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Chlamydia trachomatis IgG3 seropositivity is a predictor of reproductive outcomes in infertile women with patent fallopian tubes

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Abstract

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Objective—To determine if *Chlamydia trachomatis* (Ct) seropositivity as detected by the Ct elementary body (EB)-based enzyme linked immunosorbent assay (Ct EB ELISA) predicts pregnancy and pregnancy outcome among infertile women with documented tubal patency.

Design—Cohort study

Setting—Outpatient clinics participating in the reproductive medicine network

Patients—1250 infertile women with documented tubal patency enrolled in one of two randomized controlled trials: PPCOSII and AMIGOS

Intervention—Sera were analyzed for anti-Ct IgG1 and IgG3 antibodies using a research Ct EB ELISA. OD_{405} readings ≥0.35 and ≥0.1 were considered positive for IgG1 and IgG3, respectively.

Main Outcome Measures—Primary outcomes included pregnancy, live birth, and ectopic pregnancy. Log linear regression was used to determine the relative risk after adjusting for age, race, treatment medication, smoking status, and current alcohol use.

Results—243 (19%) women were seropositive for anti-Ct IgG3. They tended to be non-White and smokers. Anti-Ct IgG3 seropositive women were significantly less likely to conceive (RR 0.65, 95% CI 0.52-0.83) or to have a live birth (RR 0.59, 95% 0.43-0.80); these associations were weakened after adjusting for number of HSG-documented patent tubes (RR 0.73, 95% CI 0.56-0.97) and (0.73, 95% CI: 0.50-1.04), respectively. Anti-Ct IgG3 seropositive women who conceived had 2.7 (95% CI: 1.40-5.34) times the risk of ectopic pregnancy.

Conclusions—Even in the presence of tubal patency, anti-Ct IgG3 seropositivity is associated with lower likelihood of pregnancy. Anti-Ct IgG3 seropositive women have up to 3 times the risk of ectopic pregnancy.

Keywords

Chlamydia trachomatis; Infertility; Pregnancy; Ectopic Pregnancy

Introduction

Ascending *Chlamydial trachomatis* (Ct) infection induces inflammation, damage to the ciliated cells of the fallopian tubes, and pelvic adhesion formation. Furthermore, untreated upper genital tract infections can lead to irrevocable damage to the fallopian tubes including proximal and distal tubal occlusion and the formation of hydrosalpinges. This can lead to sterility if both fallopian tubes are affected. Tubal and peritoneal pathologies are the most common causes of infertility, affecting approximately 30-35% of couples (1). Symptomatic upper genital tract infections are diagnosed clinically as pelvic inflammatory disease. The risk of tubal factor infertility following one episode of pelvic inflammatory disease is approximately 10-12%; risk increases with recurrent episodes (2).

Previous exposure to Ct can be determined by assessing serostatus for anti-Ct immunoglobulin G (Ct IgG). A variety of immunoassays have been utilized for the detection of Ct IgG, including the micro-immunofluorescent antibody assay, enzyme immunoassay, and immunofluorescent assay. Commonly results are reported as titers (Ct titer, CTT). While the cut-off value for the titer that defines seropositivity varies, previous studies suggest that

CTT is a sensitive screening test for bilateral tubal obstruction among women with infertility (3-11).

The specificity of commercial assays is limited by their cross-reactivity to *Chlamydia pneumoniae*. However, more specific assays are in development. In 2012 Geisler et al. used a sensitive and specific Ct elementary body-based enzyme linked immunosorbent assay (EB ELISA) to demonstrate that IgG1 and IgG3 comprise the predominant serum anti-Ct antibody response; seropositivity appeared to be sustained for 6 months (12). In their study of 98 patients with current chlamydial infections, 73% tested seropositive using the commercially available Ct- IgG-ELISA plus Medac (Medac, Germany), compared with 90% seropositivity with the EB ELISA.

