Assessment of Intrapartum Antibiotic Prophylaxis for the Prevention of Early-onset Group B Streptococcal Disease

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Background: Most early-onset group B streptococcal (GBS) disease in recent years has occurred in newborns of prenatally GBS-negative mothers who missed intrapartum antibiotic prophylaxis (IAP). We aimed to assess the accuracy of prenatal culture in predicting GBS carriage during labor, the IAP use, and occurrence of early-onset GBS disease.

Methods: We obtained vaginal-rectal swabs at labor for GBS culture from 5497 women of \geq 32 weeks' gestation and surface cultures at birth from newborns between February 5, 2008 and February 4, 2009 at 3 hospitals in Houston, TX and Oakland, CA. Prenatal cultures were performed by a healthcare provider during routine care, and culture results were obtained from medical records. The accuracy of prenatal culture in predicting intrapartum GBS carriage was assessed by positive and negative predictive values. Mother-to-newborn transmission of GBS was assessed. Newborns were monitored for early-onset GBS disease.

Results: GBS carriage was 24.5% by prenatal and 18.8% by labor cultures. Comparing prenatal with labor GBS cultures of 4696 women, the positive predictive value was 50.5% and negative predictive value was 91.7%. IAP, administered to 93.3% of prenatally GBS-positive women, was 83.7% effective in preventing newborn's GBS colonization. Mother-to-newborn transmission of GBS occurred in 2.6% of elective cesarean deliveries. Two newborns developed early-onset GBS disease (0.36/1000 births); the prenatal GBS culture of one was negative, the other's was unknown.

Conclusions: IAP was effective in interrupting mother-to-newborn transmission of GBS. However, approximately 10% of prenatally GBS-negative women were positive during labor and missed IAP, whereas approximately 50% of prenatally GBS-positive women were negative during labor and received IAP. These findings emphasize the need for rapid diagnostics during labor.

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- Supported by the Intramural Research Program, Division of Intramural Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health.
- All authors do not have a commercial or other association that might pose a conflict of interest.
- Presented partly at the Pediatric Academic Societies' Annual Meeting May 1–4, 2010, Convention Center, Vancouver, Canada, Abstract 1370.8.
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- Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.pidj.com).

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ISSN: 0891-3668/11/3009-0759

DOI: 10.1097/INF.0b013e31821dc76f

Key Words: group B *Streptococcus*, early onset disease, predictive values, prenatal cultures, intrapartum antibiotic prophylaxis (*Pediatr Infect Dis J* 2011;30: 759–763)

ntrapartum antibiotic prophylaxis (IAP) has been the strategy of the US National Guidelines for prevention of perinatal group B streptococcal (GBS) disease.^{1,2} The widespread use of IAP in the United States has been accompanied by a reduction of neonatal early-onset GBS disease from 1.8/1000 live births in the early 1990s to 0.35 in 2003³ and has remained at this level since then.⁴ The revised guidelines of 2002 and 2010 recommend universal screening of GBS at 35 to 37 weeks' gestation and IAP for women who have had a positive prenatal GBS culture, had GBS bacteriuria during the current pregnancy, had an infant with invasive GBS disease previously, or whose GBS status is unknown, and has any of the following clinical features: preterm delivery (<37 weeks' gestation), ruptured membranes ≥ 18 hours, or fever (>38.0°C) during labor. IAP, however, is not recommended for prenatally GBS-positive women who undergo cesarean delivery without labor or ruptured membranes.^{2,5} These recommendations have been widely implemented in the United States. A survey in 2003-2004 of selected counties in 10 states in the United States reported that 85.0% of women were screened for GBS before delivery, and 85.1% of women who were eligible for antibiotic treatment during labor received chemoprophylaxis.⁶

These guidelines, however, have limitations because prenatal cultures do not accurately predict GBS carriage during labor. Prior studies have reported that 4.0% to 11.6% of prenatally GBS-negative women had positive GBS cultures during labor,⁷⁻¹³ whereas 13.0% to 54.7% of prenatally GBSpositive women had a negative culture during labor (Table 1).⁷⁻¹⁵ Thus, some women who are colonized during labor will not receive IAP, subjecting their newborns to the risk of early-onset GBS disease. Those who are colonized prenatally but cultured negative during labor are given IAP despite a low risk of delivering infants with early-onset GBS disease. Recent studies have reported that 61% to 82% of term newborns with early-onset GBS disease were born to prenatally GBS-negative mothers.^{6,16,17} In this study, we not only compared routine prenatal GBS culture with those cultures obtained during labor in a large population, but also assessed intrapartum antibiotic administration and mother-to-newborn transmission of GBS and evaluated these findings in relation to the prevention of early-onset GBS disease.

