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Chlamydia Prevalence by Age and Correlates of Infection Among Pregnant Women

Janice Leahgrace Simons, MPH, Jessica S. McKenzie, MPH,* Nicole C. Wright, PhD,* Shainela A. Sheikh, B. Pharm,* Akila Subramaniam, MD, MPH,† Alan T. N. Tita, MD, PhD,† and Jodie Dionne-Odom, MD, MSPH‡*

Background: There is a paucity of population-based data on chlamydia in pregnancy despite rising rates in US women. Our objectives were to assess chlamydia prevalence by age group and to identify factors associated with infection in pregnant women to inform screening guidelines.

Methods: This cross-sectional study included pregnant women tested for chlamydia who delivered at the University of Alabama at Birmingham between November 1, 2012, and December 31, 2017. The primary outcome was chlamydia prevalence, defined as a positive urogenital chlamydia nucleic acid amplification test result documented in the electronic medical record. Multivariable logistic regression was used to identify factors associated with infection.

Results: Among 17,796 women who delivered during the study period, 13,657 (77%) had chlamydia testing performed at the University of Alabama at Birmingham. Chlamydia prevalence (95% confidence interval) was 7.4% (7.0%–7.9%). Age-stratified prevalence rates were 14.6%, 4.3%, and 1.7% for women younger than 25 years, 25 to 29 years, and 30 years or older, respectively. Chlamydia in pregnancy remained strongly associated with age (adjusted odds ratio [95% confidence interval], 7.2 [5.6–9.2] for age <25 years, and 2.3 [1.7–3.0] for ages 25–29 years, when compared with >30 years) after adjustment for race, urban residence, and insurance status.

Conclusions: Among pregnant women living in the southeastern United States, chlamydia was detected in 1 of 14 women who were tested. Chlamydia positivity was highest among women younger than 30 years. Study findings support broad screening for chlamydia in pregnancy.

Chlamydia is the most common reportable infection in the United States, with more than 1.8 million cases reported to the Centers for Disease Control and Prevention (CDC) in 2018.[1] Women aged 15 to 29 years have high pregnancy rates and disproportionately high rates of chlamydia when compared with men of similar age and older women. Untreated chlamydia infection of the cervix in pregnant women can be transmitted vertically at delivery.[2] Because most infections are asymptomatic and effective antibiotic therapy is available, routine universal screening for chlamydia in pregnancy at the first prenatal visit is recommended by the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics.[3] In contrast, the CDC and the US Preventive Services Task Force limit chlamydia screening to pregnant women younger than 25 years with risk-based screening in older groups.[4,5] Chlamydia infection in pregnancy can lead to preventable adverse birth outcomes including a 2-fold increase in preterm delivery, low birth weight, and neonatal pneumonia in up to 30% of exposed infants.[3,6,7] Screening for chlamydia infection in pregnancy has been shown to be cost-effective when the prevalence is ≥3%.[8,9]

Although population-based surveillance data for chlamydia in pregnant women are not available in the United States because of incomplete and inconsistent reporting of pregnancy status for chlamydia cases in women, 3.5% of women tested positive for chlamydia in a US reference laboratory in 2005 to 2008.[10] There is regional variability in the prevalence of chlamydia with higher rates in the South (e.g., 777 cases per 100,000 women in Alabama compared with 693 cases per 100,000 women nationwide).[1] Risk factors for chlamydia infection in nonpregnant women include younger age, Black race, and history of sexually transmitted infection (STI).[11,12] Risk factor–based screening is inadequate if providers and women are not aware of sex partner risk and regional chlamydia prevalence. Our study objectives here were to determine the prevalence of chlamydia in pregnancy according to maternal age, identify additional factors associated with infection, and evaluate the association between age and chlamydia in pregnancy.

MATERIALS AND METHODS

Study Design and Population

The cross-sectional study design included women with chlamydia testing performed in pregnancy who delivered at the University of Alabama at Birmingham's (UAB's) Women and Infants Center between November 1, 2012, and December 31, 2017. The UAB provides prenatal care for women with and without underlying medical conditions in Jefferson County (Birmingham) and serves as a referral center for women with complicated pregnancies throughout Alabama. For women with more than one pregnancy during the study period, the initial pregnancy was used for analysis. The standard practice for diagnostic testing in outpatient obstetric clinics was to perform a urogenital chlamydia screening test at the initial prenatal visit with repeat testing based on positivity, symptoms, or exposure. Study data were extracted from the electronic medical record using an algorithm that captured

From the *Department of Epidemiology, School of Public Health, †Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Center for Women's Reproductive Health, and ‡Department of Medicine, Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, AL

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Correspondence: Jodie Dionne-Odom, MD, MSPH, Division of Infectious Diseases, University of Alabama at Birmingham, 703 19th St South, Zeigler Research Building, Birmingham, AL 35294-2050. E-mail: jdionne@uabmc.edu.