Given the prior observed relationship between CTT and tubal disease, and the development of an assay that appears to be superior in the detection of prior infection, we sought to examine the relationship between Ct seropositivity and outcomes following non-ART treatment for non-tubal factor infertility. Specifically we sought to determine if Ct seropositivity as detected by the Ct EB ELISA predicts pregnancy and pregnancy outcome among infertile women with documented tubal patency. Were this hypothesis to be confirmed, we would infer the value of screening infertile women to identify those at risk for poor reproductive outcomes despite tubal patency.

Materials and Methods

This is a cohort study of 1251 women enrolled in two trials conducted by the NICHD Cooperative Reproductive Medicine Network: PPCOS II and AMIGOS. PPCOS II was a randomized controlled trial comparing clomiphene citrate and letrozole for the treatment of infertility due to polycystic ovarian syndrome. AMIGOS was a randomized controlled trial comparing treatment with gonadotropins, clomiphene citrate, or letrozole in conjunction with intrauterine insemination in the treatment of unexplained infertility. Inclusion and exclusion criteria have been previously published (13, 14). In both trials women were between the ages of 18 and 40. Male partners had a screening semen analysis with at least 14 million sperm per milliliter (PPCOS II) or 5 million sperm per milliter (AMIGOS) with documented motility. Tubal patency was documented by one of the three following criteria: 1) a hysterosalpingogram or laparoscopy showing at least one patent fallopian tube; 2) saline infusion sonography showing accumulation of fluid in the cul-de-sac; or 3) prior uncomplicated intrauterine pregnancy resulting in live birth in the preceding 3 years (8 women or <1% of subjects). Women enrolled in AMIGOS were also required to be regularly ovulating. In both trials women provided a blood sample at baseline prior to treatment. Consent was requested of all participants for storage and use of deidentified samples for future research. IRB approval was obtained for both trials.

Women enrolled in PPCOS II (N=750) were randomized to up to 5 cycles of medications and were instructed to have regular intercourse. Women enrolled in AMIGOS (N=900) were randomized to up to 4 cycles of medications followed by intrauterine insemination. Pregnancy was detected by serum human chorionic gonadotropin levels, followed by

transvaginal ultrasound between 6 and 9 weeks to document fetal viability. Pregnancy outcomes were confirmed by a review of medical records.

Of the 1650 women enrolled in the two trials, 1251 consented for use of residual samples for future research. Serum was tested at the University of Alabama at Birmingham for anti-CT IgG1 and IgG3 antibodies using a Ct EB ELISA by reported methods (12). The optical density (OD) of reactions was measured at 405nm (OD_{405}) and cut-off values for positive IgG1 and IgG3 were ≥0.35 and ≥0.1, respectively. The reported serological responses represent the mean of triplicate determinations of 1/32 diluted serum.

Outcomes of interest for this study included conception, ectopic pregnancy, and live birth. Conception was defined as a rising serum level of human chorionic gonadotropin on two consecutive tests (AMIGOS) or a serum level of human chorionic gonadotropin of more than 10 mIU per milliliter (PPCOS II).

Chi square analyses were used to compare each outcome (conception, ectopic pregnancy [among those that conceived], and live birth) by Ct seropositivity for IgG1, IgG3, and IgG1 or IgG3. Preliminary analyses suggested the strongest relationship with the primary outcomes and anti-Ct IgG3 serostatus. For this reason, bivariate analyses including t-test, chi square analyses, and Fischer exact tests were performed, where appropriate, to assess the relationship between other covariates and anti-Ct IgG3 serostatus. Subsequently log-binomial regression models were created to determine the independent association between anti-Ct IgG3 serostatus and each outcome as measured by relative risk with 95% confidence intervals. Initially all potential confounders were included in the model but subsequently covariates that did not change the point estimate by more than 10% were removed from the model to achieve a more parsimonious model. STATA 13.0 (College Station, Texas) was used for all analyses.