METHODS

We analyzed data obtained from a prospective study with the primary aim of assessing the relation of neonatal respiratory distress and maternal GBS carriage during labor. The study enrolled a cohort of pregnant women and their newborns

 The Pediatric Infectious Disease Journal
 • Volume 30, Number 9, September 2011
 www.pidj.com | 759

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Accepted for publication March 21, 2011.

TABLE 1. Published Positive and Negative Predictive Values of Prenatal Culture for Group B Streptococcal Carriage at Labor

Study	Location	Gestational Age at Culture	Prenatal GBS + Rate (%)	No. Positive Cultures		Positive	No. Negative Cultures		Negative
				Prenatal	At Labor	Value (%)	Prenatal	At Labor	Value (%)
Allardice et al ⁷	Canada	28-34	10.3	53	29	45.3	471	452	96.0
Boyer et al ⁸	United States	First-third trimester	22.8	393	264	67.2	200	183	91.5
Yancy et al ⁹	United States	35–36	26.5	193	168	87.0	633	607	95.9
Goodman et al ¹⁰	United States	26 - 28	13.9	111	67	60.4	706	675	95.6
Edwards et al ¹¹	United States	35-37	NA	218	146	67.0	NA	NA	NA
Hiller et al ¹²	Australia	36	20.0	120	NA	77.0	480	NA	94.0
Valkenburg et al ¹⁴	Netherlands	35-37	21.0	173	136	79.0	588	530	93.6
El Helali et ¹⁵	France	35-37	12.3	115	67	58.3	818	753	92.1
Towers et al ¹³	United States	Late third trimester	15.4	227	152	67.0	1245	1101	88.4
This study	United States	≥ 32	24.5	1172	592	50.5	3524	3233	91.7

between February 5, 2008 and February 4, 2009 from 3 hospitals in Houston, TX and Oakland, CA. Using the same protocol, women of \geq 32 weeks' gestation were cultured on admission for delivery and their newborns at birth for GBS carriage. Prenatal cultures were performed by their healthcare providers during routine care.

The Institutional Review Board of Baylor College of Medicine, Children's Hospital & Research Center Oakland, Alta Bates Summit Medical Center, and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health reviewed and approved the study. Maternal consent was obtained during prenatal visits or after admission for delivery.

Study Design

Ben Taub General Hospital and St. Luke Episcopal Hospital affiliated with Baylor College of Medicine, Houston, TX and Alta Bates Summit Medical Center with the Children's Hospital and Research Center Oakland participated in enrolling mothers on admission for delivery and providing initial care for newborns. Newborns requiring level II/III nursery care received it at their birth hospital or were transferred to Texas Children's Hospital or to Children's Hospital & Research Center Oakland.

Vaginal-rectal swabs for GBS culture were obtained daily by physicians, obstetric, or study nurses during all shifts from women \geq 32 weeks' gestation on admission for delivery ("the labor culture") according to the recommended procedures.² Women were designated as GBS+/+ (prenatal/labor), GBS +/-, GBS -/+, or GBS -/- according to their prenatal and labor culture results.

Newborns had cultures taken from the throat, anus, umbilicus, and both external ear canals before their first bath.¹⁸ The nursing and study staff followed the newborns for the duration of the hospital stay. Prenatal culture results, demographic data, and antibiotic use during labor were obtained from the medical records.

Microbiological Procedures

Polyurethane-tipped swabs in transport media (BBL Culture Swab EZ/EZ11 Collection and Transport System) were used to obtain cultures from mothers' vaginal and rectal areas and newborns' surface sites. Standard microbiologic techniques were used to identify GBS. β -hemolytic colonies and suspicious nonhemolytic colonies were tested for GBS by latex agglutination (PathoDx, Diagnostic Products Corporation). Isolation and identification of GBS were performed at a designated microbiology laboratory at each study site using the same protocol.

