RESEARCH ARTICLE

The association between *Chlamydia trachomatis* genital infection and spontaneous preterm labour

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Objective. To determine the association between *Chlamydia trachomatis* genital infection, as found at the first antenatal visit, and spontaneous preterm labour.

Methods. Low-risk obstetric patients, attending the Bishop Lavis Midwife Obstetric Unit, were screened for *C. trachomatis* infection at the first antenatal visit between 16 and 23 weeks' gestation. Using a bivalve speculum, a swab was taken directly from the endocervix and examined by the polymerase chain reaction technique. At the same time a lateral vaginal smear was taken to examine for bacterial vaginosis. Analyses were done in batches after delivery. Clinicians responsible for the management of the pregnant women were therefore unaware of these test results. Patients were followed up during pregnancy and labour for complications such as delivery before 37 weeks.

Results. 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 ($p = 0.037$). The prevalence of bacterial vaginosis did not differ significantly between these two groups. There was 1 neonatal death in the preterm delivery group but no neonatal deaths among women who delivered at term.

Conclusion. An association was found between preterm delivery and *C. trachomatis* infection. An intervention study is indicated to determine whether specific treatment of this infection reduces the frequency of preterm labour.

According to a community-based study, the incidence rate of preterm delivery at Tygerberg Academic Hospital (TBH) in Cape Town, South Africa, is 20.3%. Spontaneous preterm labour is not only the most common single cause of neonatal death,[1] but also one of the major causes of delivery of a baby weighing between 750 g and 1 500 g.[2] This incidence rate of 20.3% is much higher than the 5 - 10% in industrialised countries.[3,4] Extreme preterm delivery is also a common cause of long-term disability.[5]

Infection is one of the most probable causes of preterm labour.[6,7] More specifically, it has been shown that bacterial vaginosis is a risk factor for preterm birth.[8]

In a previous study we found an association between preterm birth and *Mycoplasma hominis* and *Chlamydia trachomatis* infection.[9] This is in line with the finding that *Chlamydia* genitourinary infection at 24 weeks' gestation is associated with a doubling of the risk of preterm labour.[10] Two more recent studies also confirmed this association, as significantly more women who had had preterm deliveries than those with normal pregnancies had *C. trachomatis* IgG antibodies in their urethral and cervical smears.[11,12] The current study was designed to specifically address the effects of *C. trachomatis* genital infection on pregnancy outcome.

Methods

In a prospective study, pregnant women between 16 and 23 weeks' gestation were recruited at the booking antenatal clinic of the Bishop Lavis Midwife Obstetric Unit (MOU) in a residential area near TBH. Only low-risk pregnant mothers were included in the study, as those with previous or present complicated pregnancies were referred to TBH for further antenatal care. After the study had been explained to the pregnant women, informed consent was obtained. In the obstetric history special attention was given to risk factors for preterm labour such as a previous mid-trimester miscarriage, abortion or preterm delivery. Patients with multiple pregnancies were excluded from the study. After the general examination, a vaginal examination was done. To avoid contamination with K-Y jelly, the speculum examination was done without lubricant. A smear from the posterior vaginal fornix was then obtained by rolling a swab across the vaginal wall and then onto a glass slide. The slides were marked, heat fixed and Gram-stained. All smears were examined for bacterial vaginosis by one person, using the method described by Nugent *et al.*[13] Gestational age was determined by early ultrasound, the date of the last menstrual period or, if not available, clinically.

For detection of *C. trachomatis* by polymerase chain reaction (PCR), swabs were taken from the endocervix. Template DNA was extracted using a High Pure PCR Template Preparation kit (Roche) and PCR (primers and amplification conditions) conducted according to Class *et al.*[14] At the same examination, as part of a routine service, an endocervical swab was taken, put in a transport medium, and cultured for *Neisseria gonorrhoeae.* As part of the routine investigation blood was taken for a serological test for syphilis. Pregnant women with these two conditions were treated as soon as the positive result was found. However, analyses for *C. trachomatis* were only done in batches after completion of the pregnancy. These test results were therefore not available to the health care workers who followed these women up at the antenatal clinics. The same applies to the Nugent score for bacterial vaginosis, which was also done at the end of the study. When they gave birth the women belonging to the study were identified and clinical information regarding the pregnancy and neonatal outcome was obtained from the medical records. Endpoints were gestational age at delivery, birth weight, 5-minute Apgar score and intrauterine and neonatal deaths. Women who delivered at or after 37 weeks were compared with those who delivered before this gestation, and women who had positive tests for *C. trachomatis* were compared with those who had negative tests.