Results

Ct serostatus results were obtained in 1250 (>99%) of the samples. 243 (19%) were seropositive for IgG3, 331 (26%) for IgG1, 397 (32%) for either IgG1 or IgG3, and 177 (14%) for both. 449 (36%) of participants conceived, 311 (25%) had a live birth, and 23 (2%) had an ectopic pregnancy.

Bivariate analyses for anti-Ct IgG subclasses and each outcome are presented in Table 1. Ct seropositivity for either IgG1 or IgG3 was inversely associated with conception and the probability of live birth. However, only Ct seropositivity for IgG3 was a significant predictor of both failure to conceive and ectopic pregnancy. 26% of women who were seropositive for IgG3 conceived, while 38% of women seronegative for IgG3 conceived ($p<0.001$). Women seropositive for IgG3 had an 11% incidence of ectopic pregnancy, while those that were seronegative had a 4% incidence ($p=0.02$).

Subsequent bivariate analyses were conducted to determine predictors of IgG3 seropositivity. Women who were seropositive for IgG3 were more likely to be younger, non-Caucasian, lower-educated, and obese than women who were seronegative for IgG3 (Table 2).

Multivariate analyses evaluating the independent associations between anti Ct-IgG3 seropositivity and probability of pregnancy, live birth, and ectopic pregnancy are presented in Table 3. After adjusting for age, race, treatment medication (gonadotropins, clomid, or letrozole), smoking status, and current alcohol use, women who were seropositive for IgG3 were significantly less likely to conceive (RR 0.65, 95% CI 0.52-0.83) or to have a live birth (RR 0.59, 95% 0.43-0.80); these associations were weakened after adjusting for the number of confirmed patent tubes (RR 0.73, 95% CI 0.56-0.97) and (0.73, 95% CI: 0.50-1.04), respectively. Women, who conceived and were Ct seropositive had a 2.7 (95% CI: 1.40-5.34) fold increase in the risk of ectopic pregnancy.

Discussion

In this study, we found that Ct seropositivity decreases the probability of pregnancy and live birth and increases the risk of ectopic pregnancy in infertile women with documented tubal patency. Of the two IgG subclasses examined, anti-Ct IgG3 serostatus was most strongly associated with all three outcomes. Ct seropositivity was more commonly observed in women with other risk factors for infertility such as smoking and obesity. However, the associations between anti-Ct IgG3 seropositivity and all reproductive outcomes remained after adjusting for these potential confounders.

In this study of women with documented tubal patency receiving non-ART treatment for infertility, Ct seropositivity lowered the probability of conceiving by 35%. In a study by Coppus et al, Ct serostatus was assessed using a microimmunofluorescence assay or ELISA (15). 1882 women with documented bilateral tubal patency were followed for up to 12 months and pregnancy, but not live birth, was determined. 23% of subjects were seropositive. Seropositive subjects had a 35% reduction in fecundability. Although the current study differs by choice of assay and inclusion criteria for tubal patency, the findings are similar. Prior studies had conflicting results (6, 9, 11, 16, 17). However, in general, these studies were underpowered, included treatment dependent and independent pregnancies, and/or were case-control study designs.

In this study, we evaluated Ct serostatus based on detection of the IgG subclasses IgG1 and IgG3 using the EB ELISA as IgG1 and IgG3 comprise the predominant anti-Ct serum antibody responses (12). Women, who were Ct seropositive by IgG3 showed the greatest reduction in probability of pregnancy and live birth. It is believed that IgG3 is involved in early response to infection and then is short-lived with IgG1 emerging as the major effector in clearing infection (18). The detection of IgG3 in these women could represent either recent Ct infection that has cleared or alternatively persisting infection. In either instance, detection of anti-Ct IgG3 may reflect more recent inflammatory damage to the fallopian tube, contributing to the pregnancy difficulties but perhaps not of sufficient duration or severity to lead to blockage of the fallopian tubes.

