Published in final edited form as:

Sex Transm Dis. 2017 May ; 44(5): 272–273. doi:10.1097/OLQ.0000000000000630.

Keep Screening! Maternal Gonococcal Infection and Adverse Birth Outcomes

Chelsea L. Shannon¹ and Jeffrey D. Klausner, MD, MPH¹

¹Division of Infectious Diseases, Department of Medicine, University of California Los Angeles, CA, USA

The association between maternal *Neisseria gonorrhoeae* (NG) infection and adverse birth outcomes has rarely been adequately evaluated using population-based records. In this issue of Sexually Transmitted Diseases, Heumann, et al. used a population-based, retrospective cohort to evaluate the association between maternal NG infection and adverse birth outcomes. Data were gathered from birth certificates and hospital discharge data in Washington State between 2003 and 2014. The study compared outcomes among women identified with “present and/or treated” NG during their pregnancy to those who were not. Primary outcomes included low birth weight, small for gestational age, and preterm delivery. Secondary outcomes included prolonged premature rupture of membranes (PROM), chorioamnionitis, and neonatal intensive care unit (NICU) admission. Covariates included age, race/ethnicity, education, marital status, parity, maternal smoking, maternal diabetes, use of Women, Infants, and Children Program (WIC), prior preterm birth, prenatal care, insurance status, and presence of other maternal infections.

In their study, maternal NG infection was associated with increased odds of low birth weight and small for gestational age infants. Specifically, maternal NG infection was associated with 40% increased odds of a low birth weight infant, adjusted for maternal smoking and marital status. Women with NG infection during pregnancy also had 60% increased odds of a small for gestational age infant. No confounders were found for the associations. Women with NG infection during pregnancy were more likely to be young, less educated, black, single, multiparous, and smokers. No associations were found between maternal NG infection and preterm delivery, prolonged PROM, chorioamnionitis, or NICU admission.

The study had numerous strengths. The large, population based sample of 4,095 women was a significant advantage. Prior studies evaluating maternal NG infection and adverse birth outcomes were unable to quantify accurately the magnitude of potential risks.¹ The larger sample size provided more precise measures of the risk of NG infection during pregnancy. A second strength of this study was the biological plausibility of the results. During pregnancy, NG may cause a low-grade infection of the placenta, maternal decidua, or fetal membrane, leading to intrauterine growth restriction. Intrauterine growth restriction subsequently may result in low birth weight or small for gestational age infants.² Perhaps the most significant

Corresponding Author: Chelsea Shannon, 10920 Wilshire Blvd, Suite 350, Los Angeles, CA 90024, T: (310) 748-9794 F: (310) 794-8297, cshannon@mednet.ucla.edu.

Conflicts of Interest: No conflicts of interest.

strength of this study was that a wide array of potential confounders was evaluated, including maternal socioeconomic status, maternal health, and presence of other maternal co-infections. Those considerations help reduce the likelihood that unrelated factors influenced the findings and strengthen the specificity of the effect.

Though the use of birth certificates to collect exposures and outcome measures had advantages in terms of enabling a large study size, it also contributed to several limitations. Exposure was determined based on a checked box identifying a “present and/or treated” NG infection during pregnancy. Since those measures were gathered from hospitals within Washington State, it is likely that most women’s infections were treated according to standard medical practice. Thus, the study actually analyzed the association between treated maternal NG infection and adverse outcomes. Several studies have shown that antibiotic treatment of NG infection during pregnancy improves birth outcomes.^{3, 4} Therefore, antibiotic treatment perhaps explains why adverse outcomes previously associated with untreated NG infection, such as preterm delivery, were not found in this study. Since women whose NG infections were presumably cured with antibiotics still experienced adverse birth outcomes, women with untreated NG infections are likely at an even higher risk. The fact that treated NG infections still lead to adverse outcomes reinforces the need for primary prevention and the importance of early pregnancy NG screening.

Due to the method of data collection, the timing of infection was not addressed. Without knowing the trimester of diagnosis, the specific timing of putative mechanisms of adverse outcomes cannot be assessed. It has been suggested that NG infection during the first trimester can lead to more frequent adverse outcomes, including preterm delivery.⁵ Since this study included diagnosis of NG infection during any trimester, it is possible that associations that are present for first trimester infections were missed or mitigated by later trimester infections. The lack of information about trimester of diagnosis could explain why associations found in previous studies were not identified in this study.

The Centers for Disease Control and Prevention (CDC) currently recommends NG and *Chlamydia Trachomatis* (CT) screening at the first prenatal visit for women under 25 years of age or for women at “increased risk.”⁶ Increased risk is defined as having new or multiple sex partners, a sex partner with concurrent partners, a sex partner with a sexually transmitted disease (STD), inconsistent condom use among persons not in mutually monogamous relationships, previous or coexisting STDs, or exchanging sex for money or drugs.⁷ The CDC recommends third trimester CT screening for women considered to be at continued increased risk, but makes no further recommendation regarding NG screening. The American College of Obstetricians and Gynecologists and the United States Preventative Services Task Force (USPSTF) both recommend CT and NG screening for women under the age of 25 or for women at increased risk, as well as third trimester screening for both infections in those at continued increased risk. Interestingly, while USPSTF recommends against CT screening for pregnant women who are neither at an increased risk nor under age 25, it makes no such statement about NG screening. USPSTF has no recommendation about NG screening in pregnant women who are not at an increased risk due to insufficient evidence for or against it.

