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Chlamydia trachomatis infection and the risk of perinatal mortality in Hungary

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1 Introduction

Epidemiological evidence indicates that chlamydial infections of the genital tract are a global problem. In pregnancy, *Chlamydia trachomatis* may cause a wide range of serious complications, including premature delivery, ophtalmia neonatorum and neonatal pneumonia. Thus, *C. trachomatis* is a major cause of neonatal morbidity and mortality.

Premature delivery is the most important perinatal problem in Hungary [3] as Czeizel and [10] Orvos have reported. In most cases the underlying cause is not known. A breakthrough in the prevention of this problem requires more data about the causes leading to premature uterine contractions. A large number of anecdotal observations suggest that *C. trachomatis* infections may have a causative role in the origin of premature delivery [5, 7, 14]. Consequently, a multicenter survey was carried out in order to determine the prevalence and risk factors for *C. trachomatis* infection in the pregnant population in Hungary [8] as Nyári has reported. The data set of the Hungarian survey was reanalyzed in order to provide further information on the relationship between neonatal mortality and genital chlamydial infections and to estimate the frequency of these infections.

2 Materials and methods

2.1 The protocol

The study started in January 1994 and terminated in June 1995, in seven different hospitals of two regions (east and west) in Hungary. The nucleic acid hybridization method (PACE2 Gen-Probe, Medical System®) was applied for the examination of *C. trachomatis*. The sensitivity and specificity of this method are known to be 70 % and 99 % respectively [6] as Newhall has reported; Bayes' theorem was applied to estimate the prevalence of the infection [11]. The envisaged sample size was calculated using Hsieh's formula for logistic regression [4]. Assuming a 5 % significance test, a power of 90 %, and a 5 % estimated probability of the infection, this resulted in a sample size of 1550 women per region. The *C. trachomatis-positive* pregnant patients received roxithromycin treatment (150 mg × 2 daily 10 days). Premature uterine activity was defined as any uterine contractions before the 38th gestational week. Low birth weight was defined as birth weight less than 2500 g. The average unemployment rate in Hungary was 6−7 %. If the unemployment rate was less than 4 % or greater than 8 %, then they were regarded as low or high, respectively.

2.2 Data collection

The screening was performed before delivery. The target population was all women registered as singleton pregnant with their hospital, and all of them were asymptomatic as concerns of genital infection. The *C. trachomatis* screening was performed at the time of admission to the hospital in labor. The sample was selected using simple

random sampling. An interviewer-administered standardized questionnaire was completed, in which age, social and marital status, obstetrical and neonatal history data were recorded. To preserve confidentially, unique codes were used. Data management was carried out with self-developed software. All personal data were protected from illegal use.

2.3 Data analysis

Statistical analyses were performed with the SPSS for Windows (8.0 version) software package. To compare *C. trahomatis* infected and non-infected groups chi-square tests were employed. Odds ratios (OR), as estimators of relative risks, together with their corresponding 95 % confidence intervals (CI), were computed, using unconditional multiple logistic regression, fitted by the method of maximum likelihood allowing for several possible confounding factors. A p value of less than 0.05 was used to indicate a significant effect.

3 Results

3.1 *C. trachomatis* infection

A total of 6156 pregnant women were examined for the occurrence of *C. trachomatis*. The overall average *C. trachomatis* infection rate was 5.9 %, the data varying in the range 1.3−9.8 % (table I.). In case of the sensitivity of the PACE2 Gen-Probe test for detection of *C. trachomatis* was only 70 %, the estimated prevalence of *C. trachomatis* infection in this population could be as high as was 7.1 %, because the additional 30 % of patients with suspected infection could have been detected. These centers were categorized into two regions based on the rate of unemployment. An average rate of unemployment occurred in the western region (3.4 %) and a significant high one (7.2 %) in the eastern region.

