterium responsible for sexually transmitted infections, costing health care systems billions of dollars to treat not only the acute infection, but also the complications they cause. A major concern with Chlamydia infections is that 70% of infected women and 50% of infected men are asymptomatic. In women, this can lead to severe sequelae such as pelvic inflammatory disease (PID), which can then cause ectopic pregnancies and tubal infertility, and men can suffer from prostatitis and epididymitis. Risk factors for contracting infection include age, with those aged 15-24 most affected, gender, with women at more risk than men, and race⁽¹³⁾.

Vertical transmission from mother to infant is considered to occur mostly during vaginal delivery and may result in conjunctivitis and pneumonia in newborn. In addition, chlamydia trachomatis has been suggested to be associated with premature rupture of membranes, premature labor and birth, neonatal problems and even fetal death⁽¹⁴⁾.

The most challenging issue of the chlamydia trachomatis infections is the difficulty of diagnosis. In the past cell culture was regarded as the gold standard nevertheless this method requires an experienced team and some technical equipment. Nowadays there are new antigen determination methods such as direct fluorescent antibody (DFA) and enzyme immunoassay (EIA) which provide a rapid result. Among many molecular methods polymerase chain reaction (PCR) possesses a high sensitivity for chlamydia thus it will likely become the gold standard diagnostic modality in the future⁽¹⁵⁾.

Controversy exists regarding the association between Chlamydia trachomatis infection during

pregnancy and adverse perinatal outcome as preterm labor⁽¹⁶⁾.

PATIENTS & METHODS

This was a case-control study conducted at Ain Shams University Maternity Hospital. This study included 70 pregnant women with singleton fetus who attended the causality and were selected to participate in the study. They were divided into two groups, cases and control group each 35 patients.

Cases: Pregnant women who present with a diagnosis of preterm labor.

Control: Pregnant women with symptoms of labor at term (more than 37 weeks).

Inclusion Criteria

- 1- Pregnant women 20 to 40 years old.
- 2- Body mass index (BMI) from 20 to 35.
- 3- Gestational age from 28 to 37 weeks in the study group and > 37 weeks in the control group.
- 4- Regular uterine contraction with cervical dilatation more than 3 cm and effacement more than 80% in the study group.
- 5- Intact membranes.

Exclusion criteria

- 1- Multiple gestation.
- 2- Patients with preterm labor and ruptured membranes.
- 3- Bacterial vaginosis.
- 4- Intra-uterine fetal death.
- 5- Eclampsia.
- 6- Severe obstetric bleeding either abruptio placenta or placenta previa.

Study procedure

1. **Verbal consent** was obtained from the pregnant women on whom the study was performed and they were informed about the objectives of the study.
2. Personal history including name, age, address, date of marriage, occupation, mobile number and special habits of medical importance was taken.
3. Medical history including past medical history, chronic medical disorders was taken.
4. Menstrual history especially the first day of last menstrual period to calculate the gestational age was taken.
5. General examination was performed and included recording of the weight, height and vital signs.
6. Abdominal examination: the fundal height, clinically-estimated fetal weight and presence of uterine contractions were performed.
7. Pelvic examination: condition of the membranes, presentation and cervical status (dilatation,

- length, consistency and position) at the time of diagnosis of preterm labor were performed.
8. Diagnosis of preterm labor: Symptoms like pelvic pressure, increased vaginal discharge, backache, and menstrual-like cramps are common with advancing pregnancy and suggest preterm labor more by their persistence than by their severity ⁽¹⁷⁾. The traditional criteria for labor, persistent uterine contractions accompanied by dilatation or effacement of the cervix, or both, are reasonably accurate when the frequency is six or more contractions per hour, cervical dilatation is 3 cm or more, effacement is 80 percent or greater, and membranes rupture or bleeding occurs ^(18,19). Other means of enhancing diagnostic accuracy in preterm labor include transvaginal sonographic measurement of cervical length and testing for fetal fibronectin in cervicovaginal fluid (5). Both of these tests improve the diagnostic accuracy by reducing the possibility of a false-positive diagnosis of labor.
 9. Type of delivery.
 10. Fetal outcome was followed up and fetal data were obtained from neonatologist.
 11. Maternal outcome was followed up.