Because maternal NG infection may cause low birth weight and small for gestational age infants, all pregnant women should be screened for NG infection at least once, ideally during the first trimester. Assessing if a woman is “increased risk” is a subjective process on the part of the physician. Many women in need of NG screening may not meet the physician’s definition of increased risk, resulting in missed opportunities for identifying infection. Testing all pregnant women for NG infection would prevent those missed opportunities and likely reduce adverse infant outcomes. For example, the state of Florida currently recommends screening all pregnant women for NG and CT, regardless of perceived risk.⁸ It would be valuable to see a cost effectiveness analysis in the United States evaluating screening all pregnant women for NG and CT.

Internationally, the study has implications as well. Ten countries currently recommend NG and/or CT screening for all pregnant women: the Bahamas, Bulgaria, Canada, Estonia, Japan, Germany, Democratic People’s Republic of Korea, Romania, Sweden, and the UK. Four countries, Australia, New Zealand, Latvia, and the United States, recommend screening for both antenatal NG and CT infection in women under age 25 years or in those at increased risk.⁹ Most countries have no antenatal NG or CT screening policies. Currently, the World Health Organization’s (WHO) recommendations for antenatal sexually transmitted infection (STI) prevention only include human immunodeficiency virus and syphilis screening. There are no recommendations for NG or CT screening. In terms of treatment, the WHO suggests symptom-based treatment of NG and CT in pregnant women. However, NG and CT infections are largely asymptomatic, resulting in many undiagnosed and untreated cases. Given the documented adverse outcomes of NG infection during pregnancy, that approach is unacceptable. While screening is currently expensive and testing is not widely available, more needs to be done to reduce costs and increase access. Fortunately, several diagnostic companies are in the process of developing rapid point of care STI screening tests.¹⁰ As rapid testing becomes available, new cost-effectiveness analyses are needed to demonstrate the value of point-of-care screening interventions.

Overall, the study showed maternal NG infection was associated with increased odds of low birth weight and small for gestational age infants. The study is one of the first large, population-based studies of maternal NG and birth outcomes. The study size and design provides greater validity to the association between NG infection and adverse pregnancy outcomes than previous, smaller studies. However, the findings were limited by the fact that trimester of diagnosis and treatment status was unknown. Further studies are needed to evaluate the outcome of maternal NG infection according to the trimester of infection. It is also important to keep in mind that the results reflect the effects of a treated NG infection during pregnancy. As treated NG infection still led to adverse birth outcomes, it is likely that a study of untreated NG infection would show more dramatic adverse outcomes. The results of the study should be used to encourage NG prevention and control efforts as well as efforts to increase and monitor routine NG screening during pregnancy.

Acknowledgments

Sources of Funding: Funding provided by Center for AIDS Research (NIH grant no. AI028697) and Center for HIV Identification, Prevention, and Treatment Services (NIH grant no. MH058107).

References

1. US Preventive Services Task Force. Screening for gonorrhea: recommendation statement. The Annals of Family Medicine. 2005; 3(3):263–267. [PubMed: 15928231]
2. Germain M, Krohn MA, Hillier SL, et al. Genital flora in pregnancy and its association with intrauterine growth retardation. Journal of clinical microbiology. 1994; 32(9):2162–2168. [PubMed: 7814541]
3. Locksmith, G., Duff, P. Seminars in Perinatology. Vol. 25. WB Saunders; 2001. Infection, antibiotics, and preterm delivery.
4. Temmerman M, Njagi E, Nagelkerke N, et al. Mass antimicrobial treatment in pregnancy. A randomized placebo-controlled trial in a population with high rates of sexually transmitted disease. J Reprod Med. 1995; 210:176–180.
5. Johnson HL, Ghanem KG, Zenilman JM, et al. Sexually transmitted infections and adverse pregnancy outcomes among women attending inner city public sexually transmitted diseases clinics. Sexually Transmitted Diseases. 2011; 38:3. 167–171.
6. Centers for Disease Control and Prevention. Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources. Available at: <https://www.cdc.gov/std/tg2015/screening-recommendations.htm>. Accessed Jan 20, 2017
7. LeFevre ML. Screening for Chlamydia and Gonorrhea: US Preventive Services Task Force Recommendation Statement. Annals of Internal Medicine. 2014; 161(12):902–910. [PubMed: 25243785]
8. STD Testing Related to Pregnancy. Florida Administrative Code and Florida Administrative Register. Available at: <https://www.flrules.org/gateway/ruleno.asp?id=64D-3.042&Section=0>. Accessed Jan 20, 2017
9. Medline A, Davey DJ, Klausner JD. Lost opportunity to save newborn lives: variable national antenatal screening policies for Neisseria gonorrhoeae and Chlamydia trachomatis. International Journal of STD & AIDS. 2016
10. Herbst de Cortina S, Bristow CC, Davey DJ, et al. A systematic review of point of care testing for Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis. Infectious Diseases in Obstetrics and Gynecology. 2016