Further supporting our suggestion that Ct seropositivity may well represent undiagnosed tubal/peritoneal disease is our observation that seropositive women who conceived had almost three times the risk of ectopic pregnancy. Normal migration of the fertilized oocyte from the ampulla of the oviduct into the uterine cavity is dependent on contractions of the

tubal musculature, ciliary activity, and the flow of tubal secretions (19). Rhythmic oviduct contractions are due to a network of pacemaker like interstitial cells in conjunction with smooth muscle cells. A recent study showed that this pacemaker cell network is disrupted with Ct infections resulting in loss of normal oviduct contractile activity (20). Ct infections may also inhibit normal oviduct ciliary activity or ciliary beat frequency (21) and increase secretions, further inhibiting normal progression. Thus tubal pathology may be present even in the setting of normal appearing, patent fallopian tubes.

This study has some weaknesses. First it is a secondary analysis. Second, the criteria for documentation of tubal patency were not strict; however, they are likely consistent with clinical practice. Women did receive treatment, thus, we cannot necessarily generalize these results to those women attempting to conceive naturally. We can also not differentiate diagnosis effects from insemination effects. All women with PCOS had timed intercourse, while women with unexplained infertility received intrauterine insemination. However, none of the women received in vitro fertilization, thus pregnancy was still dependent on in vivo fertilization. While study (PPCOS II versus AMIGOS) did differ in prevalence of seropositivity, the study was not related to the probability of achieving a pregnancy. Thus, study did not act as a confounder. After adding study to the model, the effect estimates did not change significantly (pregnancy: RR 0.64 vs. RR 0.65; live birth RR 0.59 vs. RR 0.59). For a more parsimonious model, we therefore did not include this covariate in the model for the multivariate analysis. Finally the cohort is comprised of participants in two studies with different study populations; however, many of the inclusion, exclusion, and outcomes measures had been intentionally harmonized to allow for such combined analyses.

The study has many strengths. First, this study is adequately powered. Although an a priori power calculation was not conducted, a post hoc power analysis revealed that this study had 80% power to detect a 9% difference in live birth rates, given Ct seroprevalence of 20%. Second the cohort is well characterized. Third, this is one of the few studies that has live birth as the primary outcome. Finally, we used an assay that has been shown to be more sensitive than the commercial assay Medac in the detection of Ct seropositivity. In addition to being highly sensitive and specific, the Ct EB ELISA provided the opportunity to assess the relationship of IgG subclass to the different reproductive outcomes.

In conclusion, women who are Ct seropositive by IgG3 have a significantly lower chance of conceiving in the setting of documented tubal patency. This may be due to underlying damage to fallopian tubal architecture. Future screening for tubal factor infertility may include both an assessment of anti-Ct IgG3 seropositivity and a radiologic evaluation (hysterosalpingography or saline infusion sonography) for documenting tubal patency. Ct seropositivity would potentially identify those with tubal pathology and at risk for ectopic pregnancy.

