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# Catching Strep: Cost-Comparison of Peri-Natal Screening Assays for Goup B Streptococcus

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**Abstract:**

CATCHING STREP: COST-COMPARISON OF PERINATAL SCREENING ASSAYS FOR GROUP B STREPTOCOCCUS. BG Dempsey, L Leeman, S Phelan, and S Young, University of New Mexico School of Medicine, Albuquerque, NM

**Purpose:** To determine how the implementation of a rapid polymerase chain reaction (PCR) –based assay for Group B Streptococcus (GBS) affects the treatment and management of women presenting to the hospital, in labor with an unknown GBS culture status.

**Methods:** We performed a retrospective chart review of women presenting in labor with an unknown GBS culture status to a large university –based hospital. We compared two groups of women: 1. Women who presented prior to the implementation of the Rapid PCR culture who were cultured using traditional methods; 2. Women who presented after the Rapid PCR GBS culture was implemented as a standard of care. We analyzed variables such as length of hospital stay, administration of prophylactic antibiotics against GBS, GBS-associated laboratory testing, and patient demographics. **Results:** The implementation of the Rapid PCR GBS culture was associated with a higher median cost of hospital stay compared to the traditional GBS culture method, while resulting in less extended hospital stays due to concerns for neonatal GBS infections.

**Conclusion:** The implementation of Rapid PCR GBS cultures for women presenting in labor with an unknown GBS status does not correlate with cost-savings or decreased length of post-partum hospital stay despite being associated with a decrease in the number of infants with a prolonged hospital stay secondary to GBS concerns.

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**Introduction:** Group B Strep (GBS), otherwise known as *Streptococcus agalactiae*, is the leading cause of infectious morbidity and mortality among newborns in North America[1]. Between 10%-30% of pregnant women are colonized with GBS in the vagina or rectum[2], which can be transmitted vertically during labor or delivery, and potentially result in invasive neonatal infection. The rate of vertical transmission from colonized mothers to their infants during labor is reported to be approximately 50%, of which 1-2% present with early-onset GBS disease[3]. To put this in perspective, out of the approximately 4 million births in the United States, up to 600,000 of delivering women are colonized with GBS, potentially resulting in vertical transmission to ~300,000 infants and early onset disease in ~40,000 infants. The actual number of infants infected by GBS is significantly lower (see below) due to screening efforts and the use of antibiotics.

GBS infections in neonates typically belong to one of two groups: early onset disease or late onset disease. *Early onset* disease accounts for approximately 1,600 cases of GBS infection, and 80 deaths annually [4,5] and presents as typical neonatal sepsis. Newborn complications from invasive GBS infection can include sepsis or pneumonia, meningitis, osteomyelitis, or septic arthritis. GBS is the most common bacterial agent responsible for CNS infection in infants 0 to 3 months of life; neurological sequelae from GBS meningitis include sight or hearing loss and mental retardation. Death occurs in 5% of infants[6]. Early onset disease accounts for approximately 51% of GBS infections in neonates[7]. *Late onset* infections occur in infants from 1 week up to three months of age, and affected infants typically present with meningitis. Late onset disease is the result of vertical transmission or nosocomial or community acquired infection.

Coinciding with active prevention efforts, the early onset form of GBS disease has decreased by 70% from 1993 to 2002—1.7 cases per 1,000 live births (1993) to 0.4 cases per 1,000 live births (2002)[4,5]. Since 1996, the Centers for Disease Control and Prevention (CDC) has recommended obtaining recto-vaginal cultures at 35-37 weeks gestation; women who screen positive for GBS colonization are treated with antibiotic prophylaxis prior to onset of labor. A major difficulty with prenatal GBS screening has been the relatively short window of time during pregnancy in which cultures can be obtained. The CDC recommendation for GBS screening at 35-37 weeks is based on the cost burden of testing and the duration of the validity of test results. GBS cultures obtained prior to 35 weeks are poor predictors of GBS carrier status at delivery and results are only predictive up to six weeks after culture[8, 9]. Most women deliver between 39 and 41 weeks gestation, thus 35 weeks gestation is the usual time period for GBS culturing (latest CDC data show that only one out of every eight live births was pre-term)[10]. Thus, GBS testing should be performed early enough to obtain a woman's GBS carrier status prior to delivery, yet late enough that results of GBS screens are still accurate by the time most deliveries take place. Testing for GBS is typically done with a recto-vaginal culture, with results available after two to three days.

