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Relationship between *Chlamydia trachomatis* infection diagnosed in early pregnancy and adverse pregnancy outcomes

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Jarosław Kalinka[1ABDEFG], Wojciech Hanke[2ABCF], Małgorzata Wasiela[3CDEG], Paweł Krajewski[1DEF]

[1] Department of Perinatology, I Division of Gynecology and Obstetrics, Medical University of Łódź, Łódź, Poland
[2] Department of Environmental Epidemiology, Nofer Institute of Occupational Medicine, Łódź, Łódź, Poland
[3] Department of Medical Microbiology, Medical University of Łódź, Łódź, Poland

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Summary

Background: The aim was to examine the relationship between *Chlamydia trachomatis* infection diagnosed in early pregnancy (8–16 weeks) and the risk of preterm delivery, low birth weight (LBW), and small for gestational age babies (SGA) in Central Poland.

Material/Methods: The study population comprised 179 pregnant women attending 10 randomly chosen outpatient maternity units between the 8th and 16th weeks of gestation. Cervicovaginal samples were collected together with a standard questionnaire from every subject. On the basis on Spiegel's criteria, Gram-stained vaginal smears were examined for bacterial vaginosis (BV). *C. trachomatis* infection was diagnosed using a direct immunofluorescence test performed on endocervical swabs (Chlamydia Direct IF-BioMerieux). To evaluate the risk factors, the odds ratios (*OR*) were calculated. Statistical analysis was carried out using the statistical program EPI INFO.

Results: The average pregnancy duration at the time of microbiological analysis was 12.3 weeks. Of the 179 women analyzed, 21 (11.7%) had preterm births, 20 (11.1%) delivered newborns with intrauretine growth retardation (IUGR), and 26 (14.5%) delivered low birth-weight infants (LBW). BV was diagnosed in 55 of the pregnant women (28.1%), grade I microflora in 70 (35.7%), and grade II (intermediate) in 71 of the women (36.2%). *Chlamydia trachomatis* was diagnosed in 48 of the pregnant women (24.5%). 29.1% of the women with bacterial vaginosis also had *C. trachomatis* infection. We did not find a significant difference in the *C. trachomatis* infection rate at early pregnancy between women who delivered LBW infants and women from the reference group (26.9% and 24.8%, respectively). *C. trachomatis* infection was found more frequently in the group of women who delivered before the 37th week of pregnancy (33.3%) than in the control group (24.1%; *OR*=1.58. CI: 0.53–4.58). *C. trachomatis* infection at early pregnancy was not related to SGA.

Conclusions: *C. trachomatis* infection during early pregnancy could be associated with preterm delivery, but not with LBW or SGA. The high prevalence of *C. trachomatis* infection in early pregnancy observed in the Central Polish population and the negative impact of this infection on the newborns' health indicate the need for more precise evaluation of the role of *C. trachomatis* infection during pregnancy.

Key words: ***C. trachomatis*** • **risk factors** • **infection** • **pregnancy** • **low birth weight** • **preterm delivery**

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Author's address: Jarosław Kalinka, MD, Ph.D., Department of Perinatology, 1st Division of Gynecology and Obstetrics, Medical University of Łódź, ul. Wileńska 37, 94-029 Łódź, Poland, e-mail: j.kalinka@csk.am.lodz.pl

Background

Low birth weight (LBW, below 2500 g), prematurity, and small for gestational age (SGA) babies constitutes major hazards in perinatology and neonatology. The pathogenesis and etiology of these pathologies are multifactorial, but there is now substantial evidence that preterm labor and birth is associated mainly with subclinical infection ascending into the uterine cavity from the lower genital tract [1–3]. It has been demonstrated that infection, and the ensuing inflammatory response, can stimulate the production of prostaglandins and cytokines from decidual and chorioamnion cells leading to the onset of labor [4,5]. Still, the prevalence of various microorganisms isolated from the lower genital tract, their relative concentrations, and their role in the pathogenesis of LBW, preterm delivery, and SGA is unclear, mainly due to observed race, ethnicity, and population differences in vaginal flora ecology and various gestational ages at the time of examination. The data concerning the impact of *Chlamydia trachomatis (C. trachomatis)* infection on subsequent pregnancy outcome is still controversial [6–8].

The main aim of this prospective study was to determine the prevalence of *Chlamydia trachomatis* infection diagnosed during early pregnancy (8th–16th week) and to assess its association with the risk of preterm delivery, low birth-weight (LBW), and small for gestational age babies in Central Poland.

Material and Methods

The study population comprised 196 randomly selected pregnant women attending 10 district outpatient maternity units cooperating with the Department of Perinatology, Medical University of Łódź, in the Łódź (Central Poland) region. Only singleton pregnancies between 8–16 weeks of pregnancy were qualified for inclusion in the survey. Women living outside the Łódź region were excluded from the study. A standard questionnaire covering medical, socio-economic, demographic, constitutional, and environmental features was administered to every subject and verified based on medical records. Full medical data were finally available for 179 women, who constituted the study population.

