Maternal and Infant *Chlamydia trachomatis* Infections

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**Abstract**

*Chlamydia trachomatis* infections in pregnancy present several challenges. In addition to potentially affecting the pregnancy, the infection may also affect the developing fetus and be transmitted to the infant during parturition. *C. trachomatis* infection during pregnancy has been associated with a number of adverse outcomes including stillbirth, low birth weight and premature delivery. Data on the effect of treatment of maternal infection on outcome of pregnancy have been inconclusive. *C. trachomatis* infection has also been associated with postpartum endometritis and postabortal pelvic inflammatory disease. The risk of an infant born to an infected mother of acquiring *C. trachomatis* infection is approximately 50%. The infant may become infected at multiple sites including the conjunctivae, nasopharynx, rectum and vagina. The most common clinical manifestation is neonatal conjunctivitis. Although the nasopharynx is the most frequent site of infection in infants, most of these infections are asymptomatic and may persist for months. Approximately 25% of infants with nasopharyngeal infection may develop a characteristic pneumonia, usually 1–3 months after birth. The most effective approach to preventing perinatal chlamydial infection is screening and treatment of pregnant women. This has been greatly facilitated by the use of nucleic acid amplification tests for diagnosis and the availability of effective single-dose antibiotic treatment.

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**The Effect of Pregnancy on *Chlamydia trachomatis* Infection**

Various changes in pregnancy have been proposed to influence *C. trachomatis* infection [1]. Cervical ectopy (related to estrogen levels), associated with *C. trachomatis* infection and pregnancy, may increase shedding of *C. trachomatis* and/or increase the risk of chlamydial infection [2]. Furthermore, pregnancy is physiologically immunosuppressive and alters the immune responses progressively with advancing gestation, which may affect replication and shedding of *C. trachomatis*. 
The Effect of *C. trachomatis* Infection on Pregnancy

**In the First Trimester**

*C. trachomatis* has been associated with spontaneous (recurrent) abortions, though not consistently [3–8]. Various models have been proposed for the pathogenesis of chlamydia-related spontaneous abortions, being either direct zygote infection or an immune response to heat shock proteins expressed by the zygote that is triggered by previous *C. trachomatis* infection, and reactivation of latent chlamydial infection or endometrial damage from past chlamydial infection [3, 6].

**In the Second and Third Trimester**

Premature Rupture of Membranes, Premature Delivery, Prematurity

*C. trachomatis* infection during pregnancy may influence pregnancy outcome and has been associated with chorioamnionitis, premature rupture of the membranes and premature delivery [9–24]. However, the literature regarding these effects of *C. trachomatis* infection on pregnancy outcome is conflicting, which seems to be primarily due to differences in the study design, population and microbiological tests that were used. While earlier studies based on serology and cultures were at variance regarding premature delivery, studies that used nucleic acid amplification tests (NAATs) for diagnosis were more likely to find an association of prematurity with *C. trachomatis* infection [19–21].

Low Birth Weight

*C. trachomatis* infection during pregnancy has been associated with low birth weight. However, again the literature is contradictory and other studies could not confirm such an association, probably also due to heterogeneity of the methods used [21, 25]. In some studies an association of *C. trachomatis* infection with low birth weight could only be confirmed in subgroups of women with elevated anti-*C. trachomatis* IgM antibodies, which suggested acute infection [11, 26]. A major confounding variable in many of these studies was coinfection with other organisms also associated with chorioamnionitis and low birth weight, including genital mycoplasmas, *Trichomonas vaginalis* and bacteria responsible for bacterial vaginosis [25]. The Vaginitis in Pregnancy study, which was a large US multicenter study sponsored by the National Institutes of Health in the early 1990s generated much of these data [24, 25]. A total of 13,750 women were enrolled and *C. trachomatis* was isolated by culture from 1,239 (9%). The Vaginitis in Pregnancy study also included a placebo-controlled study of erythromycin for treatment of *C. trachomatis* infection in pregnant women to determine whether treatment would lower the incidence of preterm delivery and/or low birth weight. The results were equivocal, erythromycin treatment had little impact on reducing low birth weight (defined as <2,500 g) or preterm delivery. There was a 20% failure rate in the erythromycin group which was associated with a higher rate of low birth weight and preterm delivery. However, 37% of women in the placebo group
cleared the infection spontaneously; women in the placebo group were also more likely to use nontrial antibiotics that also had activity against *C. trachomatis* (clindamycin, amoxicillin), which further complicated the analysis.