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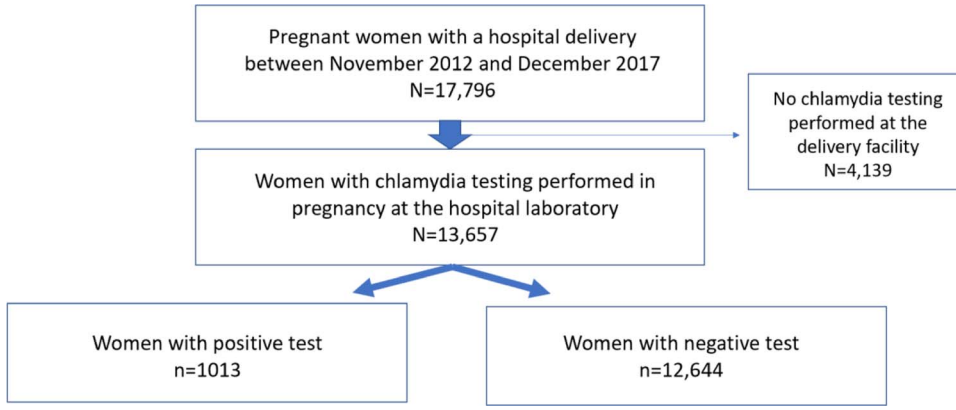

Figure 1. Study flow diagram.

relevant test results and deidentified sociodemographic information for the study population. Unique ID numbers were assigned.

Study Outcomes

The primary study outcome was the prevalence of urogenital chlamydia infection during pregnancy. Prevalence was defined as the number of women with at least one positive chlamydia test result among those screened who delivered at our center during the study period. *Chlamydia trachomatis* testing was performed on urine samples, vaginal swabs, and cervical swabs using highly sensitive nucleic acid amplification test with Roche Amplicor in 2012 and Cobas 4800 between 2013 and 2017 for clinic patients, and BD Viper in 2012 to 2013 and Aptima Hologic between 2014 and 2017 for women tested in the emergency department (ED) or as inpatients. The performance of these nucleic acid amplification tests performed on samples collected from the female genital tract or urine is similar with high sensitivity >90% and specificity >99%.[13] Chlamydia testing performed outside the UAB system or before referral was not available. For pregnancy outcome definitions, preterm delivery occurs before 37 weeks' gestation, low birth weight is <2500 g, fetal loss before 20 weeks is a spontaneous

TABLE 1. Characteristics of Pregnant Women Tested for Chlamydia

	Total Sample* (n = 13,657)	Chlamydia Positive* (n = 1013)	Chlamydia Negative* (n = 12,644)
Age at delivery, median (IQR), y	26.8 (9.2)	21.6 (5.4)	27.3 (8.9)
Age category, n (%)			
<25 y	5303	774 (14.6)	4529 (85.4)
25–29 y	3828	164 (4.3)	3664 (95.7)
30+ y	4526	75 (1.7)	4451 (98.3)
Race/Ethnicity, n (%)			
Black	7016	804 (11.5)	6219 (88.5)
White	3561	82 (2.3)	3479 (97.7)
Hispanic	2501	95 (3.8)	2404 (96.2)
Asian	244	8 (3.3)	236 (96.7)
Multiple	129	15 (11.6)	115 (88.4)
Other	206	9 (4.4)	196 (95.6)
Urban residence, n (%)	10,867	944 (8.7)	9923 (91.3)
Insurance status, n (%)			
Public	8918	827 (9.3)	8091 (90.7)
Private	3425	100 (2.9)	3325 (97.1)
Uninsured	1314	86 (6.5)	1228 (93.5)
Location of testing, n (%)			
Clinic	12,169	899 (7.4)	11,270 (92.6)
ED	1474	111 (7.5)	1363 (92.5)
Inpatient	14	3 (21.4)	11 (78.6)
Preterm delivery, n (%)	2139	154 (7.2)	1985 (92.8)
Birth weight, n (%)			
<2500 g	1794	153 (8.5)	1641 (91.5)
≥2500 g	10,930	797 (7.3)	10,133 (92.7)
Missing	933	63 (6.8)	870 (93.2)
Birth outcomes, n (%)			
Live birth	13,409	998 (7.4)	12,411 (92.6)
SAB/Stillbirth/IUFD	228	17 (7.5)	211 (92.5)
Neonatal death	23	1 (4.3)	22 (95.7)

*Row percentages.

