Utility of Routine Testing for Chlamydia and Gonorrhea in the Setting of Preterm Delivery or Premature Preterm Rupture of Membranes

Kaitlynn Ebisutani MD; Charlie K. Wang MD; Hyeong Jun Ahn PhD; Autumn J. Broady MD; and Bliss Kaneshiro MD, MPH

Abstract

This study aimed to explore the rates of positive and negative Chlamydia trachomatis and Neisseria gonorrhoeae test results in patients screened for these infections and later experienced preterm delivery or preterm premature rupture of membranes. The team conducted a retrospective chart review of patients admitted for preterm premature rupture of membranes or who experienced preterm delivery between April 1, 2009, and April 30, 2015. Patients lacking chlamydia and gonorrhea screening before admission were excluded from the study. Four hundred and six patients met the inclusion criteria. The prevalence of chlamydia infection at initial prenatal screening before admission was 13.3%. Among those for whom the prenatal chlamydia test was negative, 1.7% of patients had a positive subsequent chlamydia test on admission screening. Among those for whom the prenatal chlamydia test was positive, 18.5% had a positive subsequent chlamydia test on admission screening. Positive prenatal test (P=.002) and age 25 years or less (P<.001) were associated with positive admission screening for chlamydia, though only a positive prenatal test remained significant in a logistic regression model (odds ratio, 8.56; 95% CI, 2.67–27.49; P=.003). The prevalence of gonorrhea was low at 0.2% of patients positive for gonorrhea at prenatal testing and 0.5% of patients positive for gonorrhea at admission testing. Our results suggest that individualization based on patient characteristics may be utilized to decrease re-testing. More research is needed to identify possible additional risk factors for new infection or re-infection and the most optimal timing for re-screening during the prenatal period.

Abbreviations and Acronyms

ACOG = American College of Obstetricians and Gynecologists
CDC = Centers for Disease Control and Prevention
KMCWC = Kapi'olani Medical Center for Women and Children
NICU = neonatal intensive care unit
PTD = preterm delivery
PPROM = preterm premature rupture of membranes
STI(s) = sexually transmitted infection(s)
US = United States

Background

In the United States (US), chlamydia and gonorrhea are the first and second most commonly reported sexually transmitted infections (STIs). In 2017, more than 1.7 million cases of chlamydia and more than 550 000 cases of gonorrhea were reported to the Centers for Disease Control and Prevention (CDC).[1] Chlamydia and gonorrhea result in urogenital infections, extragenital infections, and sequelae detrimental to fertility and neonatal outcomes. Males present with symptoms of urethritis and epididymitis, and females present with urethritis, cervicitis, and pelvic inflammatory disease. In both men and women, asymptomatic infection is common.[2,3] Preterm premature rupture of membranes (PPROM) complicates 3% of pregnancies, and in turn, is responsible for one-third of all preterm births.[4]

Studies exploring the role of chlamydia infection as a cause of preterm delivery (PTD) are mainly observational and yield mixed results, so the extent to which infection adversely affects pregnancy remains controversial.[5] Most studies suggest chlamydial infection increases the risk of PTD, PPROM, and low birthweight infants.[6-10] Rours et al noted the risk of PTD before 32 weeks was significantly higher among women with chlamydia than those who tested negative after adjustment for age and socio-economic background (odds ratio [OR], 4.35; 95% CI, 1.3–15.2).[15] Some studies, however, have not demonstrated an increased risk of these outcomes.[5,11-14] A recent large observational study of more than 100 000 women did not find an association between chlamydial infection and preterm birth, small for gestational age infants, or intrauterine fetal demise.[16] Neonates who acquire chlamydia at the time of delivery are at risk for conjunctival infections and *Chlamydia trachomatis* pneumonia.[2]