Women whose culture status is unknown should be assessed for GBS risk factors. GBS risk factors include:

- pre-term delivery (defined as delivered < 37 weeks gestation
- prolonged amnionic membrane rupture (≥18 hours)
- intra-partum temperature of ≥ 100.4º F (≥38.0º C)

Women who present with an unknown culture status and a GBS risk factor should also receive intra-partum chemoprophylaxis. Intra-partum antibiotic prophylaxis is the method of choice for preventing neonatal early-onset GBS disease. Current recommendations from the American College of Obstetricians and Gynecologists[4] indicate penicillin as the first-line agent for intra-partum antibiotic prophylaxis, with ampicillin serving as an acceptable alternative. Penicillin is preferred as it has a narrower spectrum of antimicrobial activity, and may be less likely to select for resistant organisms. Intravenous administration is the only route of administration recommended for intra-partum chemoprophylaxis to prevent peri-natal GBS disease, regardless of the antimicrobial agent used, because higher intra-amniotic concentrations are achieved with this method. At least two intra-partum doses are required for successful treatment of GBS, a 5mU loading dose, and a 2.5mU dose 4 hours later. Cefazolin is the agent of choice for intra-partum chemoprophylaxis among penicillin-allergic women not at high risk for anaphylaxis.

**Women with unknown GBS status at time of delivery without associated risks of GBS infection commonly undergo a prolonged in-patient stay (minimum of 48 hours additional stay) for newborn observation, as do women who received inadequate chemoprophylaxis (due to rapid delivery).** Prolonged hospital admissions increase the cost of labor and delivery and utilize hospital resources. In order to minimize prolonged inpatient stays and chemoprophylaxis, and to appropriately direct resources to infants truly at risk for GBS disease, the use of rapid molecular testing may prove beneficial. Results from rapid molecular-based assays can be obtained within 2 hours—vs. greater than 2-3 days for culture-based methods. The 2002 statement by the CDC on prevention

of GBS disease in neonates states that "an adequate rapid intra-partum test must be as sensitive as culture, rapid, and convenient for integration into routine laboratory use."[11] Rapid GBS tests have been developed sufficiently so that sensitivity and specificity of the rapid test are at least equal to or better than traditional vaginal/peri-anal swabbing culture techniques[12,13]. Due to the increased cost of rapid testing compared with traditional culture-based strep tests (average cost of the rapid test is approximately $100-125 vs. $25-40 for the GBS culture test), rapid testing needs to be limited to an at-risk population of pregnant women with unknown GBS status in order to be cost-effective. Sensitive and accurate rapid-screening tests could reduce the risks associated with prophylactic antibiotic therapy, and may obviate the need for unnecessary observational hospital stays for mother and infant; in this way the rapid strep test may prove cost-effective in select populations despite being a more expensive test than culture-based methods.

We hypothesized that the use of rapid strep testing at an academic center should translate into cost-savings when utilized in women at risk for GBS infection with unknown GBS culture status at time of presentation to labor and delivery in labor compared with traditional GBS culture methods by decreasing mean length of hospital stay for the mother-infant dyad, additional testing of the newborn, and the need for prophylactic antibiotics.

**Methods (including Statistical Analysis):**

Prior to implementation of the protocol, we obtained HRRC (IRB) approval for the project.

We performed a retrospective chart review of women who presented at time of labor with an estimated gestational age of ≥ 35 weeks and one or more of the following:

- no prenatal care
- no GBS culture
- no available results from prior GBS culture

We obtained medical record numbers from an internal database to study all women that met the above criteria at our institution in 2006, prior to the implementation of Rapid GBS testing (pre-RGBS). We also studied women who met the above criteria from October 1, 2007-February 29, 2008, after the implementation of the Rapid GBS culture (post-RGBS) as a standard of care test at our institution (the Rapid GBS test has been standard of care at UNMH since July, 2007). We obtained the medical record numbers for the post-RGBS group directly from the laboratory that processes all of the Rapid GBS cultures at our institution. Results from Rapid GBS cultures were collected from a recto-vaginal sample and processed using the Xpert GBS Assay (Cepheid) for rapid GBS diagnosis. Xpert GBS utilizes real time and reverse transcription Polymerase Chain Reaction to detect a target in GBS DNA. Relative to culture, the Xpert GBS assay displays a sensitivity of 88.6% and a specificity of 96.7%.[14]

