SEROLOGIC EVIDENCE OF *CHLAMYDIA TRACHOMATIS* INFECTION AND RISK OF PRETERM BIRTH

Paul Claman, MD; Baldwin Toye, MD; Rosanna W. Peeling, PhD; Peter Jessamine, MD; Judy Belcher, RN

Abstract • Résumé

Objective: To determine whether serologic evidence of *Chlamydia trachomatis* during pregnancy is a risk factor for preterm delivery (before 37 weeks' gestation).

Design: Chart review.

Setting: Antenatal clinics associated with a teaching hospital.

Patients: A group of 103 unselected consecutive patients presenting for routine prenatal care.

Outcome measures: Pregnancy outcome and C. *trachomatis* serologic status.

Results: A total of 21 women (20%) were found to be seropositive for IgG antibodies to C. *trachomatis*. They were similar to the seronegative women with respect to maternal age, parity, history of preterm birth, obstetric or medical problems, smoking status, history of drug abuse, educational status and psychosocial stressors. The seropositive women were significantly more likely than the seronegative women to have a preterm birth (24% [5/21] v. 7% [6/82]; $p = 0.029$, odds ratio 3.96, 95% confidence interval 1.08 to 14.57), an infant with a lower mean gestational age at birth (262 [standard deviation (SD) 19] days v. 273 [SD 15] days; $p = 0.0052$) and an infant with a lower mean birth weight (3125 [SD 692] g v. 3473 [SD 696] g; $p = 0.0434$). The positive predictive value of a seropositive result for preterm birth was 31% (5/16); the negative predictive value of a seronegative result for preterm birth was 8% (6/76).

Conclusion: Women with serologic evidence of C. *trachomatis* may be at risk for preterm birth. Further study is required to determine whether serologic testing for C. *trachomatis* should be a routine part of prenatal care.

Objectif : Déterminer si les indications sérologiques de *Chlamydia trachomatis* au cours de la grossesse constituent un facteur de risque en cas d'accouchement avant terme (avant 37 semaines de gestation).

Conception : Examen de dossiers.

Contexte : Cliniques anténatales associées à un hôpital d'enseignement.

Patientes : Un groupe de 103 patientes consécutives, sans sélection particulière, qui se sont présentées pour des soins prénataux de routine.

Mesures des résultats : Issue de la grossesse et état sérologique par rapport à la C. *trachomatis*.

Résultats : Au total, on constaté que 21 femmes (20 %) étaient séropositives pour les anticorps de l'IgG à la C. *trachomatis*. Elles présentaient des caractéristiques semblables à celles des femmes séronégatives en ce qui a trait aux aspects suivants : âge, parité, accouchements avant terme antérieurs, problèmes obstétriques ou médicaux, tabagisme, antécédents d'abus de drogues, niveau de scolarité et facteurs de stress psychosociaux. Les femmes séropositives étaient beaucoup plus susceptibles que les femmes séronégatives d'accoucher avant terme (24 % [5/21] c. 7 % [6/82]; $p = 0,029$, ratio des probabilités 3,96, intervalle de confiance à 95 % 1,08 à 14,57), et d'accoucher d'un bébé d'âge moyen de grossesse à la naissance moins élevé (262 [écart type (ET) 19] jours c. 273 [ET 15] jours; $p = 0,0052$) et de poids moyen à la naissance inférieur (3125 [ET 692] g c. 3473 [ET 696] g; $p = 0,0434$). La valeur prédictive positive d'un résultat séropositif à l'égard d'une naissance avant terme s'est établie à 31 % (5/16) et la valeur prédictive négative d'un résultat séronégatif à l'égard d'une naissance avant terme, à 8 % (6/76).

Conclusion : Les femmes qui présentent des signes sérologiques de C. *trachomatis* peuvent risquer d'accoucher avant terme. Une étude plus poussée s'impose pour déterminer si le dépistage sérologique de C. *trachomatis* devrait faire partie des soins prénataux de routine.