Similar to results of studies examining outcomes associated with maternal chlamydia infection, studies of outcomes associated with maternal gonococcal infection have yielded mixed results. Most studies of maternal gonococcal infection note associations with low birth weight and small for gestational age infants though some studies have also found a higher risk of PPROM and PTD in individuals with gonorrhea.[14,17-21] Studies also suggest associations of maternal gonococcal infection with spontaneous abortion, intrauterine growth restriction, and chorioamnionitis.[14,17-20] A recent study in Washington state found a significantly increased risk of low birthweight, but not of PTD, PPROM, chorioamnionitis, or infant admission into a neonatal intensive care unit (NICU).[22] If untreated, transmission of gonorrhea from mother to infant occurs in 30% to 50% of cases.[23] Neonatal complications include neonatal conjunctivitis, pharyngitis, and arthritis.[3]

The American College of Obstetricians (ACOG) recommends screening all pregnant women at the initial prenatal visit for chlamydia and re-screening women at risk for a new infection

in the third trimester. Patients are considered to be at a higher risk for a new infection if they have new or multiple sex partners, a sex partner with concurrent partners, or a sex partner who has a STI.[1,2] The CDC has more limited recommendations for screening than ACOG and recommends screening pregnant women who are 25 years of age or younger and women of any age who have risk factors for infection. ACOG and the CDC recommend gonorrhea screening during pregnancy in patients 25 years of age or younger, those with risk factors for infection (previous or coexisting STI, new or multiple sex partners, inconsistent condom use among persons not in mutually monogamous relationships, exchanging sex for money or drugs), and those living in high-morbidity areas.[24]

In the current study, patients at our institution admitted for PPROM or experienced PTD during the study period were routinely screened for gonorrhea or chlamydia regardless of whether they had been previously screened. This study was not based on any national recommendation but was performed at our institution for many years. We sought to evaluate the utility of this practice. Data regarding admission to the NICU, chorioamnionitis, and neonatal sepsis were collected to assess the prevalence of these outcomes in the setting of maternal chlamydia or gonococcal infection.

Materials and Methods

The primary objective of this retrospective, descriptive study was to determine the prevalence of chlamydia among patients admitted for PPROM or experienced PTD who had a negative chlamydia test earlier in pregnancy. PTD was defined as delivery before 37 weeks' gestation, and PPROM was defined as rupture of the amniotic membrane before 37 weeks without the onset of labor. We also sought to identify risk factors for chlamydia at the time of admission so that testing could be done more selectively. Gonorrhea and chlamydia testing are typically done at the same time, with the same sample. Specimens collected were tested for chlamydia and gonorrhea using the Aptima Combo 2 assay, with associated test sensitivity of 97.8% and specificity of 99.2%. Though we planned to describe the results of gonorrhea testing, we did not seek to identify risk factors for gonorrhea because of the suspected lower prevalence of gonorrhea in the current population.

Using *International Classification for Diseases, Ninth Revision* (ICD-9) codes, we identified patients who met our inclusion criteria at Kapi'olani Medical Center for Women and Children (KMCWC) between April 1, 2009, and April 30, 2015. We further limited our cohort to women who (1) had a chlamydia test result from a date before admission, which we termed "antenatal screening", and (2) had a screening for chlamydia at the time of admission, which we termed "admission screening." We excluded those who did not have prenatal screening for chlamydia before admission as these patients should have testing done at the time of admission per ACOG guidelines.[24,25] Charts were individually reviewed to verify diagnoses and test results.

In addition to gonorrhea and chlamydia test results, we collected demographic and clinical information. At KMCWC, race is self-reported and entered into the electronic medical record. An individual could identify with more than 1 race. If an individual identified with multiple races, they were analyzed by each race they best identified. Since individuals could be counted in more than 1 racial category, we did not compare any outcome between races (for example, Asian versus white) but compared single racial categories with the rest of the population (for example, Asian versus non-Asian) because of the increased presence of multiracial individuals in the study population. We reported demographic characteristics by race for all races for which more than 30 participants were identified. We described patients' demographic and clinical characteristics by frequency and percentage for categorical variables and mean and standard deviation for continuous variables. We evaluated associations between gonorrhea and chlamydia test results and other variables using chi-square or Fisher's exact tests. All analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, NC). A P value of less than .05 was considered statistically significant. We determined the proportion of patients who had admissions to the NICU and a diagnosis of chorioamnionitis or neonatal sepsis based on ICD-9 codes. This study was granted exempt status from Institutional Review Board approval by the Hawai'i Pacific Health Research Institute (HPHRI 2015-076).