**Stillbirth**

*C. trachomatis* has been implicated as a cause of in utero infection in the fetus leading to stillbirth [10] and again results of various studies have been contradictory. IgM antibodies to *C. trachomatis* can be detected in cord blood of prematurely born neonates, which was felt to be suggestive of fetal infection. However, cord blood can often be contaminated with maternal blood, thus the antibody may be of maternal origin.

**Postpartum Effects of *C. trachomatis* Infections**

*C. trachomatis* infection during pregnancy may continue after delivery and cause postpartum endometritis, salpingitis or pelvic inflammatory disease [27–30]. In contrast to early postpartum endometritis, *C. trachomatis* usually causes late postpartum endometritis and develops between 2 days and 6 weeks after delivery [27–30]. Women are usually not seriously ill, but may present with secondary postpartum hemorrhage, with or without fever, lower abdominal pain and vaginal discharge. *C. trachomatis* infection can spread into the fallopian tubes resulting in salpingitis and increasing the risk of infertility or ectopic pregnancy.

**C. trachomatis Infections in Newborn Infants**

At the time of delivery, newborns may acquire *C. trachomatis* infection from pregnant women during passage through an infected birth canal. Hence, the occurrence of *C. trachomatis* infection in infants is directly related to the prevalence of maternal infection [31–34]. Infants born by caesarean section are at lower risk of acquiring chlamydial infection; however, several anecdotal reports of *C. trachomatis* infections in newborns after delivery by caesarean section, with and without premature rupture of the membranes, indicate that intrauterine infection can occur [35–37]. The overall risk for infants born to women with untreated chlamydial infection is approximately 50–75%, with infection occurring at one or more anatomic sites, including the conjunctivae, nasopharynx, rectum and vagina (table 1). Most of these studies were conducted in the 1980s before maternal screening was mandated in the USA and other developed countries. Approximately 30–50% of infants born to mothers with active, untreated chlamydial infection develop clinical conjunctivitis [31–34, 38]. The nasopharynx is the most frequent site of infection with 78% of infected infants having positive nasopharyngeal cultures in one study [38]. At least 50% of infants with chlamydial conjunctivitis also have nasopharyngeal infection. A recent study from China
documented nasopharyngeal infection, using PCR, in 24.2% of infants born to chlamydia-positive mothers [19]. However no details were given on when the infants were tested or if they were followed or treated. The overall risk of developing pneumonia among infants born to chlamydia-positive mothers has been reported to range from 1 to 22% but only about 25% of infants with nasopharyngeal chlamydial infection develop pneumonia [31–34, 38]. Data on the risk of acquiring rectal or vaginal infection are more limited. Bell et al. [39] demonstrated that perinatally acquired C. trachomatis infection may persist for months to years. Twenty-two infants born to women with culture-documented chlamydial infection were followed and positive cultures from the nasopharynx and oropharynx in the infants were detected as late as 28.5 months after birth. Rectal and vaginal infections were asymptomatic and persisted for at least 1 year. This can become an important confounding variable when young children are tested for the presence of C. trachomatis during evaluation for suspected sexual abuse.

Before the introduction of systematic prenatal screening for C. trachomatis infection and treatment of pregnant women, C. trachomatis was probably the most frequent infectious cause of neonatal conjunctivitis in the USA [32]. Since screening and treatment were initiated the incidence of both neonatal conjunctivitis and pneumonia have decreased dramatically. However, in countries where prenatal screening is not done, C. trachomatis remains an important cause of neonatal infection, including conjunctivitis. A retrospective/prospective study from the Netherlands demonstrated that C. trachomatis was responsible for 61% of cases of neonatal conjunctivitis in infants presenting to a pediatric hospital and ophthalmologists in Rotterdam [40]. Prevalence of C. trachomatis infection among pregnant women in that population was 4%; however, prenatal screening and treatment is not standard practice in the Netherlands. Similar data were reported from Ireland, between July 2002 and December 2006, 17 cases of neonatal conjunctivitis due to C. trachomatis and one due to Neisseria gonorrhoeae were identified in infants presenting to a major Irish regional teaching hospital [41]. The incidence of chlamydial ophthalmia was 0.65/1,000 live births.