Cervicovaginal samples were obtained from all the pregnant women under study. Gram-stained vaginal smears were examined for bacterial vaginosis (BV) and BV-associated flora were sought by culture. BV was diagnosed by Gram's stain according to Spiegel's criteria [9] and the flora were graded as follows:

grade I – normal: predominantly lactobacillus morphotypes,
grade II – intermediate: mixed lactobacillus morphotypes and other morphotypes,
grade III – bacterial vaginosis: few or no lactobacillus morphotypes, but greatly increased number of *G. vaginalis* and other bacterial morphotypes.

C. trachomatis infection was diagnosed using a direct immunfluorescence test performed on endocervical swabs (Chlamydia Direct IF-BioMerieux). This method is based on monoclonal antibodies directed against *C. trachomatis* serotypes D-K.

Delivery of a newborn with birth weight below 2500 g was classified as LBW. SGA was defined as a birth weight below the 10th percentile according to the Central Poland percentile scale, taking into account the newborn's gender and gestational age at delivery.

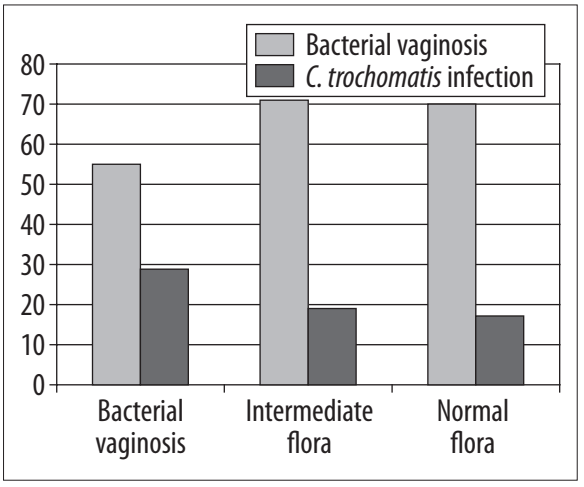

Figure 1. Prevalence of *C. trachomatis* infection according to bacterial flora grading during pregnancy.

To evaluate the risk factors, the odds ratios (*OR*) were calculated. Statistical analysis was carried out using the statistical program EPI INFO.

Results

The average pregnancy duration at the time of microbiological analysis was 12.3 weeks and the average age of the subjects was 26.1 years. 12.6% of the women were under 18 years of age and 18.5% were ever 30. 38% of the examined women had primary education only. Almost 25% of the pregnant women declared single marital status, and 31.2% were unemployed during pregnancy. 25% of the women smoked during pregnancy and half of them declared smoking more than six cigarettes a day. Poor or very poor economic situation were declared by 20.1% of the women under study.

According to the Gram stains, bacterial vaginosis was diagnosed in 55 of the pregnant women (28.1%), grade I microflora in 70 (35.7%), and grade II (intermediate) in 71 women (36.2%). *Chlamydia trachomatis* was diagnosed in 48 of the pregnant women (24.5%). The relationship between *C. trachomatis* infection and bacterial flora grading during pregnancy is shown in Figure 1. 29.1% of the pregnant women with BV also had *C. trachomatis* infection. Of the 179 women analyzed, 21 (11.7%) had preterm births, 20 (11.1%) delivered newborns with intrauterine growth restriction (IUGR), and 26 (14.5%) delivered low birthweight infants.

We did not find a significant difference in *C. trachomatis* infection rate in early pregnancy between the women who delivered LBW infants and women from the reference group (26.9% and 24.8%, respectively) (Table 1). *C. trachomatis* infection was found more frequently in the group of women who delivered before the 37th week of pregnancy (33.3%) compared with the control group (24.1%; *OR*=1.58, *CI*=0.53–4.58) (Table 2). *C. trachomatis* infection in early pregnancy was not related to SGA (Table 3).

Table 1. Association between *C. trachomatis* infection in early pregnancy and the risk of delivering a low birth-weight (LBW) infant.

	Newborn birth weight				*OR* (95% *CI*)
	<2500 g (n=26)		≥2500 g (n=153)		
C. trachomatis					
No Infection	19	73.6%	115	75.2%	Reference group
Infection	7	26.9%	38	24.8%	1.11 (0.39–3.09)

Table 2. *C. trachomatis* infection in early pregnancy and the risk of preterm delivery.

	Gestational age at delivery				*OR* (95% *CI*)
	<37 weeks (n=21)		≥37 weeks (n=158)		
C. trachomatis					
No Infection	14	66.6%	120	75.9%	Reference group
Infection	7	33.3%	38	24.1%	1.58 (0.53–4.58)

Table 3. *C. trachomatis* infection in early pregnancy and the risk of intrauterine growth restriction (IUGR).