Results

The demographics and clinical characteristics of the study population are presented in Table 1. Among the demographics listed in Table 1, a previous positive prenatal chlamydia test was the only factor significantly associated with a positive chlamydia test result upon admission screening. During the study period, there were 406 patients admitted for PPROM or resulting PTD who had both antepartum and admission test for chlamydia. Of the 406 patients who met our inclusion criteria, 352 patients (86.7%) had negative prenatal chlamydia tests, and 54 (13.3%) had positive prenatal chlamydia tests (Figure 1). Of the 352 patients who had negative prenatal chlamydia tests, 346 (98.3%) had negative chlamydia tests on admission, and 6 (1.7%) had positive chlamydia tests on admission. Of the 54 patients with positive prenatal chlamydia tests, 44 (81.5%) had negative chlamydia tests on admission, and 10 (18.5%) had positive chlamydia tests on admission. Regardless of prenatal chlamydia test results, of the 406 patients, 16 (3.9%) had positive chlamydia tests on admission, and 390 (96.1%) had negative chlamydia tests on admission.

Of the 54 patients with positive prenatal chlamydial tests, treatment was documented in the medical record for 46 (85.2%) of them. Of the 8 patients with positive prenatal chlamydial tests who did not have documented treatment, 1 (12.5%) tested positive, and 7 (87.5%) tested negative upon admission screening for chlamydia. The resolution of positive test results for patients without documented treatment is likely because of the incomplete nature of some medical records, as explained

Table 1. Demographics and Clinical Characteristics of the Study Population			
Characteristics	**Negative Admission Chlamydia (n=390) n (%)**	**Positive Admission Chlamydia (n=16) n (%)**	***P* Value[a]**
Positive antenatal test	44 (11.3)	10 (62.5)	<.001
Age, 25 years or younger	166 (42.6)	13 (81.3)	.002
PPROM at admission	126 (32.3)	2 (12.5)	.107
History of preterm delivery	39 (10.0)	0 (0.0)	.38
Insurance type			
Unknown/uninsured	2 (0.6)	0 (0.0)	.56
Public	187 (47.9)	11 (68.8)	
Private	185 (47.4)	5 (31.3)	
Military	16 (4.1)	0 (0.0)	
Gestational age at delivery, weeks			
Less than 24	10 (2.6)	0 (0.0)	.76
24 to 27+6[b]	47 (12.1)	3 (18.3)	
28 to 31+6[b]	62 (15.9)	3 (18.3)	
32 to 36+6[b]	271 (69.5)	10 (62.5)	
Race			
Filipino	181 (46.4)	8 (50.0)	.78
White	179 (45.9)	5 (31.3)	.25
Hawaiian	152 (39.0)	5 (31.3)	.53
Chinese	102 (26.2)	4 (25.0)	.92
Japanese	80 (20.5)	2 (12.5)	.43
Micronesian	27 (6.9)	4 (25.0)	.008

Abbreviations: PPROM, preterm premature rupture of membranes.
[a] *P* values <.05 considered to be statistically significant, reflecting an association with a positive chlamydia test.
[b] "+6" in reference to number of days of gestation, in addition to the previous value indicating weeks of gestation.