IUFD indicates intrauterine fetal demise; SAB, spontaneous abortion.

abortion, and fetal loss after 20 weeks is an intrauterine fetal demise. Neonatal death occurs within 28 days of birth.

Potential Factors of Interest

Variables of interest were maternal age (continuous and categorized into 13–24, 25–29, and 30+ years based on current prenatal screening guidelines), self-reported race (non-Hispanic Black, non-Hispanic White, Asian, multiple and other), ethnicity (Hispanic, non-Hispanic), insurance status (private, public [Medicaid or Medicare], none), urban residence (defined as a resident of Jefferson County, the most populous county in Alabama with 650,000 residents) versus nonurban, and location of chlamydia testing (clinic, ED, inpatient).

Statistical Analysis

To describe the study population, χ^2 procedures were used to analyze categorical variables with stratification by chlamydia test results. Bivariate analysis was used to explore associations between variables of interest and chlamydia positivity. Logistic regression was used to calculate unadjusted and adjusted odds ratios (ORs) along with 95% confidence intervals (95% CIs) for the outcome of interest. We included all variables with significance in crude models at a P value <0.05 in the multivariable model. The analysis was performed using SAS version 9.4 (Cary, NC).

Ethics

The study was approved by the UAB Institutional Review Board with waiver of informed consent.

RESULTS

A total of 17,796 pregnant women delivered at UAB hospital during the 5-year study period. Among these, 13,657 women (77%) had chlamydia testing performed at UAB. The prevalence (95% CI) of chlamydia infection in this group was 7.4% (7.0%–7.9%; Fig. 1). Table 1 shows the characteristics of the total sample of pregnant women, and Table 2 shows differences in characteristics stratified by chlamydia test results. The median age for our study sample was 27 years, and 51% were Black women. Chlamydia prevalence varied by age: 14.6% in women younger than 25 years, 4.3% in women aged 25 to 29 years, and 1.7% in women 30 years and older (Table 1). The median age of pregnant women with chlamydia was 22 years compared with 27 years in those without chlamydia ($P < 0.001$; Table 2). We also observed significant differences in chlamydia positivity by race and ethnicity ($P < 0.001$; Table 2). Among pregnant women with chlamydia, 93% lived in urban areas compared with 79% of women without chlamydia ($P < 0.001$). A larger proportion of women with chlamydia had public insurance compared with those without chlamydia (82% [79.1%–84.0%] vs. 64% [63.1%–64.8%], $P < 0.001$). No difference was noted in testing location ($P = 0.13$) or birth outcomes ($P = 0.81$) according to chlamydia positivity (Table 2). Preterm delivery occurred in 15.2% of women with chlamydia and 15.7% of women without chlamydia ($P = 0.68$).

Factors associated with chlamydia infection are shown in Table 3. In crude models, younger age (odds ratios [ORs], 10.1 [95% CI, 8.0–12.9] for age <25 years and 2.7 [95% CI, 2.0–3.5] for ages 25–29 years, both compared with age >30 years);

TABLE 2. Evaluating Differences in Characteristics by Chlamydia Test Positivity

	Chlamydia Positive* (n = 1013)	Chlamydia Negative* (n = 12,644)	$P^{\dagger}$
Age at delivery, median (IQR), y	21.6 (5.4)	27.3 (8.9)	<0.001
Age category, n (%)			
<25 y	774 (76.4)	4529 (35.8)	<0.001
25–29 y	164 (16.2)	3664 (29.0)	
30+ y	75 (7.4)	4451 (35.2)	
Race/Ethnicity, n (%)			
Black	804 (79.4)	6219 (49.1)	<0.001
White	82 (8.1)	3479 (27.5)	
Hispanic	95 (9.4)	2404 (19.0)	
Asian	8 (0.8)	236 (1.9)	
Multiple	15 (1.5)	115 (0.9)	
Other	9 (0.9)	196 (1.6)	
Urban residence, n (%)	944 (93.2)	9923 (78.5)	<0.001
Insurance status, n (%)			
Public	827 (81.6)	8091 (64.0)	<0.001
Private	100 (9.9)	3325 (26.3)	
Uninsured	86 (8.5)	1228 (9.7)	
Location of testing, n (%)			0.13
Clinic	899 (88.8)	11,270 (89.1)	
ED	111 (11.0)	1363 (10.8)	
Inpatient	3 (0.3)	11 (0.1)	
Preterm delivery, n (%)	154 (15.2)	1985 (15.7)	0.68
Birth weight, n (%)			
<2500 g	153 (15.1)	1641 (13.0)	0.13
≥2500 g	797 (78.7)	10,133 (80.1)	
Missing	63 (6.2)	870 (6.9)	
Birth outcomes, n (%)			
Live birth	998 (98.5)	12,411 (98.2)	0.81
SAB/Stillbirth/IUFD	17 (1.7)	211 (1.6)	
Neonatal death	1 (0.1)	22 (0.2)	