Dr. Claman and Ms. Belcher are in the Division of Reproductive Endocrinology, Department of Obstetrics and Gynecology, Ottawa Civic Hospital and University of Ottawa, Ottawa, Ont. Dr. Toye is in the Division of Infectious Disease, Department of Medicine, and the Division of Microbiology, Department of Pathology and Laboratory Medicine, Ottawa General Hospital and University of Ottawa, Ottawa, Ont. Dr. Peeling is with the National Laboratory for Sexually Transmitted Diseases, Laboratory Centre for Disease Control, Ottawa, Ont. Dr. Jessamine is in the Division of Microbiology and Immunology, Department of Laboratory Medicine, and the Division of Infectious Disease, Department of Medicine, Ottawa Civic Hospital and University of Ottawa, Ottawa, Ont.

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Reprint requests to: *Dr. Paul Claman, 552–737 Parkdale Ave., Ottawa ON K1Y 4E9; fax 613 724-4942*

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An association has been described between tubal infertility, preterm birth and *Chlamydia trachomatis* infection.[1-3] However, antenatal screening for *C. trachomatis* infection is not done routinely because it has not been shown to be cost-effective. Furthermore, screening asymptomatic women with the widely used antigen detection assays may yield significant numbers of false-negative results.[4]

Serologic evidence of previous *C. trachomatis* infection has been found to be associated with ectopic pregnancy,[5] tubal infertility[6,7] and possibly miscarriage.[8,9] However, few studies have examined the relation between serologic evidence and preterm birth.[3,10] Cohen and colleagues[10] failed to identify an association between serologic evidence of IgG antibodies to *C. trachomatis* and preterm labour. However, they used a case–control design to determine the prevalence of *C. trachomatis* infection in a small number of women experiencing preterm labour, not all of whom went on to preterm delivery. Furthermore, they used a relatively insensitive single-serovar immunoperoxidase assay to detect the antibodies.

Martin and associates[2] found that in a group of pregnant women with active *C. trachomatis* infection 28% delivered before 37 weeks' gestation, as compared with 6% of uninfected women. Harrison and collaborators[3] studied the serologic status of 72 pregnant women for whom culture results were positive for *C. trachomatis*. They found that active infection did not constitute a risk factor for premature rupture of membranes or low-birth-weight infants unless IgM antibodies were also present: 41% and 23% of the women with IgM antibodies had premature rupture of membranes and low-birth-weight infants respectively, as compared with 7% and 2% of those who were IgM negative. Their data differed from those of Martin and associates, who found that women with positive cultures alone constituted a group at high risk for preterm labour.

To explore further the association between *C. trachomatis* exposure and preterm birth, we studied the serologic status of 103 consecutive patients at an antenatal clinic using a microimmunofluorescence (MIF) assay.

Methods

Serologic testing for IgG and IgM antibodies to *C. trachomatis* was performed in an unselected consecutive series of 103 women attending antenatal clinics associated with the Ottawa Civic Hospital. Routine antenatal care did not include screening for *C. trachomatis* infection. None of the patients had a multiple pregnancy or was symptomatic for cervical chlamydial infection.

Delivery-room and clinic records were examined retrospectively to determine the gestational age at birth, birth weight, maternal age, parity, history of preterm birth, illnesses or obstetric complications known to lead to preterm birth (e.g., abruptio placentae, placenta previa, preeclampsia or insulin-dependent diabetes mellitus), smoking status, history of drug abuse (e.g., cocaine or narcotics), educational status (completion of high school) and psychosocial stressors during pregnancy (e.g., single teenaged parent, recent divorce or move).[11-13]

Serum was aliquoted from blood samples taken routinely during antenatal care. MIF assay was then performed with the use of purified formalin-fixed elementary bodies.[6,14] The samples were screened at a dilution of 1:8 and titred at twofold dilutions to the end point. *C. trachomatis* seropositivity was defined as a titre of 1:8 or greater.[15]

The data were analysed with the use of the χ^2 test, Student's *t*-test and Fisher's exact test as appropriate.[16]

Results

Of the 103 women 21 (20%) were found to be positive for IgG antibodies to *C. trachomatis* (Table 1). All of the patients were negative for IgM antibodies. Compared with the seronegative women, those who were seropositive were significantly more likely to deliver before 37 weeks' gestation and to have infants with a lower mean gestational age at birth and a lower mean birth weight. The two groups did not differ significantly with respect to mean maternal age, parity, history of preterm birth, presence of illness or obstetric complications known to lead to preterm birth, smoking status, history of drug abuse, completion of high school or psychosocial stressors during pregnancy. Two of the five seropositive women and three of the six seronegative women who had a preterm birth had important obstetric or medical problems (e.g., placentia previa, preeclampsia or diabetes mellitus) during pregnancy.