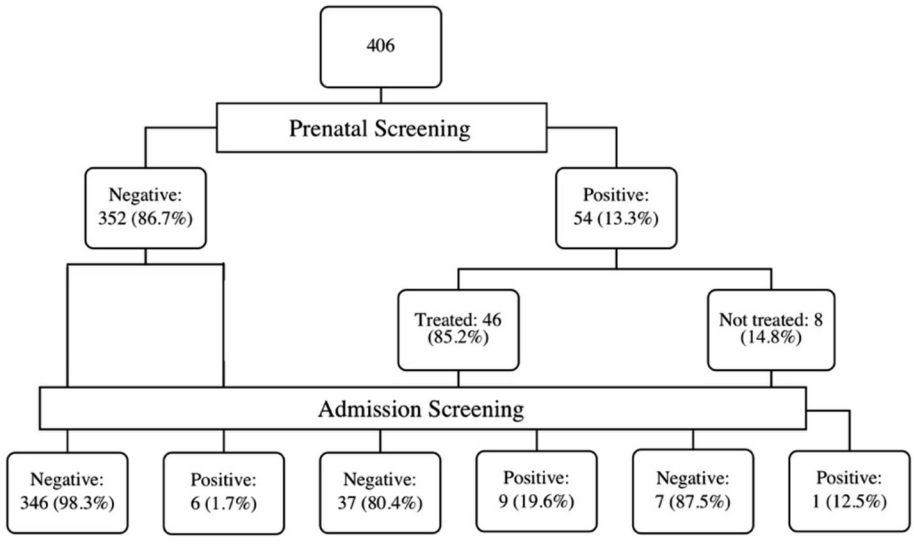

Figure 1. Chlamydia Prenatal Screening Results and Subsequent Admission Screening Results for Patients Admitted for PPROM or Experienced PTD.

Table 2. The Association of Chorioamnionitis, Neonatal Intensive Care Unit Admission, and Neonatal Sepsis Events with Chlamydia Test Results

Diagnosis	Negative Admission Chlamydia (n=390) n (%)	Positive Admission Chlamydia (n=16) n (%)	*P* Value[a]
Chorioamnionitis	43 (11.0)	3 (18.8)	.34
NICU admission	310 (79.5)	12 (75.0)	.66
Sepsis in newborn	46 (11.8)	1 (6.3)	.49

Abbreviations: NICU, neonatal intensive care unit.
[a] *P* values <.05 considered to be statistically significant, reflecting an association with a positive chlamydia test.

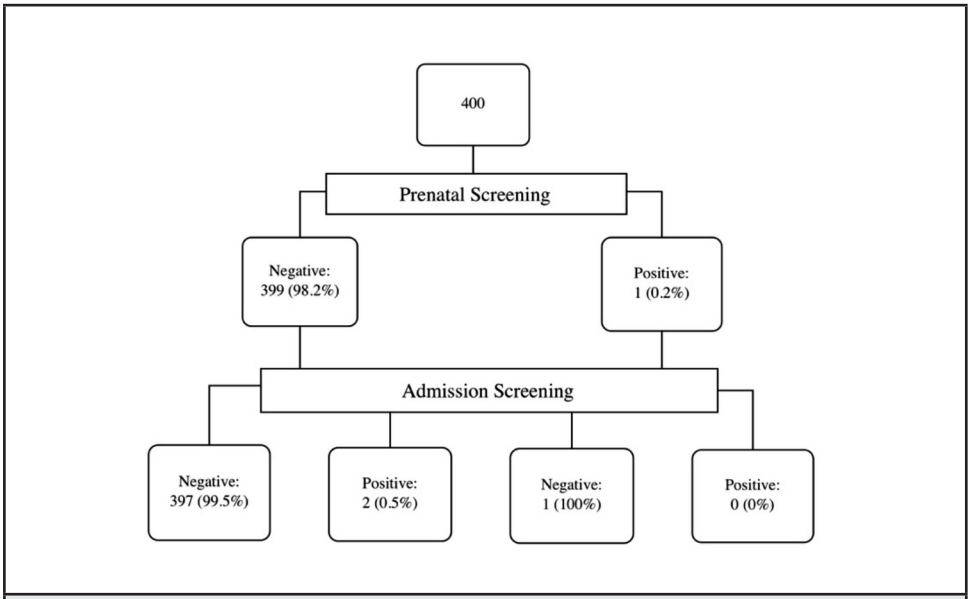

Figure 2. Gonorrhea Prenatal Screening Results and Subsequent Admission Screening Results for Patients Admitted for PPROM or Experienced PTD.