*Column percentages.

†Significance determined using χ^2 tests for proportions and t test for continuous variables.

TABLE 3. Factors Associated With Chlamydia in Pregnancy

	Crude Odds Ratio (95% CI)
Age, y	
<25	10.1 (8.0–12.9)
25–29	2.7 (2.0–3.5)
30+	Referent
Race/Ethnicity	
White	Referent
Black	5.5 (4.4–6.9)
Hispanic	1.7 (1.2–2.3)
Other	2.5 (1.6–3.8)
Urban residence	3.8 (2.9–4.8)
Insurance status	
Private	Referent
Uninsured	2.3 (1.7–3.1)
Public	3.4 (2.8–4.2)

self-reported Black (OR, 5.5 [95% CI 4.4–6.9]), Hispanic (OR, 1.7 [95% CI, 1.2–2.3]), or other race (OR, 2.5 [95% CI, 1.6–3.8]) compared with White race; urban residence (OR, 3.8 [95%, CI 2.9–4.8]); having public insurance (OR, 3.4 [95% CI, 2.8–4.2]); and being uninsured (OR, 2.3 [95% CI 1.7–3.1]) compared with private insurance were significantly associated with chlamydia.

Table 4 shows 3 adjusted models for the association between age and chlamydia in pregnancy. All models show similar results. In model 3, women younger than 25 years had 7-fold higher odds of chlamydia compared with women older than 30 years (adjusted OR [95% CI], 7.2 [5.6–9.2]). Women aged 25 to 29 years had 2-fold higher odds of having chlamydia compared with women older than 30 years (2.3 [1.7–3.0]). This model was adjusted for race/ethnicity, urban residence, and insurance status.

DISCUSSION

Among more than 13,500 women who delivered at our university hospital facility in urban Alabama, the prevalence of chlamydia infection during pregnancy was 7.4%. Women younger than 30 years had a significantly higher prevalence of infection compared with older women. Nearly 1 in 4 infections would have been missed if chlamydia testing had been limited to women younger than 25 years. We also found evidence of disparity in infection rates according to race, urban residence, and socioeconomic status: women who were uninsured or had public insurance (mostly Medicaid) had higher odds of chlamydia infection compared with women with private insurance.

Few contemporary studies estimate the prevalence of chlamydia infection in pregnancy in the United States. An analysis from a large laboratory database (Quest Diagnostics) 10 years ago showed that 59% of women had been tested for chlamydia in pregnancy, and the positivity rate was 3.5%.[10] In Atlanta, chlamydia prevalence in pregnant women tested was similar to our study at 9%.[14] A CDC-funded system called the Pregnancy Risk Assessment Monitoring System surveyed nearly 13,000 women about STI in pregnancy in 5 states from 2009 to 2011: 2.4% reported chlamydia infection, but this highlights the limitations of self-report and likely underestimates prevalence.[12] In a retrospective matched cohort study of 358 pregnant women with and without HIV who delivered at our UAB facility between 2000 and 2014, chlamydia prevalence rates were 17% in women with HIV and 12% in women without HIV ($P = 0.2$).[15]

In the current study, 77% of women who delivered had laboratory testing for chlamydia at our center. This likely underestimates the true prenatal screening rate because women referred to the UAB for pregnancy complications may have been tested for chlamydia before the transfer of care. External laboratory records were not incorporated in the current analysis. In a recent CDC analysis from the National Survey of Family Growth (n = 1155), 48% of women with pregnancy in the past year reported that they were tested for chlamydia during prenatal care.[16] National surveillance systems capture valuable information about chlamydia infection in women because chlamydia is a reportable condition, but pregnancy status is not consistently included in case reports to the CDC.[17] As a result, stratified analysis of population-based national data to look at screening rates and positivity rates according to pregnancy status is not possible.