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References

1. Miller JH, Weinberg RK, Canino NL, Klein NA, Soules MR. The pattern of infertility diagnoses in women of advanced reproductive age. Am J Obstet Gynecol. 1999; 181:952–7. [PubMed: 10521760]
2. Westrom LV. Sexually transmitted diseases and infertility. Sex Transm Dis. 1994; 21:S32–7. [PubMed: 8042113]
3. Akande VA, Hunt LP, Cahill DJ, Caul EO, Ford WC, Jenkins JM. Tubal damage in infertile women: prediction using chlamydia serology. Hum Reprod. 2003; 18:1841–7. [PubMed: 12923136]
4. Broeze KA, Opmeer BC, Coppus SF, Van Geloven N, Alves MF, Anestad G, et al. Chlamydia antibody testing and diagnosing tubal pathology in subfertile women: an individual patient data meta-analysis. Hum Reprod Update. 2011; 17:301–10. [PubMed: 21227996]
5. Coppus SF, Opmeer BC, Logan S, van der Veen F, Bhattacharya S, Mol BW. The predictive value of medical history taking and Chlamydia IgG ELISA antibody testing (CAT) in the selection of subfertile women for diagnostic laparoscopy: a clinical prediction model approach. Hum Reprod. 2007; 22:1353–8. [PubMed: 17234674]
6. Keltz MD, Gera PS, Moustakis M. Chlamydia serology screening in infertility patients. Fertil Steril. 2006; 85:752–4. [PubMed: 16500355]
7. Land JA, Evers JL, Goossens VJ. How to use Chlamydia antibody testing in subfertility patients. Hum Reprod. 1998; 13:1094–8. [PubMed: 9619578]
8. Logan S, Gazvani R, McKenzie H, Templeton A, Bhattacharya S. Can history, ultrasound, or ELISA chlamydial antibodies, alone or in combination, predict tubal factor infertility in subfertile women? Hum Reprod. 2003; 18:2350–6. [PubMed: 14585886]
9. Malik A, Jain S, Rizvi M, Shukla I, Hakim S. *Chlamydia trachomatis* infection in women with secondary infertility. Fertil Steril. 2009; 91:91–5. [PubMed: 18635168]
10. Mol BW, Dijkman B, Wertheim P, Lijmer J, van der Veen F, Bossuyt PM. The accuracy of serum chlamydial antibodies in the diagnosis of tubal pathology: a meta-analysis. Fertil Steril. 1997; 67:1031–7. [PubMed: 9176440]
11. Perquin DA, Beersma MF, de Craen AJ, Helmerhorst FM. The value of *Chlamydia trachomatis*-specific IgG antibody testing and hysterosalpingography for predicting tubal pathology and occurrence of pregnancy. Fertil Steril. 2007; 88:224–6. [PubMed: 17296194]

12. Geisler WM, Morrison SG, Doemland ML, Iqbal SM, Su J, Mancevski A, et al. Immunoglobulin-specific responses to Chlamydia elementary bodies in individuals with and at risk for genital chlamydial infection. J Infect Dis. 2012; 206:1836–43. [PubMed: 23045619]
13. Legro RS, Brzyski RG, Diamond MP, Coutifaris C, Schlaff WD, Casson P, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. N Engl J Med. 2014; 371:119–29. [PubMed: 25006718]
14. Diamond MP, Mitwally M, Casper R, Ager J, Legro RS, Brzyski R, et al. Estimating rates of multiple gestation pregnancies: sample size calculation from the assessment of multiple intrauterine gestations from ovarian stimulation (AMIGOS) trial. Contemp Clin Trials. 2011; 32:902–8. [PubMed: 21787883]
15. Coppus SF, Land JA, Opmeer BC, Steures P, Eijkemans MJ, Hompes PG, et al. *Chlamydia trachomatis* IgG seropositivity is associated with lower natural conception rates in ovulatory subfertile women without visible tubal pathology. Hum Reprod. 2011; 26:3061–7. [PubMed: 21926058]
16. El Hakim EA, Epee M, Draycott T, Gordon UD, Akande VA. Significance of positive Chlamydia serology in women with normal-looking Fallopian tubes. Reprod Biomed Online. 2009; 19:847–51. [PubMed: 20031027]
17. Idahl A, Boman J, Kumlin U, Olofsson JI. Demonstration of *Chlamydia trachomatis* IgG antibodies in the male partner of the infertile couple is correlated with a reduced likelihood of achieving pregnancy. Hum Reprod. 2004; 19:1121–6. [PubMed: 15121732]
18. Collins AM, Jackson KJ. A Temporal Model of Human IgE and IgG Antibody Function. Front Immunol. 2013; 4:235. [PubMed: 23950757]
19. Jansen RP. Endocrine response in the fallopian tube. Endocrine Reviews. 1984; 5:525–51. [PubMed: 6094174]
20. Dixon RE, Hwang SJ, Hennig GW, Ramsey KH, Schripsema JH, Sanders KM, et al. Chlamydia infection causes loss of pacemaker cells and inhibits oocyte transport in the mouse oviduct. Biol Reprod. 2009; 80:665–73. [PubMed: 19109220]
21. Leng Z, Moore DE, Mueller BA, Critchlow CW, Patton DL, Halbert SA, et al. Characterization of ciliary activity in distal Fallopian tube biopsies of women with obstructive tubal infertility. Hum Reprod. 1998; 13:3121–7. [PubMed: 9853868]