Semiquantitative Culture of Maternal Vaginal-rectal Swab

Vaginal-rectal swabs were refrigerated and processed within 72 hours by placing in 2 mL Todd-Hewitt Broth containing polymyxin B (10 μ g/mL), nalidixic acid (15 μ g/mL), and crystal violet (0.1 μ g/mL), and vortexed. A 0.01 mL aliquot of the broth was removed using a calibrated loop, streaked onto a colistin-nalidixic acid (CNA) agar plate similar to the way urine culture is performed and incubated at 37°C for 18 to 24 hours. The GBS colonies were then counted and recorded as 0, 1-50 colonies (<10,000 CFU/swab), 51-100 colonies (10,000-20,000 CFU/swab), and >100 colonies (>20,000 CFU/swab).¹⁹ If no GBS colonies were found on the CNA plate, the original broth (which had been incubated overnight) was subcultured onto a 5% sheep blood agar plate. Because the organisms multiply in the broth during incubation, the subcultured plate could only be interpreted as positive or negative. For analyses, the density of growth was defined as follows: grade I if no GBS colonies were found on the CNA plate but the broth subculture was positive; grade II when 1 to 50 colonies of GBS were counted on the CNA plate; grade III, 51 to 100 colonies; and grade IV when >100 colonies were counted.

Newborn Culture

The swabs were refrigerated and processed within 72 hours by placing each swab into Todd-Hewitt broth containing antibiotics as described earlier and incubated for 18 to 24 hours. The broth was then subcultured on sheep blood agar plates at 37°C for 24–48 hours. β -hemolytic colonies and suspicious nonhemolytic colonies were tested for GBS.

Statistical Analyses

The accuracy of prenatal culture in predicting intrapartum GBS carriage was assessed by positive (PPV) and negative (NPV) predictive values. PPV was determined by calculating [(number of GBS+/+ women)] \times 100%, and NPV by [(number of GBS -/- women)] \times 100%, and NPV by [(number of GBS -/- women)] \times 100%. The efficacy of IAP in interrupting mother-to-newborn transmission was calculated by (1 - transmission rate in treated mother \div transmission rate in untreated mothers) \times 100%. Confidence intervals (CIs) for the efficacy of IAP were obtained by transforming the asymptotic CIs for the relative risk. Fisher exact test was used for the comparisons of proportions. CIs for proportions were based on the exact formula for the binomial distribution.

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TABLE 2. Discordance in Group B *Streptococcus* Detection Between the Prenatal and the Labor Cultures

Study Site	F	Positive Prena (N = 1) Labor Cu	tal Culture 172) 1lture	Negative Prenatal Culture (N = 3524) Labor Culture			
	No. Cultured	No. Positive	Positive Predictive Value %, 95% CI	No. Cultured	No. Negative	Negative Predictive Value %, 95% CI	
Houston Oakland Total	$425 \\ 747 \\ 1172$	267 325 592	62.8, 58.0-67.4 43.5, 39.9-47.2 50.5, 47.6-53.4	1834 1690 3524	1680 1553 3233	91.6, 90.2–92.8 91.9, 90.5–93.2 91.7, 90.8–92.6	

RESULTS

Vaginal-rectal cultures were obtained from 5497 women on admission for delivery (2688 in Houston and 2809 in Oakland) among 15,461 deliveries (7797 in Houston and 7664 in Oakland). The cohort was racially and ethnically diverse and not different from those of the total maternal population of the study sites. Mothers' ages ranged from 15 to 47 years (median: 29.3 years). Overall, 27.3% of the women were primigravidas and 25.6% had cesarean deliveries, of which 25% were elective. Multiple births occurred in 1.2%. The newborns' birth weights ranged from 1060 to 5456 g with a median of 3359 g, and 93.5% of newborns were full term (\geq 37 weeks' gestation) (Table, Supplemental Digital Content 1, http://links.lww.com/INF/A858, describes the characteristics of mothers and their newborns).

Prenatal Culture

Among the women in the cohort, 4778 (86.9%) had prenatal cultures: results were available in 4696 (98.3%); 1172 (24.5%) of them were positive. Prenatal cultures were positive in 30.2% of women in Oakland compared with 18.5% in Houston (P < 0.001). The timing of prenatal cultures was not available for 1535 (32.1%) women (1117 in Oakland and 418 in Houston). For those whose gestational age at the prenatal cultures was recorded (n = 3243, 67.9%), 12.5% were at <35 weeks' gestation, 75.7% at 35 to 37 weeks, and 11.8% at \geq 38 weeks. Of women who had prenatal cultures at <35 weeks, 72% delivered at term.