Current CDC and US Preventive Services Task Force recommendations for universal chlamydia screening in pregnancy is limited to younger woman (<25 years). This guidance is based on prevalence and cost-effectiveness analyses from the United States and other countries.[9,18,19] In our study setting where universal screening per ACOG guidelines was standard practice, 1 in 4 cases of chlamydia in pregnancy would have been missed if testing had been restricted to women younger than 25 years. Risk-based STI screening in pregnancy can be limited: for example, in a recent CDC study of pregnant women with primary and secondary syphilis, 49% had no reported risk factor for infection.[20] Although chlamydia rates are consistently highest in women younger than 25 years, Hu et al.[8] showed that annual chlamydia screening in the general population of women aged 15 to 29 years can be cost-effective. Another factor in support of ACOG's universal screening guidelines for chlamydia in pregnancy relates to demographic changes in the US population: the mean maternal age at the time of first pregnancy has increased to 26.3 years.[21] Because fewer pregnant women are younger than 25 years, age-restricted screening guidelines may lead to reduced screening rates.

Younger age in women has long been associated with higher rates of chlamydia acquisition, and age is the strongest predictor of chlamydia in pregnant women in our study.[1] Whether this is due to anatomy (cervical ectropion that resolves with age), immunology (acquired immunity to chlamydia with age), or behavioral patterns (more sex partners or higher risk sex partners in younger women) remains unclear.[22] In HIV-discordant couples, pregnancy is associated with 2-fold increased risk of HIV

TABLE 4. Association Between Age and Chlamydia in Pregnancy

	Crude Odds Ratio (95% CI)	Model 1, Adjusted Odds Ratio* (95% CI)	Model 2, Adjusted Odds Ratio† (95% CI)	Model 3, Adjusted Odds Ratio‡ (95% CI)
Age, y				
<25	10.1 (8.0–12.9)	7.9 (6.2–10.1)	7.8 (6.1–9.9)	7.2 (5.6–9.2)
25–29	2.7 (2.0–3.5)	2.4 (1.8–3.1)	2.3 (1.8–3.1)	2.3 (1.7–3.0)
30+	Referent	Referent	Referent	Referent

*Model 1 adjusted for race.

†Model 2 adjusted for race and urban residence.

‡Model 3 adjusted for race, urban residence, and insurance status.

acquisition compared with nonpregnant women (7.4 vs. 3.0 incident infections per 100 person-years).[23] Other independent predictors of chlamydia infection in pregnancy in our study included Black race. Persistent disparities in STI rates have been consistently documented in national surveillance reports where chlamydia infection rates are 4 to 5 times higher in Black women compared with White women.[1,24,25] Sexual networks have been shown to explain much of the elevated risk of STI acquisition among Black adolescents and women compared with other racial/ethnic groups.[26] Lack of health insurance or having public insurance instead of private insurance is another independent predictor of chlamydia in pregnant women in our study. This may be a proxy for access to health care, but it is most likely a proxy for socioeconomic status, which has been associated with STI risk.[11] Many adverse outcomes have been documented in adults without medical insurance, including pregnancy outcomes.[27] Improving access to high-quality prenatal care is critical to improving health outcomes that depend on the detection and treatment of chlamydia in asymptomatic and symptomatic women.[28,29]

Our study has important limitations. It is a retrospective study limited to women who delivered at a single center in the Southeastern United States, which may not be representative of other regions or women who reside in predominantly rural regions. Our study was not able to distinguish women who presented for testing because of symptoms, known exposure, or routine screening. Complete information about potential risk factors for chlamydia acquisition (such as sex partner number and characteristics, STI history, drug use, alcohol use, education level, and income) was not routinely available for this analysis. This may have led to bias due to residual confounding that we were unable to adjust for. Our estimates of screening and positivity rates may be underestimates if women were screened and/or treated for chlamydia at other facilities before transfer to our center. There may be a testing bias if women who were not screened had different characteristics from women who were screened. This should have been minimized by the protocol for universal screening. Study strengths include the sample size, the use of highly sensitive diagnostic testing, and the data set quality.

One in 14 pregnant women who were tested in our academic center during the past 5 years had chlamydia infection. Factors associated with infection included younger age (<30 years), Black race, and lower socioeconomic status. In the midst of rising chlamydia rates in the United States, study findings support current ACOG guidelines for universal chlamydia screening in pregnancy.

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