further in the limitations of the study. Patients also might have gone to different facilities or providers and received treatment that was not documented in the electronic medical record. Of the 46 patients with positive prenatal chlamydial tests who did receive treatment, 9 (19.6%) tested positive, and 37 (80.4%) tested negative upon admission screening for chlamydia. The higher rates of positive chlamydia results upon admission for patients with documented treatment might be related to incomplete treatment or re-infection.

Six patients who had antepartum tests and admission tests for chlamydia did not have concurrent gonorrhea tests, including 4 patients who did not have prenatal tests for gonorrhea and 2 patients who did not have admission tests for gonorrhea, leaving 400 patients available for the analysis of gonorrhea test results. We could not ascertain the reason for this testing discordance from reviewing the medical record. Of the 400 patients who had prenatal and admission tests for gonorrhea, 2 tested positive at admission (0.5%), as shown in Figure 2. One patient had a positive prenatal test (0.2%) but tested negative at admission.

The mean age of patients who tested positive for chlamydia on admission was 21.8 (standard deviation [SD], 4.9) years, compared to a mean of 27.2 (6.2) years for patients who tested negative on admission (*P*=.16). Mean gestational age on admission was no different in those who tested positive and those who tested negative for chlamydia on admission, with a mean (SD) of 229.9 (26.2) days versus a mean (SD) of 223.0 (24.3) days.

The 3 factors that showed significant association with a positive chlamydia test on admission were age 25 years or younger (OR, 5.85; 95% CI 1.64–20.85), a positive antepartum test for chlamydia (OR, 13.11; 95% CI, 4.54–37.82) and Micronesian race (OR, 4.48; 95% CI, 1.35–14.84) (Table 1). From a logistic regression model adjusting for the 3 significant variables, only a positive antepartum test for chlamydia remained significantly associated with a positive test on admission (OR, 8.56; 95% CI, 2.67–27.49; *P*=.003), while age 25 years or younger (*P*=.089) and Micronesian race (*P*=.650) were not significant.

If admission testing for chlamydia were done only in women who were 25 years of age or younger, we would have tested 179 individuals and detected 13 of 16 (81.3%) chlamydia infections. If we had tested only patients with a positive antepartum test and those who were 25 years of age or younger, we would have tested 192 individuals and detected 14 of 16 (87.5%) chlamydia infections on admission.

Table 2 reports the percentages of patients with positive and negative admission chlamydial tests who had chorioamnionitis, NICU admission, or a diagnosis of neonatal sepsis. A higher percentage of patients with positive chlamydia tests on admission had chorioamnionitis, though this was not statistically different (18.8% versus 11.0%; *P*=.34).

Discussion

During pregnancy, routine screening for chlamydia is recommended by ACOG and the CDC in women 25 years of age or younger and those with risk factors for infection.[24,25] These recommendations are important because most patients with chlamydia are asymptomatic, and most studies suggest a higher risk of neonatal morbidity when a pregnancy is complicated by infection.[2] At our institution, it was common to re-screen patients at the time of admission for PTD or PPROM regardless of risk factors or the results of screening earlier in pregnancy. Among those who were re-screened at the time of admission, 3.9% had a positive test for chlamydia, and 0.5% had a positive test for gonorrhea. Despite the abundance of STI statistics in non-pregnant women, there are minimal data reflecting the prevalence of STIs among pregnant women. In a study using self-reported data from the Pregnancy Risk Assessment Monitoring System in 5 states (Arkansas, Delaware, Mississippi, Missouri, and New York State), 2.4% of patients reported being diagnosed with a positive chlamydia result, and 0.5% of patients reported being diagnosed with a positive gonorrhea result.[26] In comparison, our population had a slightly higher percentage of chlamydia and a similar percentage of gonorrhea.

