

Predictability of Negative Group B Streptococcus at Time of Delivery in Pregnant Women Who Were Negative at 35-37 Weeks

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Introduction

Group B streptococcus (GBS), also known as *Streptococcus agalactiae*, is the leading cause of neonatal morbidity and mortality in the United States. Early-onset GBS disease (EOGBS) in newborns occurs within the first week of life. Clinical syndromes associated with EOGBS include meningitis, pneumonia, and sepsis, which can ultimately lead to death. Neonates acquire GBS colonization or infection from the mother, whose primary sources of GBS vaginal and rectal colonization are the gastrointestinal and genitourinary tracts, respectively.^{7,32,33} Although asymptomatic, 6-45% of pregnant women have GBS rectal and/or vaginal colonization.^{4,8-13} The pathogen GBS is transmitted vertically from GBS-positive mothers to their babies. Only 1-3% of colonized infants develop severe syndromes; however, approximately 30-70% of infants born to GBS positive mothers become transiently colonized by the pathogen.^{6,23,26,28,30,35,36} In 2002, the Centers for Disease Control and Prevention (CDC) published updated guidelines advising all pregnant women be screened at 35-37 weeks' gestation for vaginal and rectal GBS colonization. The gold standard for GBS identification is enrichment followed by subculture. Women with positive cultures, in addition to women with GBS bacteriuria anytime during pregnancy or who had a previous infant affected by GBS, receive intrapartum antibiotic prophylaxis (IAP). Although the incidence of EOGBS disease has declined 27% since the implementation of the current guidelines for IAP administration, EOGBS cases

continue to occur.^{6,7,28} This culture-based screening during the third trimester was found to be 50% more effective than other possible screening options for identifying maternal GBS colonization. However, GBS colonization is transient during pregnancy, and increased intervals between screening and delivery decreases the positive predictive value (PPV) for GBS cultures, especially when the interval exceeds six weeks; negative predictive value (NPV) remains unchanged.^{4,5,7,17-21} Many of the reported cases of EOGBS occur in infants whose mothers had negative cultures at 35-37 weeks' gestation or in preterm infants born before their mothers could receive the recommended universal screening.^{1,5} To address these missed cases, in 2010 the CDC revised the guidelines to include separate algorithms for threatened preterm delivery and true preterm labor. The need for improved laboratory screening methods was also addressed in this revision with a detailed procedure for specimen collection and processing. These revisions are hoped to decrease the incidence of EOGBS in preterm infants who have an increased risk of morbidity and mortality from the disease⁷ and to improve the accuracy of the current recommended prenatal screening.^{6,26,27,31} With knowledge of the transiency of GBS colonization, the revision does not address the pregnant women that become positive after the culture-based screening at 35-37 weeks' gestation. The objective of this study is to evaluate the reproducibility of a negative GBS culture at the initiation of labor in a single, small maternity service in West Alabama.

Materials

Liquid Stuart media
Todd-Hewitt CNA (Lim) broths
Columbia CNA Agar with 5% sheep blood plate

Methods

Study Population

This study enrolled 30 pregnant women who presented to DCH Regional Hospital (Tuscaloosa, Alabama) at term with expected delivery of their pregnancy during that presentation. Approval of the study as designed was obtained from the Institutional Review Board of DCH Regional Hospital prior to enrolling subjects. Each enrolled patient had received her prenatal care with our group at the University of Alabama School of Medicine-Tuscaloosa. Each enrolled patient had had an ultrasound no later than the second trimester of her pregnancy, and gestational age was determined using a combination of last menstrual period and the earliest ultrasound examination. Per our clinic's prenatal care protocol, each patient had had a lower genital tract culture for screening of group B streptococcus (GBS) colonization. This culture was obtained between 35 and 37 completed weeks' gestation. Patients that failed to keep scheduled appointments between 35 and 37 weeks' gestation were excluded from this study. Each of the enrolled patients had a negative GBS culture between 35 and 37 weeks. These prenatal cultures were variously obtained by a medical student, a resident physician, or an attending physician. The enrolled patients that presented for delivery had the GBS culture repeated upon their hospitalization. The repeat culture was obtained during one of their cervical examinations or at the time of delivery. In many instances the culture was obtained following the patient having received epidural anesthesia. The intrapartum culture was obtained by either a post-graduate fellow physician or attending physician.

Written consent was obtained for intrapartum GBS testing in English and in Spanish. Patients who did not speak English or Spanish were excluded from the study.

