

Early Neonatal Infection by *Chlamydia trachomatis*

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Rec date: Jun 30, 2014; Acc date: Jul 29, 2014; Pub date: Aug 05, 2014

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Abstract

Chlamydia trachomatis infection in pregnant women is a critical condition because the infection can induce an ectopic gestation, preterm delivery, premature rupture of membranes, and chorioamnionitis. Furthermore, the newborn may become infected by vertical transmission; however, at present there are evidences that intrauterine infections can occur. Here we examine this evidence and describe the clinical manifestations shown by these newborns after their delivery. We suggest the possibility of multi-systemic infection in these newborns.

Keywords: *Chlamydia trachomatis*, Intrauterine infection; Pregnancy

Commentary

Chlamydia trachomatis infections are a public health problem because of their high prevalence; infections are asymptomatic in 70% of women and affect fertility because they are not found and treated promptly [1]. The World Health Organization estimates that about 100 million new infections take place each year worldwide [2]. Pelvic inflammatory disease (PID), infertility due to tubal occlusion, and chronic abdominal pain are the most common sequels in women infected with this pathogen [1]. However, when a woman is pregnant, the situation becomes more critical, because the infection can provoke an ectopic pregnancy, preterm delivery, premature rupture of membranes, chorioamnionitis, spontaneous miscarriages, and perinatal mortality [3]. In addition, the newborn may become infected when passing through the birth canal of an infected mother or during premature rupture of membranes [3]. There is also the possibility of an intrauterine infection since there are reports on newborns delivered by cesarean and without premature rupture of membrane that coursed with chlamydial infection [4]. In the newborn, the most common clinical manifestations are conjunctivitis and/or pneumonia, which appear between 4 and 11 weeks after birth [3]. However, our research group has reported infants infected with this pathogen showing clinical manifestation of pneumonia at a few hours after birth [5]. In 2007, we reported a clinical case of a term new-born that died 14 days after birth of respiratory distress syndrome [5], with moderate to severe eosinophilia and positive culture for *Chlamydia trachomatis* in the bronchial aspirate sample. Furthermore, *Chlamydia trachomatis* DNA was detected in different organs such as heart, kidney, and lung [5]. In the same year, similar events were reported by Gorbunov et al. [6]; they found 23 cases of chlamydia identified at perinatal autopsy, and found several tissues infected, especially the kidney. This suggests that *C. trachomatis* is capable of causing a generalized infection in newborns and, possibly, transmission can occur in utero. Research conducted in 2011 by Rours et al. [7] demonstrated a high proportion of placentas (25%) from women with preterm birth (signs of less than 32 weeks gestation) with *C. trachomatis* DNA, associated with

histological evidence of placental inflammation. These results suggest that this bacterium ascends, colonizes the placenta, and causes an inflammatory response that can trigger preterm delivery, intrauterine growth retardation or pre-eclampsia. The ability of this bacterium to infect trophoblast and syncytiotrophoblast cells has been reported in both mouse model and humans [8,9]. The cellular damage mechanism is triggered by apoptosis [9]. These results support the idea regarding the capacity of *C. trachomatis* to infect the placenta. Despite the above, it has not been established if the newborn can get infected through the placenta; however, our research group has provided support for the ability of *C. trachomatis* to infect many different organs of the newborn [10]. The latter study was double-blinded, and the aim was to detect this bacterium in infants with early neonatal mortality. The mortality cases analyzed were of infants who died from various causes; the results demonstrated the presence of *C. trachomatis* DNA in those infants who suffered sepsis and in whom the etiologic agent of the disease had not been identified. In summary, these infants were invaded with *C. trachomatis* DNA in tissues such as the liver, kidney, lung, and brain [10].

The finding of *C. trachomatis* DNA in more than two different tissues suggests the possibility of a multivisceral infection and the discovery of this DNA repeatedly in the brain and liver suggests strongly a systemic infection by this pathogen. Moreover, in this same study, we tried to identify serotypes causing this infection. Nevertheless, only one was identified as serotype D, this newborn was a preterm baby (25 weeks gestation) with an 8-day premature rupture of membranes and with clinical data of sepsis [10]. The autopsy revealed congenital pneumonia and a placental histological lesion that showed chorioamnionitis. The three most common serotypes that cause genitourinary infections in the world are: E, F, and D [11]. Gallo et al. [12] reported that genotypes E, G, D, and F are the most frequently identified in neonatal conjunctivitis of babies from Argentina, whereas serotypes E, F, Ja, D, and G have been identified in Chilean infants with pneumonia [13].

In Mexico, genotypes F, E, and G are the most usually identified in genitourinary infections in infertile women [11], so that the D genotype is rare in these women. Despite the above, the genotype D is one of the serotypes showing virulence factors, such as production of

cytotoxin, which acts on cytoskeleton proteins of the infected cells [14] and can cause changes in the structural integrity, reduce ATP hydrolysis, decrease cell adhesion, induce changes in the outer membrane, and decrease intracellular transport [15]; all of these events could cause damage to the cells of the newborn and produce loss of their functionality and, eventually, provoke the death of the newborn. However, the mechanisms by which *C. trachomatis* can spread to different organs have not yet been identified.

Perhaps the mononuclear phagocytic cells could be participating significantly, since it has been shown that these cells are susceptible to infection by this pathogen [16]. Finally, it should be noted that the placenta not only serves as a reservoir for *C. trachomatis*, but also acts as a risk factor for infection of newborns within the uterus. Due to this, it is necessary to identify the mechanisms by which this pathogen can carry out the intrauterine infection. A possible mechanism is that *C. trachomatis* could cross the placenta; this bacterium has been found in amniotic fluid [17], suggesting its ability to go through several strata of the placenta such as the decidua, amnion chorion, and amniotic epithelium. Jerchel et al. [18,19] developed an in vitro model, using human Fallopian tubes, and by means of scanning electron microscopy (SEM) and transmission electron microscopy (TEM) were able to identify the epithelial damage of Fallopian tubes caused by serotype D of *C. trachomatis*. A similar model could be employed to demonstrate the harm that this bacterium can cause on the placenta. Another possibility is identifying structural changes of various tissues during chlamydial infection in pregnant mice. Placenta and fetus of these animals could be studied under the microscope. Mathematical/computational models could be another tool useful in identifying the mechanism by which *C. trachomatis* infects newborns. Recently, a software package about in-silico simulation of sexual transmitted disease was designed. The STI-GMA software (Sexually-Transmitted Infections-Graphical Modelling and Simulation) is aimed at monitoring indirectly the STI progression in humans by means of mathematical modelling. This software could be used not only in cervical tissue infections, but also in other regions such as the Fallopian tubes. This would allow performing research about scarring, inflammation, and development of PID or it could be used to analyze how chlamydial genital infection occurs in pregnant women and how it is transmitted to the newborn.

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