Labor Culture

Of women cultured during labor, 1031 (18.8%) were positive for GBS (19.0% in Houston and 18.4% in Oakland). The carriage rate of black women (27.9%) was higher than of white (17.7%), Hispanic (17.5%), or Asian women (13.6%) (P < 0.001). Among colonized women, 46.6% had grade I, 29.7% had grade II, 15.6% had grade III, and 8.2% had grade IV growth density. The proportion of women who had heavy carriage of GBS (grade II–IV growth density) was higher among the GBS+/+ than the GBS -/+ women (60.0% vs. 43.6%, P < 0.001).

Discordance of GBS Carriage Between the Prenatal and Labor Periods

Of the 1172 prenatally GBS-positive women, 592 (50.5%) had positive, and 580 (49.5%) had negative cultures during labor. The PPV of prenatal culture for GBS carriage during labor was 50.5% (95% CI: 47.6%–53.4%); higher in Houston than in Oakland (62.8% vs. 43.5%, P < 0.001) (Table 2). Among the 3524 prenatally GBSnegative women, 91.7% had negative and 8.3% had positive culture during labor. The NPV was 91.7%, similar at the 2 study sites. The PPV was highest for women whose cultures were taken within 1 week of delivery and lowest among those whose cultures were taken at ≥ 6 weeks of delivery (69.7% vs. 54.4%, P = 0.03). For women whose prenatal cultures were taken at 35–37 weeks' gestation as recommended, the PPV was 60.6% and the NPV 89.5%. The PPV was significantly lower in women with unknown timing of prenatal culture than those with a known timing (28.7% vs. 61.1%, P < 0.001).

The proportion of women who received antibiotics during pregnancy was not statistically different between the GBS +/- and the GBS+/+ women (18.6% vs. 15.2%, P = 0.29).

Antibiotic Administration During Labor

Overall, 38.3% of mothers received antibiotics during labor (45.7% in Oakland and 30.4% in Houston, P < 0.001). Of the prenatally GBS-positive women, 93.3% received IAP, similar for GBS+/+ and GBS+/- mothers (93.8% vs. 92.9%). Of the prenatally GBS-negative women, 20.0% received antibiotics for reasons such as suspected maternal infection, cesarean delivery, preterm labor, or prolonged ruptured membranes. The proportion of women who received antibiotics was similar for GBS -/+ and GBS -/- mothers (21.6% vs. 19.9%).

For women who received IAP, 35.5% had the first dose at ≤ 2 hours, 10.1% at 2 to 3.9 hours, and 54.4% at ≥ 4 hours prior to delivery. β -lactam antibiotics were used in 94% of women who received IAP. One woman (0.2/1000 deliveries) experienced an itchy throat, difficulty in breathing, and swollen lips after receiving ampicillin for GBS in the prenatal culture.

Mother-to-newborn Transmission of GBS

Transmission of GBS from mother-to-newborn was determined by isolation of GBS from at least one of the 4 surface sites of the neonate born to a labor GBS-positive mother. Transmission rate of GBS from mother-to-newborn was 16.1% for all deliveries: higher among newborns of mothers who did not receive antibiotics (untreated) than of those who received antibiotics during labor (treated) (38.2% vs. 6.3%, P < 0.001). Overall, IAP was 83.7% (95% CI: 77.6%–88.1%) effective in interrupting the mother-tonewborn transmission of GBS (Table 3).

For untreated mothers, the mother-to-newborn transmission rate was 4-fold higher for vaginal than for cesarean deliveries (45.1% vs. 10.9%, P < 0.001) and 10-fold higher for nonelective than for elective cesarean deliveries (25.0% vs. 2.5%, P = 0.009) (Table 3). Transmission was highest in women who had grade IV (68.4%), intermediate in those who had grade II (40.2%) or grade III (38.9%), and lowest in those who had grade I (33.7%) growth density (P =0.02). In treated mothers, the transmission rate varied from 6.6% in those who had grade I growth density to 9.4% in those with grade IV (P = 0.56).