Statistical analyses were carried out using the statistical package for the social sciences (SPSS) version 10. Categorical data were analysed using the chi-square test; the odds ratio and the 95% confidence intervals were calculated where applicable. Where an expected cell value was less than 5, Fisher's exact test was used. Continuous data were analysed with the Student's *t*-test, and for non-parametric data the Mann-Whitney *U*-test. A *p*-value of 0.05 was regarded as significant.

The study was approved by the Committee of Human Research of Stellenbosch University, and was done between February 2002 and November 2003.

Results

There were 343 patients in the study, of whom 36 (10.5%) delivered before 37 completed weeks. When women who had preterm deliveries were compared with those who had term deliveries, no significant differences were found regarding age, gravity, parity, previous early pregnancy losses and body mass index (data not shown). *C. trachomatis* was found in 22.2% of mothers who had preterm deliveries, in contrast to 10.4% in the term delivery group (Table I). The frequency of other sexually transmitted diseases did not differ significantly. Perinatal outcomes are set out in Table II. All perinatal deaths occurred in the preterm delivery group. When the demographic data of mothers with positive and negative tests for *C. trachomatis* were compared, the only significant differences were the lower age and lower body mass index in the positive group (Table III). Only 1 woman in the *C. trachomatis* group was electively delivered before 37 weeks (for pre-eclampsia), while 3 in the other group were delivered before 37 weeks (2 for pre-eclampsia and 1 for antepartum haemorrhage). *N. gonorrhoeae* occurred more frequently in mothers who were positive for *C. trachomatis*. In addition, significantly more women with *C. trachomatis* infection also had bacterial

Table I. Sexually transmitted diseases and duration of pregnancy (*N* = 343)

	< 37 weeks (*N* = 36)	**>37 weeks (*N* = 307)**	**Significance**
C. trachomatis	8 (22.2%)	32 (10.4%)	$p = 0.037$
Syphilis	1 (2.8%)	19 (6.2%)	$p = 0.707$
N. gonorrhoeae	1 (2.8%)	2 (0.7%)	$p = 0.285$
Bacterial vaginosis			
Negative (A)	24 (66.7%)	181(59.1%)	A in comparison with B+C:
Intermediate (B)	1 (2.8%)	26 (8.5%)	$p = 0.384$
Positive (C)	11 (30.6%)	99 (32.4%) *	

*Result for 1 patient not available.

Table II. Perinatal outcome (*N* = 343)

	< 37 weeks	> 37 weeks	Significance
Delivery			
Vaginal	29 (73.3%)	283 (92.5%)	$p = 0.026$
Caesarean	7 (20%)	23 (7.5%)	(caesarean v. vaginal delivery)
Birth weight (g)			
Mean	1 880	3 098	$p = 0.0000$
SD	715	427	
Median	1 858	3 080	
5 min Apgar			
Mean	7.7	9.8	$p = 0.0000$
SD	3.3	0.6	
Median	9	10	
Outcome			
Normal	31	307	
Miscarriage	1	0	
IUD	3	0	
NND	1	0	

IUD = intrauterine death; NND = neonatal death.

Table III. Obstetric data for mothers with positive and negative *C. trachomatis* findings (*N* = 343)

	***C. trachomatis* pos. (*N* = 40)**	***C. trachomatis* neg. (*N* = 303)**	**Significance**
Age (yrs)			
Mean	20.6	23.1	$p = 0.0016$
SD	4.6	5.5	
Median	19	22	
Gravidity			
Mean	1.6	1.8	$p = 0.1531$
SD	0.9	1.1	
Median	1	2	
Parity			
Mean	0.6	0.8	$p = 0.1588$
SD	0.9	1.0	
Median	0	0	
Previous miscarriage	1	23	
Previous ectopic	0	1	
Previous TOP	2	3	
BMI			
Mean	22.9	24.7	$p = 0.036$
SD	4.1	5.4	
Median	22.1	23.8	

vaginosis (Table IV). The frequencies of other sexually transmitted diseases did not differ significantly between these groups. There were no perinatal deaths in the *C. trachomatis*-positive group. All the perinatal deaths occurred in preterm babies born to mothers in whom *C. trachomatis* was not found.