Study Protocol

After obtaining informed consent, GBS swabs were collected from the lower vagina and anus of pregnant women at 35-37 weeks by the attending physician, resident physician, or medical student that had been taught how to collect GBS specimens. Each culturette was placed in liquid Stuart media made of calcium chloride, mercaptoacetic acid, and sodium glycerophosphate. The samples were brought to the lab within 24 hours and were inoculated into Todd-Hewitt CNA (Lim) broths. The broths were then placed in an incubator at 35-37°C for 24 hours. Standard protocol was then followed for GBS screening via Columbia CNA agar. The plates were then assessed for hemolysis. The patients who tested negative for group B streptococcus colonization were re-tested at the time of delivery irrespective of rupture of membranes via the same

method to determine current group B streptococcus status by the attending physician or post-graduate fellow physician. The intrapartum cultures were delivered to the laboratory as soon as possible following collection. However, this could be as many as 60 hours in instances where the culture was obtained on a Friday afternoon then delivered to the laboratory on a Monday morning. The swabs were stored in a safe area from Friday afternoon till Monday morning. This delay could have possibly changed the outcome of the study. Such delay could potentially make even more negative GBS culture results that, if handled more expeditiously, might have been, in fact, positive.

Results

Based on the study criteria of having received prenatal care at our center, having a negative group B streptococcus culture obtained between 35 and 37 weeks gestational age, and consenting to have a repeat group B streptococcus culture when in active labor, a total of 30 patients were enrolled in this study. The consent was obtained following admission to the hospital as the patient was either in labor or scheduled for induction of labor. Of these 30 patients, 9 had positive Group B streptococcus cultures when the culture was repeated as the patient was in labor. Nine of thirty or 30% of the patients with negative cultures at gestational age 35-37 were found to be Group B streptococcus positive at the time of labor.

Discussion

We do have an understanding of the transience of the discoverability of the presence of GBS in the female lower genital tract; however, we have come to rely upon a negative culture when obtained between 35 and 37 completed weeks. This current study reveals that that reliance was misplaced as often as 30% of the time. Thus, 30% of the women included in this study did not receive prophylactic antibiotics against GBS to protect their newborn infants from EOGBS. Although this study was performed in a small maternity service, if the current guidelines are unreliable 30% of the time, we need more effective screening measures to decrease the risk to neonates at the time of delivery. One way to help ensure that a pregnant woman's GBS status is reliable is to screen for colonization at the onset of labor. We need a cost effective, rapid screening method in order to properly care for our patients. With a rapid screening method in place, we will be able to provide antibiotic prophylaxis only to women that are GBS positive. This measure will reduce unnecessary exposure to antibiotics that can result in antibiotic tolerance. Thus, in order to better predict a woman's GBS status at the time of delivery we need better screening methods in place. The development of a cost effective, rapid screening method will decrease the risk of EOGBS in preterm and term neonates; decrease the risk of antibiotic resistance; and, in the long term, decrease costs. This study did not compare rapid testing verses traditional testing. This study was to see if mothers who tested negative at 35-37 weeks were GBS positive at delivery. Through the before mentioned results, it was found that 30% of negative mothers were later found to be positive.