GBS transmission occurred in 3 of 116 (2.6%) labor GBSpositive women who underwent elective cesarean deliveries, 2 received antibiotics and 1 did not (Table 3). The 3 colonized newborns (2 full terms, one 36 weeks' gestation) were born to mothers who were not in labor and without ruptured membranes who received no intrapartum procedures other than epidural anesthesia. All 3 mothers were GBS+/+. The first had grade III

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TABLE 3. Mother-to-newborn Transmission of Group B *Streptococcus* by Antibiotic Use During Labor and by Types of Delivery

Antibiotic During Labor	Type of Delivery	Labor GBS-positive Mothers (Number)*	GBS-colonized Newborns Number (%)*
Yes	Vaginal	507	34 (6.7)
	C/S-nonelective [†]	120	8 (6.7)
	C/S-elective	76	2(2.6)
	All types	703	44 (6.3)‡
No	Vaginal	253	$114 (45.1)^{\$}$
	C/S-nonelective	24	$6 (25.0)^{\$}$
	C/S-elective	40	$1 (2.5)^{\$}$
	All types	317	$121 (38.2)^{\ddagger}$
Total	All types	1020	$165\ (16.2)$

*Not included in the table are 21 mothers and their newborns due to missing data (newborns of 16 mothers were not swabbed and 5 mothers did not have data on antibiotic use).

[†]C/S: Cesarean section.

 $^{\ddagger}\text{Antibiotic}$ use (treated) versus no antibiotic use (untreated): 6.3% vs. 38.2%: P < 0.001.

[§]For untreated: vaginal delivery versus nonelective C/S: 45.1% versus 25.0%; P < 0.001; vaginal delivery versus elective C/S: 45.1% versus 2.5%; P < 0.001; nonelective versus elective C/S: 25.0% versus 2.5%; P = 0.009.

growth density in the labor GBS culture, received no antibiotics during labor, and her newborn had GBS grown from all 4 surface sites (heavily colonized).¹⁸ The second had grade IV growth, received 1 dose of cefazolin intravenously 2 hours before delivery, and her newborn had GBS identified from all 4 surface sites (heavily colonized). The third who received cefazolin shortly before delivery had grade I growth and her newborn's GBS grew only from the external ear canals (lightly colonized).¹⁸

Early-onset GBS Sepsis

Early-onset GBS disease occurred in 2 newborns, one at Houston and the other at Oakland; an incidence of 0.36/1000 live births. Both newborns had GBS isolated from blood cultures. Both were full-term infants of mothers who delivered vaginally, had no fever or prolonged rupture of membranes. Neither of the mothers received antibiotics during labor.

The mother of the first case-patient had a negative prenatal culture at 35 weeks' gestation, yet her culture during labor had grade II growth of GBS and her newborn had GBS identified from all 4 surface sites. Her newborn developed respiratory distress 3 hours after birth, required supplemental oxygen, and was admitted to the intensive care nursery. Spinal fluid showed a white blood cell count of 91 WBC/mL and a positive GBS antigen test. The mother of the second case-patient had no documented prenatal GBS culture; her urine culture during the first trimester was negative for GBS. Neither the mother nor the newborn was swabbed for culture during labor and delivery. The newborn developed respiratory distress 11 hours after birth, required supplemental oxygen, and was admitted to the intensive care nursery. The spinal fluid had white blood cell counts of 27 WBC/mL, showed no growth in culture, and was negative for GBS antigen. Both newborns received 2 weeks of antibiotic treatment and were discharged home.

DISCUSSION

Similar to reports from elsewhere in the United States^{6,20,21} IAP was widely used to prevent perinatal GBS disease in the 3 participating hospitals of this study and was highly effective in interrupting the mother-to-newborn transmission of GBS. None of the newborns of prenatally GBS-positive mothers in this study developed early-onset GBS disease. However, 2 cases of early-

onset GBS disease (0.36/1000 live births) occurred in full-term newborns of mothers who had either negative prenatal culture or an unknown history of prenatal GBS culture. These data reaffirm the effectiveness of IAP in preventing early-onset GBS disease and are consistent with the observations that the majority of recent cases of early-onset GBS disease occurred in newborns of prenatally GBS-negative mothers.^{6,16,17}

In this study, we compared GBS prenatal cultures from the nearly 5000 women to their vaginal-rectal cultures at labor and demonstrated a 50.5% PPV and 91.7% NPV (Table 2). Our findings are consistent with published reports which showed that both PPVs and NPVs of prenatal culture for GBS carriage during labor are not optimal (Table 1). These findings revealed limitations of prenatal culture-based IAP. First, nearly 10% of prenatally GBS-negative mothers who were positive during labor would have missed IAP, resulting in the occurrence of early-onset GBS disease. Second, one-third to approximately 50% of prenatally positive mothers would have received IAP despite negative labor cultures and low risk of delivering infants with early-onset GBS disease.