	IUGR (n=20)		Non-IUGR (n=159)		*OR* (95% *CI*)
C. trachomatis					
No Infection	15	60.0%	117	73.6%	Reference group
Infection	5	20.0%	42	26.4%	0.95 (0.25–2.98)

Discussion

In an indigenous population of Central Poland we observed a relatively high prevalence of *C. trachomatis* infection (24.5%) among pregnant women diagnosed by a direct immunfluorescence test performed on endocervical swabs during early pregnancy. This relatively high prevalence of *C. trachomatis* infection could be partly explained by the negative socioeconomic and demographic characteristic of the population under study, e.g. high rate of unemployment, single marital status, poor educational level, and high incidence of cigarette smoking during gestation. Rastogi et al. [10] noted almost the same prevalence of *C. trachomatis* infection in a population of northern India (21.3%) diagnosed in the 12th week of gestation using the same method. According to the results obtained by Paul et al. [11], the infection rate was 17% during pregnancy and 18.6% during labor. A lower incidence of *C. trachomatis* (11%) was reported by Andrews et al. [7], determined by a ligase chain reaction assay of voided urine samples at 24 weeks of gestation, and Kovacs et al. [12] (5.74%), determined by the Gen-Probe method. The observed differences could be explained by the different methods used for *C. trachomatis* identification, the different populations under study, and various gestational ages at the time of sampling.

We observed a relatively high prevalence of *Chlamydia trachomatis* infection among women who delivered before the 37th week of gestation (33.3%). Gencay et al. [13] found serum antibody against *Chlamydia trachomatis* in 18.8% of women who delivered prematurely, diagnosed between 23 and 29 week of gestation. Andrews et al. [7] also observed a higher infection rate in 24th week of pregnancy among women who subsequently delivered before the 37th week of gestation compared with women who delivered at term (15.8% vs. 6.3%).

Though in our study *C. trachomatis* infection was found more frequently in the group of women who delivered before the 37th week of pregnancy, the calculated risk of preterm delivery for infected women was *OR*=1.58, *CI*=0.53–4.58. The lack of statistical significance was probably due to the small number of analyzed cases. Similar results were obtained by Kovacs et al. [12]; Paul et al. [11], and French et al. [13]. Paul et al. [11] did not find any differences in LBW rate, prematurity rate, and mean birth weight of their newborns between women with and without the infection during pregnancy. In contrast, Andrews et al. [7] calculated the risk of preterm delivery among women with *Chlamydia trachomatis* infection as *OR*=2.2 for delivery before the 37th week and as *OR*=3.2 for delivery before the 35th week of gestation. Rastogi et al. [10] also noted a statistically significant increased incidence of still-birth, prematurity, and low birth weight in *C. trachomatis*-positive women.

There are only a few papers regarding the association between *C. trachomatis* infection during pregnancy and intrauterine growth restriction. The results of The John

Hopkins Study of Cervicitis and Adverse Pregnancy Outcome [14] suggests that maternal genital tract colonization with *C. trachomatis* diagnosed between the 22nd and 30th weeks of pregnancy was significantly associated both with intrauterine growth restriction (*OR*=2.4) and preterm delivery (*OR*=1.6). These findings confirm the probable role of infection in preterm and IUGR births. Our results do not support an important role for *C. trachomatis* infection in the pathogenesis of SGA.

In our study, *C. trachomatis* infection was diagnosed in 29.1% of the women with BV and in 18.6% of the women with normal flora. Similar results were obtained by Hillier et al. [15], who diagnosed *C. trachomatis* infection in 28.4% women with BV compared with 14.8% in women without BV. These results suggest that *C. trachomatis* is probably an independent infection. Andrews et al. observed that women with chlamydia infection were more likely to have bacterial vaginosis (57.1% vs. 32.9%, *p*=0.02). The relatively high incidence of BV diagnosed in our population could also partly explain the high prevalence *of C. trachomatis* we observed.

The results of various studies evaluating the impact of *C. trachomatis* infection during pregnancy on adverse pregnancy outcome are still controversial. These controversies could be explained by the different populations under study, the different methods used for *C. trachomatis* identification, and the different gestational ages at the time of investigation. Not only colonization by selected microorganisms, but also impairment of the mucosal and local immune system are probably responsible for specific subsequent negative perinatal outcomes observed among pregnant women with *Chlamydia trachomatis* infection.

Taking into account the well-known negative impact of *Chlamydia trachomatis* infection during pregnancy on neonate health and the possible role of this infection in preterm delivery, further, carefully designed intervention studies are needed.

CONCLUSIONS

1. *Chlamydia trachomatis* infection in early pregnancy could be associated with the additional risk of preterm delivery, but not with delivering low birth-weight or small for gestational age infants.
2. The high prevalence of *Chlamydia trachomatis* infection diagnosed in early pregnancy observed in our study and the negative impact of this infection on the newborns' health indicate the need for more precise evaluation of the role of *Chlamydia trachomatis* infection during pregnancy.

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