- lithotomy position
- Separation the two labia
- A swab obtained from endocervix by rolling across it, soaked into a sample tube in chlamydia transport media S, then, stored at -80 at the department of Medical microbiology Samples were analyzed by real time polymerase chain reaction (PCR).and immunology, Faculty of Medicine Ain Shams University.

The study was done after approval of ethical board of Ain Shams university and an informed written consent was taken from each participant in the study.

Results were analyzed by Chi-square *test*.

RESULTS

In the current study the mean of age of the studied cases was 27.86 years with a SD± 5.24years. The mean of maternal BMI of cases was 29.17 kg with a SD ± 3.75 kg. PG represented 31.4% of cases, while the mean of age of the control group was 28.40 years with a SD± 6.10 years. The mean of maternal BMI of cases was 29.80 kg with a SD ±12.01 kg. PG represented 28.6% of cases.

All patients were instructed to do the following:

Table (1): Comparison between preterm and full term cases as regard personal data:

| | | Preterm | | | | P | Sig |
|--------------------------|------|---------|-------|--------|-------|---------|-----|
| | | Yes | | No | | | |
| | | Mean | ±SD | Mean | ±SD | | |
| Age (yrs.) | | 27.86 | 5.24 | 28.40 | 6.10 | 0.691‡ | NS |
| BMI | | 29.17 | 3.75 | 29.80 | 12.01 | 0.769‡ | NS |
| Systolic blood pressure | | 111.14 | 9.93 | 110.29 | 11.50 | 0.740‡ | NS |
| Diastolic blood pressure | | 72.29 | 8.69 | 71.57 | 8.97 | 0.736‡ | NS |
| Parity | PG | 11 | 31.4% | 10 | 28.6% | 0.891* | NS |
| | P0-2 | 15 | 42.9% | 17 | 48.6% | | |
| | >=P3 | 9 | 25.7% | 8 | 22.9% | | |
| Previous PTL | Yes | 5 | 14.3% | 3 | 8.6% | 0.710** | NS |
| | No | 30 | 85.7% | 32 | 91.4% | | |
| Number of abortion | 0 | 27 | 77.1% | 24 | 68.6% | 0.758** | NS |
| | 1 | 7 | 20.0% | 10 | 28.6% | | |
| | 2 | 1 | 2.9% | 1 | 2.9% | | |

The above table shows that no significant difference between pre- and full term cases as regard personal data