The positive predictive value of a seropositive *C. trachomatis* test result for the occurrence of preterm birth (i.e., the number of seropositive women who had a preterm birth divided by the number of seropositive women who did not) was 31% (5/16). The negative predictive value of a seronegative result for preterm birth (i.e., the number of seronegative women who had a preterm birth divided by the number of seronegative patients who did not) was 8% (6/76).

Discussion

Our data indicate that serologic evidence of *C. trachomatis* infection is associated with an increased risk for preterm delivery. An odds ratio of 3.96 for preterm birth among the seropositive women suggests that the serologic status may be more important than other known risk factors for preterm birth. The observed preterm

birth rate of 7% among the seronegative patients was similar to that reported among low-risk obstetric patients attending antenatal clinics in developed countries.[11]

Our findings differ from those of Cohen and colleagues,[10] who were unable to identify differences in the prevalence of antibodies to *C. trachomatis* between a small group of 28 women with premature contractions and 43 women who delivered at term. Their case–control design with small numbers may have resulted in a type II error. In addition, they studied patients who had premature contractions rather than preterm delivery. Many patients admitted to hospital with premature contractions do not deliver preterm. Furthermore, the single-serovar immunoperoxidase assay they used is not as sensitive or as specific as the MIF assay, which uses purified *C. trachomatis* elementary bodies of multiple serovars.[17]

The overall seroprevalence rate in our study (20%) was similar to that in a study by Witkin and Ledger[8] involving pregnant women who had had recurrent spontaneous abortion. Our rate was much higher than the rate of active infection (as detected by means of culture or antigen-detection techniques) among women of childbearing age.[18] This is not surprising, since in most cases a seropositive status would occur with either active infection or a history of infection.

Whereas IgM antibodies are usually associated with a primary infection, the presence of IgG antibodies in our cohort provides evidence of a prior or possibly a persistent *C. trachomatis* infection. Tubal infertility in women with prior *Chlamydia* infection is also strongly correlated with seropositivity and is believed to be immune mediated.[6] Perhaps late-pregnancy complications due to *C. trachomatis* infection require a robust immunologic response with initial IgM production followed by long-term IgG seropositivity. Further studies are needed to determine whether the pathophysiologic mechanism behind the association between *C. trachomatis* seropositivity and the risk for preterm birth is due to microbial or immune-mediated factors. Also, serologic evidence of *C. trachomatis* might be a marker for other sexually transmitted diseases (e.g., mycoplasmal infection[3]) that would place patients at risk for preterm delivery.

Because genital *Chlamydia* infection is now the most prevalent bacterial sexually transmitted disease in most countries and because 50% to 70% of affected women are asymptomatic, further studies are needed to determine whether serologic screening for *C. trachomatis* would be a useful part of routine prenatal care to identify patients at risk for preterm delivery.

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Table 1: Characteristics of 103 consecutive patients attending antenatal care clinics who were or were not seropositive for *Chlamydia trachomatis* and outcome of pregnancy

Characteristic/outcome	Seropositive women *n* = 21	Seronegative women *n* = 82	*p* value*
Mean maternal age (and standard deviation [SD]), yr	31 (6)	30 (5)	NS
Nulliparous, no. (and %) of women	7/21 (33)	23/82 (28)	NS
History of preterm birth, no. (and %) of women	3/21 (14)	6/82 (7)	NS
Obstetric or medical problems, no. (and %) of women	7/21 (33)	14/82 (17)	NS
Cigarette smoking, no. (and %) of women	6/21 (29)	21/82 (26)	NS
Drug abuse, no. (and %) of women	1/21 (5)	2/82 (2)	NS
High school graduate, no. (and %) of women	15/17 (88)	51/53 (96)	NS
Presence of psychosocial stressors, no. (and %) of women	6/21 (29)	22/82 (27)	NS
Preterm birth, no. (and %) of women	5/21 (24)	6/82 (7)	0.029†
Mean gestational age (and SD), days	262 (19)	273 (15)	0.0052
Mean birth weight (and SD), g	3125 (692)	3473 (696)	0.0434