Certain potential risk factors for *C. trachomatis* infection were examined: age, unemployment rate and family status. Young age (less than 24 years old), unmarried status and the high unemployment rate were statistically significant predictors of the infection (table II).

There was a significant difference ($p = 0.001$) between the rate of premature uterine activity that occurred in the infected group (8.1 %), and the non-infected group (5.3 %). Premature rupture of the membranes (PROM) occurred in 21.0 % of the *C. trachomatis*-positive group and 19.9 % of those without infection.

3.2 Perinatal mortality

Perinatal mortality occurred in 148 (2.4 %) of 6156 pregnancies. There was a significantly higher ($p = 0.042$) mortality rate (4.1 %) in the

Table I. Observed *C. trachomatis* infection rates for the centers

Center	N	*C. trachomatis* positive	Observed rate of infection (%)
Western region (average rate of unemployment)	2146	73	3.4
Szeged	996	32	3.2
Budapest I	187	15	8.0
Budapest II	674	20	3.0
Szombathely	289	6	2.1
Eastern region (high rate of unemployment)	4010	289	7.2
Debrecen	473	6	1.3
Miskolc	2112	208	9.8
Nyíregyháza	1416	75	5.3
Total	6156	362	5.9

Table II. Risk factors for *C. trachomatis* infections among 6156 pregnant women

Risk factors	N	Number of *C. trachomatis*-infections	Rate of chlamydial infection (%)	Odds ratio (95% CI)	p value*
Age					p = 0.0002
< = 24 years	2469	196	7.9	1.6 (1.3−2.0)	
> 24 years	3687	166	4.5	1.0	
Family status					p = 0.0014
unmarried	1152	98	8.5	1.5 (1.2−1.9)	
married	5004	264	5.3	1.0	
Rate of unemployment					p = 0.0001
high	4010	289	7.2	2.1 (1.6−2.7)	
normal	2146	73	3.4	1.0	

* Adjusted odds ratios and p values from multivariate logistic regression analysis. The Hosmer and Lemeshow statistics to assess model goodness of fit had a value of 5.47 with 4 df (p = 0.24). Thus this measure supports the model's adequacy for the data.

group of *C. trachomatis*-positive patients than in the group of negative patients (2.3 %). In the group of 148 perinatal deaths, the maternal *C. trachomatis* infection rate was 10.1 %.

With regard to the *C. trachomatis* infection and perinatal mortality rates in the normal and low birth weight groups, among the 28 infants under 2500 g the maternal *C. trachomatis* infection rate was 21.4 %, whereas in the group of 120 infants above 2500 g the maternal infection rate was only 7.5 %. This difference was significant (p = 0.044).

In the multiple logistic regression analysis some potential risk factors of perinatal mortality were examined: age, demographic and social status, *C. trachomatis* infection, previous pregnancy, previous delivery, low birth weight, premature rupture of membrane, premature uterine activity, intrauterine distress and intrauterine growth retardation of the neonate. As shown in table III. *C. trachomatis* infection (OR and 95 % CI: 1.9 (1.1−3.3)), low birth weight (1.7 (1.1−2.7), no previous delivery (1.9 (1.3−2.7) and the high unemployment rate (1.5 (1.2−2.2)) were all significant predictors of the neonatal mortality (p < 0.05) in the multiple regression analysis.

4 Discussion

Numerous surveys have been carried out to study the prevalence of urogenital *C. trachomatis* infections. It is necessary to estimate the true prevalence of *C. trachomatis* infection because detection and treatment of asymptomatic cases should have a major impact on the incidence of chlamydial infection, as these asymptomatic individuals are an active source of new infections. Precise estimation of the prevalence of *C. trachomatis* infection is important in cost-effectiveness analysis [15]. In developed countries, the debate on *Chlamydia* control has centered on the cost-effectiveness of different approaches for identifying infected persons. Studies have concluded that, among women, case findings using laboratory tests is cost-effective at *C. trachomatis* prevalence rates as different as 6 % to 16 % [13] as Sellors et al found. In epidemiology, some methods have been suggested to correct for measurement error. In our analyses a Bayesian approach was employed for correcting measurement errors [2, 12]. In our study the observed overall rate of *C. trachomatis* infection in Hungary was 5.9 %, increased to 7.1 % based on the Bayesian approach. In the eastern region, where the rate of unemployment is high the prevalence is estimated to be 7.2 %.