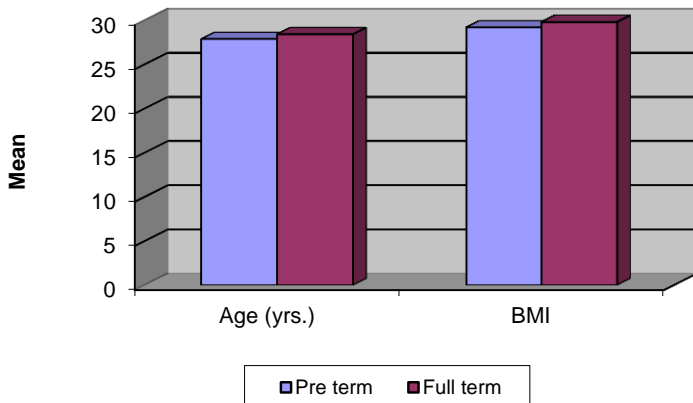


Figure (1): Comparison between preterm and full-term as regard age and BMI

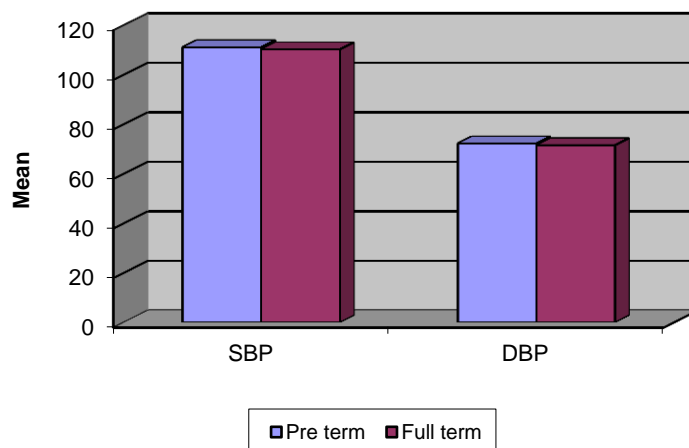


Figure (2): Comparison between preterm and fullterm as regard SBP and DBP

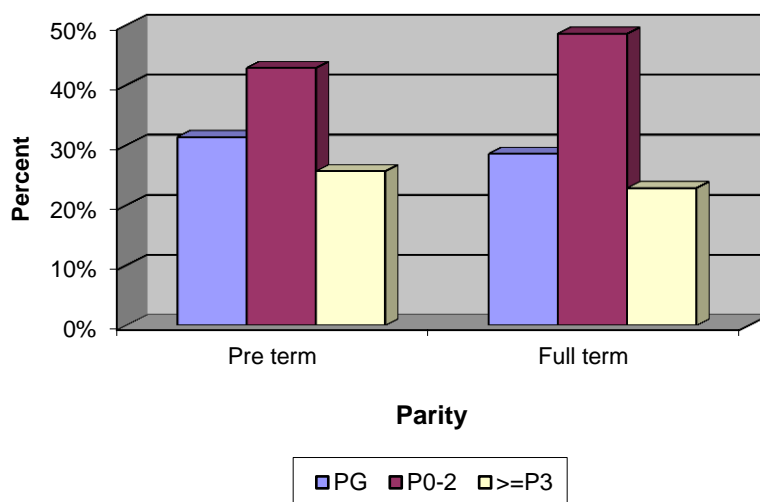


Figure (3): Comparison between preterm and full term as regard parity

Table (2): Comparison between preterm and full term as regard Obstetric data:

| | Preterm | | | | P | Sig | |
|--------------------------|----------|------|-------|------|--------|---------|----|
| | Yes | | No | | | | |
| | Mean | ±SD | Mean | ±SD | | | |
| GA (wk) | 34.06 | 2.35 | 39.11 | .93 | 0.001‡ | HS | |
| Cervical dilatation (cm) | 5.03 | 1.36 | 5.49 | 1.25 | 0.147‡ | NS | |
| Mode of delivery | C.S | 5 | 14.3% | 3 | 8.6% | 0.710** | NS |
| | NVD | 30 | 85.7% | 32 | 91.4% | | |
| Chlamydia infection | Positive | 8 | 22.9% | 2 | 5.7% | 0.04* | S |
| | Negative | 27 | 77.1% | 33 | 94.3% | | |

The above table shows that no significant difference between pre and full term cases as regard obstetric data with an exception to gestational age as preterm had lower mean GA compared to full term. As regard Chlamydia, a significant difference was present between pre and full-term cases with higher prevalence among preterm cases (22.9% Vs 5.7%)

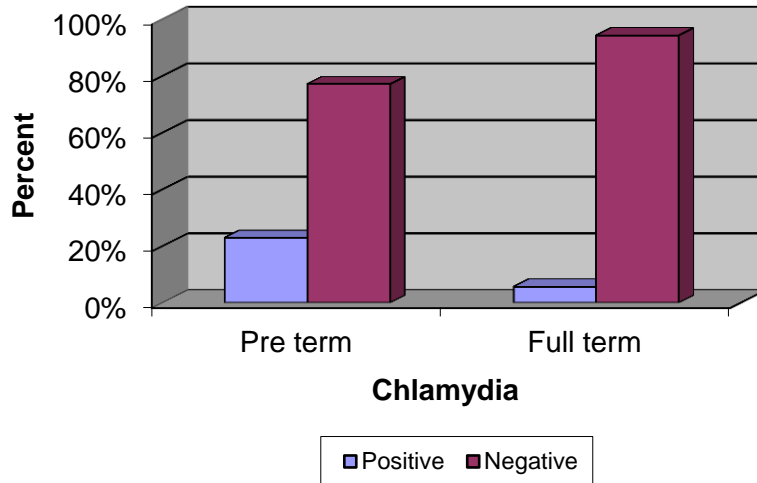


Figure (4): Comparison between preterm and full term as regard chlamydia infections