The current recommendation of not administering antibiotics to GBS-positive women who undergo elective cesarean delivery was based on the lack of early-onset GBS disease in a retrospective study in a single hospital²² and a review of Centers for Disease Control and Prevention surveillance data of early-onset GBS disease as evidence for low risk of transmission.² These studies did not address the transmission of GBS from mother to newborn. A recent study in Sweden reported that none of 29 GBS-positive women who underwent elective cesarean section transmitted GBS to their newborns.²³ Our data, however, showed that the transmission of GBS did occur in 3 of the 116 GBS-colonized mothers who underwent elective cesarean delivery, especially in heavily colonized women. Because newborn swabs were taken at birth before their first bath, it is unlikely that they acquired GBS after delivery. Colonized newborns are at risk for developing early-onset GBS disease with an attack rate of 1.2%.24 Our observations warrant further studies on the transmission of GBS among elective cesarean deliveries.

The cohort in this study was racially and ethnically diverse. When race was adjusted to the entire US population, our data estimate that for 4.2 million births annually and a cesarean section rate of 32%²⁵: (1) 772 cases early-onset GBS disease could occur in newborns of GBS -/+ mothers, an incidence of 0.18/1000 live births; (2) relying on prenatal cultures could result in overtreatment with IAP to about 310,000 parturient women; and (3) without IAP, the motherto-newborn transmission of GBS in mothers who undergo elective cesarean delivery without labor or rupture of membrane to newborns could result in 14 cases of early-onset GBS disease nationwide (Fig., Supplemental Digital Content 2, http://links.lww.com/INF/A859, shows the estimates of (1) the annual incidence of early-onset GBS disease in newborns of prenatally GBS-negative mothers, and in those of prenatally GBS-positive women who undergo elective cesarean deliveries; and (2) the number of prenatally GBS-positive women who receive IAP despite being culture-negative during labor).

The change of GBS carriage state between the prenatal and labor period in this study could not be explained by the antibiotic use during pregnancy because the proportion of women who received antibiotics during pregnancy was not different between the GBS +/- and GBS+/+ women. Longitudinal studies of GBS carriage have demonstrated that about half of pregnant women remained GBS-negative during gestation; of the remaining women who tested positive, 16% to 60% showed continuous positivity.^{7,26}

The PPV differed between the study sites (62.8% in Houston vs. 43.5% in Oakland, P = <0.001). The GBS cultures during labor were performed using a single protocol and the positive rates in these sites were similar (19.0% in Houston vs. 18.4% in Oakland, P =

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0.49). Their positive prenatal culture rates, however, differed significantly (18.5% in Houston vs. 30.2% in Oakland, P < 0.001). Prenatal cultures were performed by various providers and processed at different microbiology laboratories and the results of the prenatal cultures were then transcribed to medical records. The lower PPV in Oakland than in Houston remains unexplained. We found that the PPV was lower in women with unknown timing of prenatal cultures than that in those with known timing (29 vs. 61%, P < 0.001). This might explain the lower PPV in Oakland because a large proportion of women in Oakland had unknown timing of their prenatal cultures. Additionally, the low PPV in those with unknown timing suggest that the timing of prenatal cultures may serve as a quality indicator for a screening program.

The discordance of GBS carriage between the prenatal and labor periods emphasizes the need for a reliable and prompt identification of GBS carriers at delivery to guide the administration of IAP. Most efforts have focused on the development of GBS-specific deoxyribonucleic acid-based real-time polymerase chain reaction assays. The use of polymerase chain reaction for intrapartum identification of GBS has advantages and limitations.^{27–31} Despite its availability, the use of such tests in intrapartum settings is limited.⁵ Active immunization of mothers with a GBS vaccine rather than antibiotic treatment would be the logical choice for prevention of perinatal GBS disease in the future.