Table III. Risk factors for perinatal mortality in pregnancies screened for *C. trachomatis*

Risk factors	N	Number of perinatal mortality outcome	Rate of mortality (%)	Odds ratio (95 % CI)	p value*
C. trachomatis infection					p = 0.033
infected	362	15	4.1	1.8 (1.1−3.3)	
non infected	5794	133	2.3	1.0	
Low birth weight					p = 0.020
Yes	645	24	3.7	1.7 (1.1−2.7)	
No	5400	120	2.2	1.0	
Previous delivery					p = 0.001
no previous delivery	3219	100	3.1	1.9 (1.3−2.7)	
previous delivery	2937	48	1.6	1.0	
Rate of unemployment					p = 0.010
high	4010	108	2.7	1.5 (1.1−2.2)	
normal	2146	40	1.9	1.0	

* Adjusted odds ratios and p values from multiple logistic regression analysis. (Data missing up to 111 women) The Hosmer and Lemeshow statistics to assess model goodness of fit has a value of 4.058 with 5 df (p = 0.54). This measure supports the model's adequacy for the data.

The perinatal mortality rate is one of the most important indicators of the quality of perinatal care. As with [7] Ngassa and [9] Orfila et al., our results suggest that *C. trachomatis* infection is of great importance in perinatal pathologies. The perinatal mortality rate was significantly higher in the *C. trachomatis* positive patients. The difference was more marked in the low birth weight group than in the normal birth weight cases. In the multiple regression analysis the *C. trachomatis* infection, low birth weight, no previous delivery and the high unemployment rate were independent statistically significant predictors of neonatal mortality.

In summary, testing pregnant women for diseases that can be transmitted perinatally is an important part of obstetric care. Screening for *C. trachomatis* is suggested only in high-risk pregnancies such as those involving an unfavorable obstetric history, a poor socio-economic situation and a young age less than 24 years old. Any attempt to prevent the spread of STDs must include the provision of contraceptives, sex education, efforts to arouse a more responsible attitude to pregnancy, and attempts to improve the social environment [1].

Abstract

Introduction: Chlamydial infections of the genital tract are thought to often lead to preterm birth, which is the most important perinatal problem in Hungary.
Aim of study: A multicenter study was carried out to determine the prevalence of *Chlamydia trachomatis* infection, risk factors for the infection and to relate the infection to perinatal mortality, accounting for potential confounding effects.
Methods: The nucleic acid hybridization method (PACE2 Gen-Probe) was applied for the examination of *Chlamydia trachomatis*. Logistic regression analysis was used to assess risk.
Results: A total of 6156 pregnant women were examined for the occurrence of *Chlamydia trachomatis*. The observed overall rate of *chlamydial* infection was 5.9 %. Young age (less than 24 years old) (OR and 95 % CI:1.6 (1.3−2.0)), unmarried status (1.5 (1.2−1.9)) and the high unemployment rate (2.1 (1.6−2.7)) were statistically significant predictors of the infection.

In logistic regression analysis, chlamydial infection (1.9 (1.1−3.3)), high unemployment rate (1.5 (1.2−2.2)) and low birth weight (1.7 (1.1−2.7) were significant predictors of perinatal mortality.

Conclusions: Testing pregnant women for diseases that can be transmitted perinatally is an important part of obstetric care. Screening for *C. trachomatis* of unmarried women under 24 years of age is suggested and need increased observation during labor.

Keywords: *Chlamydia trachomatis*, perinatal mortality, poor perinatal outcome, preterm birth, preventive care.

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