Discussion

The fact that preterm deliveries occurred in 10.9% of low-risk mothers illustrates the problem of preterm delivery in this community. The overall frequency of *C. trachomatis* in the study was 11.7%. The present study confirms the high rate of *C. trachomatis* in this population, as was found in a previous hospital-based study conducted in 1992, where a rate of 11% among pregnant women was reported.[15] Screening for *C. trachomatis* is not part of the antenatal care programme at Tygerberg Hospital, and as a research initiative, the PCR tests for *C. trachomatis* were performed in batches after the patient had delivered. For these reasons patients and their newborns could not be treated for this infection. The tests for *C. trachomatis* were done blindly and patients' codes were only broken when the data were analysed. The significantly higher rate of preterm labour in mothers with positive tests for *C. trachomatis* raises the question whether the organism causes preterm labour. No randomised controlled trial could be found on the treatment of *C. trachomatis* during pregnancy. However, in an uncontrolled study 42 *Chlamydia*-positive patients, who were lost to follow-up, were compared with 17 women who received treatment. Duration of pregnancy was increased by 2.4 weeks in the treated group.[16]

In one of the first publications on the diagnosis of bacterial vaginosis by Gram stain, Spiegel *et al.*

Table IV.	Other sexually transmitted diseases in mothers with and without *C. trachomatis* (*N* = 343)		
	***C. trachomatis* pos**	***C. trachomatis* neg**	
	(*N* = 40)	**(*N* = 303)**	**Significance**
Syphilis	2 (5%)	18 (6%)	$p = 1$
N. gonorrhoeae	2 (5%)	1 (0.3%)	$p = 0.0373$
Bacterial vaginosis			
Negative (A)	17 (42.5%)	189 (62.4%)	A in comparison with
Intermediate (B)	8 (20%)	19 (6.3%)	B+C: $p = 0.0158$
Positive (C)	15 (37.5%)	95 (31.3%)	OR = 2.24
			(95% CI 1.10 - 4.61)

OR = odds ratio; CI = confidence interval.

concentrated mainly on *Lactobacillus* and *Gardnerella* morphotypes.[17] Nugent *et al.* expanded on this by adding *Bacteroides* spp. morphotypes and curved Gram-variable rods.[18] In a population-based microbiological study on 4 596 pregnant women, it was found that the dominating micro-organisms were *M. hominis, G. vaginalis* and anaerobic bacteria.[19] However, many other organisms were also found, further indicating that bacterial vaginosis is a rather general diagnosis.[19] It should also be remembered that *M. hominis* is associated with several genital signs and symptoms, even after exclusion of bacterial vaginosis.[20] A specific diagnosis should therefore always be made if possible, rather than relying on a very general diagnosis such as bacterial vaginosis. In a previous study we failed to demonstrate prolongation of pregnancy by treating bacterial vaginosis with metronidazole.[21] The most likely reason for this finding is that the specific underlying cause was not identified. Bacterial vaginosis was treated while the underlying problem could have been *C. trachomatis*.

In the present study an association was also found between *C. trachomatis* infection and low body mass index (BMI) and maternal age. However, low BMI or low maternal age was not associated with preterm labour. The younger maternal age and lower BMI, as we found in the *C. trachomatis*-positive group, are therefore more likely to be part of the profile of women with sexually transmitted diseases. The present study failed to demonstrate an association between bacterial vaginosis and preterm labour, but the association of *C. trachomatis* and bacterial vaginosis was confirmed. In the future, positive screening tests for bacterial vaginosis should be followed by more specific tests and intervention studies are indicated to establish whether *C. trachomatis* causes some of the deliveries before term. The aim of the study was not to find a way of predicting preterm labour (for this the sensitivity and positive predictive values are too low) but to learn more about the factors causing preterm labour. At this stage it is still unknown whether *C. trachomatis* causes or is associated with preterm labour. Intervention studies are needed.

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