We used a standardized one page data collection form to review labor and delivery and newborn nursery records and abstract data that included information on the following variables: demographic characteristics of the mother and newborn (including gestational age at delivery and APGARs), adequacy of prenatal care, length between presentation and delivery, length of hospital stay for mother and newborn, clinical risk factors for GBS disease (i.e., gestation of less than 37 weeks, rupture of membranes ≥18 hours prior

to delivery, intrapartum temperature ≥38°C, group B streptococcal bacteriuria, previous infant with group B streptococcal disease), intrapartum and post-partum antibiotic use, and utilization of blood cultures and complete blood count with differential.

Hospital charges are incurred every midnight, and we calculated length of hospital stay for study subjects based on the number of midnights each subject spent in the hospital. Costs of laboratory testing and antibiotics were calculated using our institution's standard charges (see Table 1-1). The total cost of hospital stay was analyzed using the median cost to avoid skewing the data from subjects with lengthy hospital stays (eg, neonates requiring methadone weaning or those born with congenital anomalies). The total cost was calculated to include cost of hospital room charge by length of hospital stay, administration of antibiotics, complete blood count with differential, blood culture, and cost of GBS test for each study group.

| **Table 1-1 Standard Charges** | (price) |
|---|---|
| Standard GBS culture: | $37.09 |
| Rapid GBS culture: | $98.08 |
| CBC with differential: | $58.00 |
| Blood Culture: | $129.00 |
| Post-partum Maternal Hospital Room Charge: | $716.00 |
| Post-partum Neonatal Hospital Room Charge: | $590.00 |
| Dose of IV Penicillin G with administration fee: | $50.00 |
| Dose of IV Ampicillin with administration fee: | $106.00 |
| Dose of IV Cefazolin with administration fee: | $63.00 |

When chart review was insufficient to determine causes of extended hospital stay, individual cases were reviewed by the Medical Directors of the University Hospital Newborn Nursery to determine if the cause of extended hospital stay was due to concerns for GBS infection or other reasons. Prolonged hospital stays were defined as greater than 48 hours post-partum for vaginal deliveries.

Using SAS statistical software, cost analysis of the pre-RGBS and post-RGBS populations was performed with Chi Square analysis of the study variables (length of hospital stay, use of antibiotics, complications, and other variables) and a Wilcoxon Rank Sum Test to compare total estimated costs of the two study populations.

**Results**: Active surveillance for women presenting with an unknown GBS status at time of delivery yielded 234 potential subjects in 2006. 72 subjects (30%) from the pre-RGBS population underwent C-sections and were excluded from our study as the number of C-sections was not comparable in the post-RGBS group that contained 11 subjects with C-sections (7.1% of post-RGBS subjects). In addition, we excluded two cases of stillborn births. This yielded 150 subjects from the pre-RGBS population.

The post-RGBS population consisted of 159 eligible subjects, of which eleven were excluded for undergoing C-sections (see above). In addition, we excluded two deliveries of twins, yielding 144 post-RGBS subjects.

Costs of antibiotics associated with treatment for chlamydia/gonorrhea were not included in the cost analysis as this did not affect management of concerns for unknown GBS

culture status. Demographic characteristics of each study group were compared and are shown in table 1.2 below:

| **Table 1.2 Demographics** | Pre-Rapid GBS Population | Post-Rapid GBS Population |
|---|---|---|
| Mean age— | 25.9 ± 5.9 years | 26.3 ± 6.5 years |
| Ethnicity— | | |
| African American: | <1% | 2.5% |
| Asian: | 2.7% | 1.3% |
| Hispanic: | 66.1% | 58.5% |
| Native American: | 14.5% | 15.7% |
| Non-Hispanic White: | 12.5% | 17.0% |
| Other: | 3.2% | 5.0% |
| Gestational Age (mean)— | 38.0 ± 1.8 weeks | 38.5 ± 1.6 weeks |
| Reason for GBS unknown— | | |
| Inadequate Prenatal Care: | 32.3% | 33.9% |
| Unable to Locate Results: | 66.4% | 60.4% |
| Results >6 weeks old: | 0% | 2.5% |
| Other: | 1.3% | 3.2% |