*NS = not significant.
†Odds ratio = 3.96, 95% confidence interval = 1.08 to 14.57.

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Aug. 16–19, 1995: Canadian Society for Epidemiology and Biostatistics Conference '95
St. John's
CSEB Conference '95 Office, c/o Health Research Unit, PO Box 23068, St. John's NF A1B 4J6; tel 709 737-6720, fax 709 737-7382

Aug. 17–18, 1995: Discoveries in Heart Failure: Exploiting New Understanding for Novel Therapeutic Development
Philadelphia
International Business Communications USA Conferences Inc., 225 Turnpike Rd., Southborough MA 01772-1749; tel 508 481-6400, fax 508 481-7911

Aug. 24–26, 1995: Canadian Health Economics Research Association 6th Canadian Conference on Health Economics: Change and Resistance in Health Care Systems
Waterloo, Ont.
Dr. Doug McCready, School of Business and Economics, Wilfrid Laurier University, Waterloo ON N2L 3C5; tel 519 884-1970, fax 519 884-0201

Sept. 7–9, 1995: American Association of Critical-Care Nurses Leadership Institute — Innovations in Healthcare: Continuing to Transform the Environment
San Francisco
Study credits available.
American Association of Critical-Care Nurses, 101 Columbia, Aliso Viejo CA 92656-1491, tel 714 362-2000, fax 714 362-2020

Sept. 8–10, 1995: Pri-Med (Primary Medicine Today) Conference and Exhibition for Primary Care Practitioners
Boston
Study credits available.
Hill Holliday Exhibition Services Inc., The John Hancock Tower, 200 Clarendon St., Boston MA 02116; tel 617 859-4476, fax 617 859-4357

Sept. 10–13, 1995: 12th European Conference on Biomaterials
Porto, Portugal
12th European Conference on Biomaterials, Instituto de Engenharia Biomédica, Praça Coronel Pacheco, 1, 4000 Porto, Portugal; tel 011 351 2 208-7131, fax 011 351 2 208-7310

Sept. 13–16, 1995: Canadian Transplantation Society and Canadian Association of Transplantation Annual Meeting
Montreal
Collette Birks, director of communications, Quebec Transplant, 1560 Sherbrooke St. E, Montreal QC H2L 4K8; tel 514 876-6768

Sept. 13–17, 1995: Royal College of Physicians and Surgeons of Canada 64th Annual Meeting (in association with the Canadian Society for Clinical Investigation and 37 national specialty societies)
Montreal
Anna Lee Chabot, head, Meetings and Assemblies Section, Office of Fellowship Affairs, Royal College of Physicians and Surgeons of Canada, 774 Echo Dr., Ottawa ON K1S 5N8; tel 613 730-6201, fax 613 730-8252

Sept. 14, 1995: Biomedical Communication Workshops (presented by the Canada Chapter of the American Medical Writers Association and held in conjunction with the Royal College of Physicians and Surgeons of Canada Annual Meeting)
Montreal
Ann Bolster, Publications Department, Canadian Medical Association, PO Box 8650, Ottawa ON K1G 0G8; tel 613 731-8610 or 800 663-7336, ext. 2117; fax 613 523-0937; abolster@hpb.hwc.ca

Sept. 20, 1995: Symposium on Advances in Reproductive Endocrinology and Infertility (precedes the Canadian Fertility and Andrology Society Annual Meeting Sept. 21–23)
Montebello, Que.
Canadian Fertility and Andrology Society, 409–2065 Alexandre de Sève St., Montreal QC H2L 2W5; tel 514 524-9009, fax 514 524-2163

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