Table (3): Comparison between preterm and full term as regard fetal and maternal outcome:

| | | Preterm | | | | P | Sig |
|-----------------------|-----|---------|--------|---------|--------|---------|-----|
| | | Yes | | No | | | |
| | | Mean | ±SD | Mean | ±SD | | |
| Fetal weight(gram) | | 2448.57 | 658.04 | 3217.14 | 206.53 | 0.001‡ | HS |
| Fetal complication | Yes | 17 | 48.6% | 3 | 8.6% | 0.001** | HS |
| | No | 18 | 51.4% | 32 | 91.4% | | |
| Maternal complication | Yes | 3 | 8.6% | 4 | 11.4% | 1.0** | NS |
| | No | 32 | 91.4% | 31 | 88.6% | | |

The above table shows a high significant difference between pre and full term cases as regard **fetal weight and fetal** complication. As regard maternal complication, no significant difference was found between pre and full term cases.

DISCUSSION

Chlamydia trachomatis (CT) is responsible for the most prevalent sexually transmitted bacterial infection worldwide. The World Health Organization (WHO) estimates that 92 million new cases occur annually, four million in the United States and 10 million in Europe^(20,21). Besides high prevalence, another concern is the high annual cost resulting from the sequels of this infection, estimated at four billion dollars, thus achieving second place among the most expensive sexually transmitted diseases⁽²⁰⁾.

The lack of diagnosis contributes considerably to the high prevalence of untreated CT leading to seriously damaging consequences⁽²²⁾. In the United States, 2% to 13.7% of pregnant women are carriers of CT⁽²³⁾.

Finally, recent studies suggest that chlamydial infection of lower genital tract may be an important risk factor facilitating sexual transmission of HIV infection⁽²⁴⁾. For all of these reasons, improved means for prevention and control of C. trachomatis infection are urgently needed.

Preterm delivery refers to birth between the onset of viability and 37 completed weeks gestation. It is a common problem occurring in 5-25% pregnancies and is a major cause of death or disability in newborns⁽²⁵⁾.

Controversy exists regarding the association between Chlamydia trachomatis infection during pregnancy and adverse perinatal outcome as preterm labor⁽¹⁶⁾.

The aim of our study was to compare the prevalence of chlamydia trachomatis cervicitis in women with preterm labor and control at term.

This is a case-control study which was carried out on pregnant women attending the causality of Ain Shams University Maternity Hospital after approval of the research and ethics committee. All included women were having a singleton

pregnancy and fulfilling the inclusion and exclusion criteria.

Results of our study are matching those of **El-Shourbagy et al.**⁽²⁶⁾ who performed a case control study to determine the incidence of chlamydial infection in these high risk Egyptian women, the study included 501 patients with cervicitis (n = 58), abnormal cervical smear (n = 256), tubal infertility (n = 85), ectopic pregnancy (n = 22), preterm labor (n = 80) and 192 controls, reported significant increase of Chlamydial infection among different clinical conditions compared to controls (56.3% among subjects with preterm labor).

Results of our study are also agree with those of **Odendaal et al.**⁽²⁷⁾ who performed a prospective study to determine the association between Chlamydia trachomatis genital infection, as found at the first antenatal visit, and spontaneous preterm labor. A total of 343 pregnant women were recruited, of whom 36 (10.5%) delivered before 37 weeks' gestation. C. trachomatis was found in 8 (22.2%) of women who had preterm deliveries in contrast to 32 (10.4%) women who had term deliveries (p = 0.037).

Results of our study are accord with those of **Blas et al.**⁽²⁸⁾ who measured the relative risk between chlamydia infection and pregnancy outcomes, by a population-based retrospective cohort study using Washington State birth certificate data. All women diagnosed with Chlamydia trachomatis infection (n = 851), noted with a check box on the birth certificate from 2003, and a randomly selected sample of women not diagnosed with C trachomatis (n = 3404) were identified. After adjusting for age and education, chlamydia-infected women were at an increased risk of preterm delivery (RR 1.46, 95% CI 1.08 to 1.99) compared with non-infected women.