Table 1

Incidence of pregnancy, live birth, and ectopic pregnancy by *Chlamydia trachomatis* IgG1 and IgG3 serostatus.

	Pregnant	Live birth	Ectopic
IgG1 or IgG3			
Seropositive (N=397)	128 (32%)	84 (21%)	10 (8%)
Seronegative (N=853)	321 (38%)	227 (27%)	13 (4%)
P-value	0.06	0.04	0.10
IgG1			
Seropositive (N=331)	107 (32%)	68 (21%)	8 (7%)
Seronegative (N=919)	342 (37%)	243 (26%)	15 (4%)
P-value	0.11	0.03	0.21
IgG3			
Seropositive (N=243)	62 (26%)	39 (16%)	7 (11%)
Seronegative (N=1007)	387 (38%)	272 (27%)	16 (4%)
P-value	<0.001	<0.001	0.02

Table 2

Patient characteristics by *Chlamydia trachomatis* IgG3 serostatus

	Ct Seronegative 1007 (81%)	Ct Seropositive 243 (19%)	P-value
Age (years)			0.02
18-26	166 (16%)	55 (23%)	
27-31	400 (40%)	100 (41%)	
32-34	223 (22%)	35 (14%)	
35-41	218 (22%)	53 (22%)	
Race			<0.001
Caucasian	890 (88%)	165 (68%)	
Other	117 (12%)	78 (32%)	
Education level			<0.001
High school or earlier	126 (13%)	56 (23%)	
Some college	256 (25%)	96 (40%)	
College degree	413 (41%)	59 (24%)	
Graduate degree	212 (21%)	32 (13%)	
Nulligravid	608 (60%)	156 (64%)	0.27
Current smoker	92 (9%)	42 (17%)	<0.001
Current alcohol use	703 (70%)	179 (74%)	0.24
Body mass index (kg/m^2)			0.001
< 18.5	15 (1%)	4 (2%)	
18.5-24.9	362 (36%)	54 (22%)	
25-29.9	221 (22%)	61 (25%)	
≥30	409 (41%)	124 (51%)	
Study			0.004
PPCOS II	399 (40%)	121 (50%)	
AMIGOS	609 (60%)	122 (50%)	
Treatment			0.35
Clomiphene	401 (40%)	102 (42%)	
Letrozole	403 (40%)	102 (42%)	
Gonadotropins	203 (20%)	39 (16%)	
Number of documented patent tubes			0.06
At least 1	289 (29%)	87 (36%)	
1	86 (8%)	28 (11%)	
2	632 (63%)	128 (53%)	

[a] Fisher's exact test

Table 3

Independent association between IgG3 *Chlamydia trahomatis* seropositivity and pregnancy, live birth, and ectopic pregnancy.

	Model 1		**Model 2**	
	RR	**95% CI**	**RR**	**95% CI**
Pregnancy	0.65	0.52-0.83	0.73	0.56-0.97
Live birth	0.59	0.43-0.80	0.73	0.50-1.04
Ectopic	2.7	1.40-5.34		
Model 1: adjusts for age, race, treatment medication, current smoker, current alcohol use				
Model 2: adjusts for age, race, treatment medication, current smoker, current alcohol use and number of confirmed patent tubes				