The CDC reports a rate of 542 chlamydia cases per 100 000 population in Hawai‘i, similar to the US average of 539 chlamydia cases per 100 000 population.[1] Reported rates of chlamydia are dependent on the actual burden of disease in a population and the likelihood of getting screened. Women's rate of chlamydia is twice that of men because of a higher likelihood of being screened (692.7 per 100 000 for US women versus 380.6 for US men).[1] Chlamydia infection also varies by age, with rates being highest in women ages 20 to 24 (4064 per 100 000) and ages 15 to 19 (3307 per 100 000).[1] As women get older, rates decline. The rate of chlamydial infection is 176.6 per 100 000 in US women ages 40 to 44 years.[1] In our cohort, we similarly noted that age was associated with having a positive admission screening test upon admission for PTD and PPROM. However, this was not significant after adjustment for having a previous test in pregnancy. This retrospective study suggests limiting re-screening to those who were 25 years of age or younger or had a positive test earlier in pregnancy would reduce the number of tests while identifying most patients with chlamydia. In this cohort, approximately half of patients would not have required re-testing, and still, the majority (87.5%) of positive cases would have been identified on admission. Based on results of past studies examining maternal chlamydia infection, missing 12% of maternal chlamydia infections by reducing re-screening could result in increased rates of associated adverse neonatal outcomes.[6-10] Further research is needed to identify better factors that could safely be used to select patients who would most benefit from re-screening.

Gonorrhea is less common than chlamydia, and this was also demonstrated in our population, with 1 patient testing positive during antepartum testing and 2 patients with positive tests on admission. The rate of gonorrhea in Hawai‘i is 105 per 100 000 population.[1] The lower rate of gonorrhea in this cohort limits the ability to make recommendations beyond those already established by national organizations. Both ACOG and CDC recommend re-screening patients for gonorrhea based on whether an individual has an ongoing risk of infection.[2,24] In clinical practice, gonorrhea and chlamydia tests are commonly conducted and processed from the same specimen, so it is often practical to do the tests simultaneously.

There are several limitations to this study. The data were limited to information available in the electronic medical record, so we were not able to ascertain information about some risk factors, particularly those that pertained to sexual partners. Prenatal records and test results for many patients were gathered through a review of prenatal records from outpatient offices and laboratories rather than from the hospital's electronic medical record because most physicians did not use the same electronic medical record system as the hospital. Some records were incomplete, which may explain why some patients who had a positive prenatal chlamydia test but did not have a documented treatment tested negative for chlamydia on admission. Incorporating risk factors (new or multiple sex partners, inconsistent condom use, STI identified in a sexual partner, persons not in mutually monogamous relationships, exchanging sex for money or drugs) outlined by the CDC for gonorrhea or chlamydia would have further enhanced our ability to identify those in whom screening on admission was warranted. The wide confidence intervals generated in our analysis are a reflection of the limited sample size. In particular, given limitations of sample size, particularly in the group of patients who tested positive for chlamydia on admission, conclusions cannot be drawn about the associations between a positive test for chlamydia and chorioamnionitis, NICU admission, and sepsis.

Findings from this study have implications for clinical practice. During the study period, patients at our institution admitted for PTD or PPROM were routinely screened for gonorrhea or chlamydia regardless of previous screening results or their age.

This study suggests that re-screening at the time of admission can be more personalized based on patient characteristics, and repeat testing in many individuals can be eliminated. Further studies are needed to determine the optimal timing and frequency of re-screening in high-risk populations.

Conflict of Interest and Disclosure Statement

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Authors' Affiliations:
- Department of Obstetrics, Gynecology & Women's Health, John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI (EB, HJA,BK)
- The Permanente Medical Group of Kaiser South Sacramento, Sacramento, CA (CKW)
- Sutter West Bay Medical Group, San Francisco, CA (AJB)

Correspondence to:
Kaitlynn Ebisutani MD; 1319 Punahou St., #824, Honolulu, HI 96826;
Email: ebisutan@hawaii.edu

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