Results of our study are compatible with those found by **Schmidt et al.**⁽²⁹⁾ who evaluated the prevalence of and associated factors for CT among cases of PTB attended at a University Hospital in Vitoria, Brazil by cross-sectional study performed among parturient who had preterm birth from June 2012 to August 2013. Odds ratio was used as a measure of association with a 95% confidence interval. The prevalence of PTB during the period of the study was 26% and the prevalence of CT among them was 13.9%.

Data of our works concur those of **Dubey et al.**⁽³⁰⁾ who established the role of maternal serum C- reactive protein and Chlamydia trachomatis IgG antibodies as predictors of preterm delivery

by a prospective study conducted in UISEMH, Department of Obstetrics and Gynecology, GSVM Medical College, Kanpur from September 2011 to September 2013. This study comprised of a total of 100 cases, out of which 50 were in study group and 50 in control group.. 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).

Results of our study are in the contrary to **Silveria et al.**⁽³¹⁾ who performed a case control study to define the risks of preterm birth associated with Chlamydia trachomatis (CT) and other sexually transmitted infections (STIs) among pregnant women. They estimated the impact of CT and other STI on the odds of preterm birth using logistic regression. The study population included all pregnant women who gave birth to a singleton newborn of at least 20 weeks' gestation, and who had antenatal care information. 2127 women were included in this analysis. The prevalence of CT infection was 4.7%. CT diagnosis was not associated with preterm birth. This study did not find an as sociation between CT and preterm birth. The lack of an association may be explained by early treatment.

Also, the present results seem to disagree with those of **Yalti et al.**⁽³²⁾ who determine the prevalence of chlamydia trachomatis infection and to line out whether there is a correlation between the presence of chlamydia trachomatis and the development of preterm delivery, PROM and abortion by a prospective study, 55 pregnant women with a preterm labor and/or premature rupture of membranes, 51 women with spontaneous abortion and 51 patients with uncomplicated pregnancies were analyzed. The prevalence of Chlamydia trachomatis in pregnant women and in pregnant women with preterm labor was found to be 1.2% and 3.6%, respectively. This finding was statistically insignificant.

This study showed that there is no significant difference between cases and control as regard maternal age and parity (Table 1). This is consistent with the study conducted by **Andrews et al.**⁽³³⁾ where there were no statistical difference between cases of preterm labor and controls regarding the maternal age and the parity. It is in contrast to the study conducted by **Schmidt et al.**⁽²⁹⁾ where there were a statistical significant difference between two groups as regard maternal age (p = 0.022).

This study indicated that there is no statistically significant difference between cases and control as regard BMI (Table 1). It is similar to that carried by **Odendaal *et al.***⁽²⁷⁾ where there were no statistical significant difference between two groups as regard BMI.

This study revealed that (Table 1) there is no statistically significant difference between cases and control as regard previous PTL. It is in contrast to **Hosny *et al.***⁽³⁴⁾ who performed a case control study to investigate risk factors for PTL before 37 gestational weeks among Egyptian women. It included 117 pregnant women. The control group (n=45) had term labor (gestational weeks \geq 37 weeks), and the case group (n=72) had PTL (gestational weeks < 37 weeks). There were a high statistical significant difference between two groups as regard previous PTL ($p = 0.037$).

This study indicated that (Table 1) there is no statistically significant difference between cases and control as regard the previous history of abortion. This is consistent with the study conducted by **Karinen *et al.***⁽³⁵⁾ where there were no statistical difference between cases of preterm labor and controls regarding previous abortions. It is in contrast to the study conducted by **Hosny *et al.***⁽³⁴⁾ where there were a high statistical significant difference between two groups as regard previous abortions ($p = 0.002$).

This study manifested that (Table 2) there is no statistically significant difference between cases and control as regard mode of delivery. It is matching with the study conducted by **Odendaal *et al.***⁽²⁷⁾ that there were no statistical significant difference between two groups as regard mode of delivery.

In this study, (Table 3) there was a high significant difference between cases and controls as regard fetal outcome ($p=0.001$). It is similar with the study conducted by **Odendaal *et al.***⁽²⁷⁾ where there were a statistical significant difference between two groups as regard fetal outcome.

CONCLUSION

This study proved that there is an association between chlamydia trachomatis cervicitis and preterm labor.

The prevalence of chlamydia trachomatis cervicitis in women with preterm labor was 22.9% as compared to women with term labor was 5.7%.

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