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References

- Pupolo KM, Madoff LC, Eichenwald EC. Early-Onset Group B Streptococcal Disease in the Era of Maternal Screening. *Pediatrics*. 2005;115:1240-46.
- Boyer KM, Gadzala CA, Kelly PC, et al. Rapid Identification of Maternal Colonization with Group B Streptococci by Use of Fluorescent Antibody. *J Clin Microbiol*. 1981;14:550-56.
- Kaanbwa B, Bryan S, Gray J, et al. Cost-effectiveness of rapid tests and other existing strategies for screening and management of early-onset group B streptococcal during labour. *BJOG*. 2010;117:1616-1627.
- Valkenburg-van den Berg AW, Houtman-Roelofson RL, Oostvogel PM, et al. Timing of Group B Streptococcus Screening in Pregnancy: A Systematic Review. *Gynecol Obstet Invest*. 2010;69:174-183.
- Helalil NE, Nguyen JC, Ly A, et al. Diagnostic Accuracy of a Rapid Real-Time Polymerase Chain Reaction Assay for Universal Intrapartum Group B Streptococcus Screening. *Clin Infect Dis*. 2009;49:417-23.
- Melin P. Neonatal group B streptococcal disease from pathogenesis to preventive strategies. *Clin Microbiol Infect*. 2011;17:1924-303.
- Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease - revised guidelines from CDC, 2010. *MMWR Recomm Rep*. 2010;59(RR-10):32.
- Valkenburg-van den Berg AW, Sprij AJ, Oostvogel PM, et al. Prevalence of colonisation with group B Streptococci in pregnant women of a multi-ethnic population in The Netherlands. *Eur J Obstet Gynecol Reprod Biol*. 2006;124:178-183.
- Ferrieri P, Cleary PP, Seeds AE. Epidemiology of group B streptococcal carriage in pregnant women and newborn infants. *J Med Microbiol*. 1977;10:103-114.
- Dillon HC Jr, Gray E, Pass MA, Gray BM. Anorectal and vaginal carriage of group B streptococci during pregnancy. *J Infect Dis*. 1982;145:794-799.
- Bergseng H, Bevanger L, Rygg M, Bergh K. Real time PCR targeting the sip gene for detection of group B Streptococcus colonization in pregnant women at delivery. *J Med Microbiol*. 2007;56:223-228.
- Gavino M, Wang E. A comparison of a new rapid real-time polymerase chain reaction system to traditional culture in determining group B streptococcus colonization. *Am J Obstet Gynecol*. 2007; 197:388.e1-4.
- Barcaite E, Bartusevicius A, Tameliene R, et al. Prevalence of maternal group B streptococcal colonization in European countries. *Acta Obstet Gynecol Scand*. 2008;87:260-271.
- Boyer KM, Gadzala CA, Kelly PD, Burd LI, Gotoff SP. Selective intrapartum chemoprophylaxis of neonatal group B streptococcal early-onset disease. II. Predictive value of prenatal cultures. *J Infect Dis*. 1983;148:802-809.
- Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. *MMWR Recomm Rep*. 2002;51:1-22.
- Easmon CS, Hastings MJ, Neill J, Bloxham B, et al. Is group B streptococcal screening during pregnancy justified? *Br J Obstet Gynaecol*. 1985;92:197-201.
- Yancey MK, Schuchat A, Brown LK, Ventura VL, Markenson GR. The accuracy of late antenatal screening cultures in predicting genital group B streptococcal colonization at delivery. *Obstet Gynecol*. 1996;88:811-815.
- Goodman JR, Berg RL, Gribble RK, et al. Longitudinal study of group B streptococcus carriage in pregnancy. *Infect Dis Obstet Gynecol*. 1997;5:237-243.
- Anthony BF, Okada DM, Hobel CJ, et al. Epidemiology of group B Streptococcus: longitudinal observation during pregnancy. *J Infect Dis*. 1978;137:524-530.
- Yow MD, Leeds LJ, Thompsom PK, et al. The natural history of group B streptococcal colonization in the pregnant woman and her offspring. I. Colonization studies. *Am J Obstet Gynecol*. 1980;137:34-38.
- Centers of Disease Control and Prevention. Prevention of perinatal group B streptococcal disease: revised guidelines from CDC. *MMWR Recomm Rep*. 2002;51(RR-11)1-22.
- Goodman JR, Berg RL, Gribble RK, et al. Longitudinal study of group B streptococcus carriage in pregnancy. *Infect Dis Obstet Gynecol*. 1997;5:237-43.
- Baker C, Stevens DL, Kaplan EL, et al. Group B streptococcal infections. In *Streptococcal infections*. New York, NY: Oxford University press, 2000; 222-237.
- Centers for Disease Control and Prevention. Perinatal group B streptococcal disease: a public health perspective. *MMWR Recomm Rep*. 1996;45(RR-7):1-24.
- Schrag SJ, Zell ER, Lynfield R, et al. A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates. *N Engl J Med*. 2002;347:233-9.
- Centers for Disease Control and Prevention. Perinatal group B streptococcal disease after universal screening recommendations-United States, 2003-2005. *MMWR Morb Mortal Wkly Rep*. 2007;56:701-705.
- Van Dyke MK, Phares CR, Lynfield R, et al. Evaluation of universal antenatal screening for group B streptococcus. *N Engl J Med*. 2009;260:2626-2636.
- Verani JR, Schrag SJ. Group B streptococcal disease in infants: progress in prevention and continued challenges. *Clin Perinatol*. 2010; 37:375-392.
- Bergeron MG, Menard C, et al. Rapid detection of group B streptococci in pregnant women at delivery. *N Engl J Med*. 2000;343:175-9.
- Heath PT, Schuchat A. Perinatal group B streptococcal disease. *Best Pract Res Clin Obstet Gynecol* 2007;21:411-24. Epub 2007 Mar 2.
- Poyart C, Reglier-Poupet H, Tazi A, et al. Invasive Group B streptococcal infections in infants, France. *Emerg Infect Dis*. 2008;14:1647-1649.
- Phares CR, Lynfield R, Farley MM, et al. Epidemiology of invasive group B streptococcal disease in the United States, 1999-2005. *JAMA*. 2008;299:2056-65.
- Schrag SJ, Zywicki S, Farley MM, et al. Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis. *N Engl J Med*. 2000;342:15-20.
- Yancey MK, Schuchat A, Brown LK, et al. The accuracy of late antenatal screening cultures in predicting genital group N streptococcal colonization at delivery. *Obstet Gynecol*. 1996;88:811-5.
- Boyer KM, Gotoff SP. Prevention of early-onset neonatal disease with selective intrapartum chemoprophylaxis. *N Engl J Med*. 1986;314:1665-1669.
- Schuchat A. Group B streptococcus. *Lancet*. 1999;353:51-6.