Total median costs of hospital stay were not significantly different between the two study groups: $2649.00 for the pre-RGBS population vs. $2710.00 for the post-RGBS population (two-tailed p=.11). The implementation of the Rapid GBS culture was associated with a decline in prolonged hospital stay **due to concerns for GBS culture status** (17% of the pre-RGBS population vs. 5% of post-RGBS population, p=.002), however there was no difference in length of hospital stay between the two study groups (47% of the pre-RGBS population had prolonged hospital stays vs. 56% of the post-RGBS population). The two study groups were similar in regards to the number of subjects that did not have prolonged hospital stays for any reason (p=.0001).

Use of prophylactic antibiotics in mothers was not significantly different in each group, 27% in the pre-RGBS population vs. 19% in the post-RGBS population (p=.12). Nor was use of antibiotics in the neonatal populations significantly different: 11% in the pre-RGBS population vs. 9% in the post-RGBS population (p=.61). Analysis of laboratory testing revealed that 36% of neonates in the pre-RGBS population had complete counts performed, vs. 26% of the post-RGBS population (p=.06). Neonates in the pre-RGBS population had significantly more blood cultures performed—32% vs. 21% of the post-RGBS population (p=.03).

**Conclusion**: While the introduction of the Rapid GBS culture resulted in a decrease of prolonged hospital stays due to concerns for GBS culture status, this did not appear to be associated with cost-savings. Many of the neonates that were eligible for discharge based on known GBS culture status (established with Rapid GBS cultures) ended up staying in the hospital for other reasons, such as hyperbilirubinemia or substance dependence, or from maternal issues such as pre-eclampsia and anemia. While the total cost of hospital stay was not decreased by implementing the Rapid GBS culture in our study population, this finding is not likely to affect usage of the Rapid GBS culture at our institution as Rapid GBS culturing has become a standard of care at UNMH, irrespective of costs.

The two study populations are demographically similar; however given the difference in C-section rates between the two groups the groups do not appear to be homogenous (see ***Methods*** above). A possible source of this difference could be the result of using a different subject database for each group that results in a slightly different patient population being studied. It may be impossible to identify if all eligible candidates

actually received the rapid GBS test. It is unlikely that the two study groups differ significantly in prevalence of maternal drug use, congenital defects, maternal anemia, difficulty breastfeeding, or other issues that account for prolonged hospital stays given that the populations being studied are from the same institution and are drawn from a similar time period.

A possible confounding variable could be that more Rapid GBS cultures were being performed as a result of the test being recently implemented. Attending physicians, hospital staff, and residents received training about the Rapid GBS culture, and reminders of how to order the test and who was eligible for the culture were posted in work areas. This may have led to an increased awareness of testing for GBS in patients that present in labor with unknown GBS culture status compared to the time period prior to the implementation of the Rapid GBS culture. Another confounding variable in our study is the opening of an Intermediate Care Nursery (ICN) at UNMH in January, 2008, which falls in the middle of the time period of the Rapid GBS study group. Infants admitted to the ICN are subject to different treatment and management, and generally have longer hospital stays than infants admitted to the Newborn Nursery at our institution. Six study subjects were admitted to the ICN from the post-RGBS population.

Use of the Rapid GBS culture could be improved by enhanced access to laboratory results between different healthcare institutions. A large portion of our study population had prior GBS culture results from other healthcare institutions that were unavailable at the time of delivery, resulting in an increased need for the Rapid GBS cultures. A more detailed study evaluating the use of the Rapid GBS culture in a population of women who

deliver via C-section is reasonable. The implementation of the Rapid GBS culture may increase hospital costs in the C-section population; women who deliver via C-section do not require rapid GBS testing as GBS is transmitted vertically via vaginal delivery. In our study, hospital stays were not categorized for analysis for reasons other than concerns for GBS culture status or GBS infection; further study of the reasons for prolonged hospital stay in our patient population is warranted.

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