ACKNOWLEDGMENTS

The authors thank mothers and newborns who participated in the study, to the physicians and nurses of the obstetric and newborn services, the staff at the microbiology laboratories and administrators at Ben Taub General Hospital, St. Luke Episcopal Hospital, Houston, TX, and Alta Bates Summit Medical Center, Oakland, CA, medical and nursing staff of the NICUs at the Texas Children Hospital and Children's Hospital & Research Center, Oakland for their support and participation of this project; to the following who contributed to the conduct of the study: research coordinators: Daniel Peters, Julie Woods, Michelle Vest, and Julia Yoshino; research nurses: Debra Duncan, RN, Samantha Capehart, RN, and Julie de la Garza, RN, ; research technicians: Hedda Leeming, Briana McDaniel, Kimberly Veal, Jessica Myers, Ashley Odukoya, Onika Chambers, Megan McElfresh, and John Yoon; and microbiologists: Vera A. Concho and Neeraja Vaidya, ND, MS, for their expertise and tireless efforts; to Asma Idriss and staff of the Unit on Computer Support Services for data management.

REFERENCES

- Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease. *Morb Mortal Wkly Rep.* 1996;45(RR-7):1–24.
- Centers for Disease Control and Prevention. Prevention of perinatal group b streptococcal disease. Revised guidelines from CDC. *Morb Mortal Wkly Rep.* 2002;51(RR-11):1–24.
- Centers for Disease Control and Prevention. Rate of early-onset and late-onset invasive group B streptococcal disease in infants, by year, 1996–2004, Active Bacterial Core Surveillance system, United States. *Morb Mortal Wkly Rep.* 2005;54:1205–1208.
- Centers for Disease Control and Prevention. Trends in perinatal group B streptococcal disease—United States, 2000–2006. *Morb Mortal Wkly Rep.* 2009;58:109–112.
- Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease. *Morb Mortal Wkly Rep.* 2010;59(RR-10):1–32.
- Van Dyke MK, Phares CR, Lynfield R, et al. Evaluation of universal antenatal screening for group B *Streptococcus*. N Engl J Med. 2009;360: 2626–2636.
- Allardice JG, Baskett TF, Seshia MM, et al. Perinatal group B streptococcal colonization and infection. Am J Obstet Gynecol. 1982;142(6 Pt 1):617–620.
- Boyer KM, Gadzala CA, Kelly PD, et al. Selective intrapartum chemoprophylaxis of neonatal group B streptococcal early-onset disease. II: predictive value of prenatal cultures. *J Infect Dis.* 1983;148:802–809.

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- Yancey MK, Schuchat A, Brown LK, et al. 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.
- Edwards RK, Clark P, Duff P. Intrapartum antibiotic prophylaxis 2: positive predictive value of antenatal group B streptococci cultures and antibiotic susceptibility of clinical isolates. *Obstet Gynecol*. 2002;100:540–544.
- Hiller JE, McDonald HM, Darbyshire P, et al. Antenatal screening for Group B *Streptococcus*: a diagnostic cohort study. *BMC Pregnancy Childbirth*. 2005;5:12.
- Towers CV, Rumney RN, Asrat T, et al. The accuracy of late third-trimester antenatal screening for group B *Streptococcus* in predicting colonization at delivery. *Am J Perinatol.* 2010;27:789–790.
- Valkenburg-van den Berg AW, Sprij AJ, Oostvogel PM, et al. Prevalence of colonisation with group B Streptococci in pregnant women of a multiethnic population in The Netherlands. *Eur J Obstet Gynecol Reprod Biol.* 2006;124:178–183.
- El Helali N, 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;49:417–423.
- Puopolo KM, Madoff LC, Eichenwald EC. Early-onset group B streptococcal disease in the era of maternal screening. *Pediatrics*. 2005;115:1240–1246.
- Pulver LS, Hopfenbeck MM, Young PC, et al. Continued early onset group B streptococcal infections in the era of intrapartum prophylaxis. *J Perinatol.* 2009;29:20–25.
- Lin FY, Philips JB III, Azimi PH, et al. Level of maternal antibody required to protect neonates against early-onset disease caused by group B *Streptococcus* type Ia: a multicenter, seroepidemiology study. *J Infect Dis.* 2001; 184:1022–1028.
- Kontnick CM, Edberg SC. Direct detection of group B streptococci from vaginal specimens compared with quantitative culture. J Clin Microbiol. 1990;28:336–339.
- Centers for Disease Control and Prevention. Adoption of perinatal group B streptococcal prevention recommendations by prenatal care providers—Connecticut and Minnesota, 1998. *Morb Mortal Wkly Rep.* 2000;49:228–232.
- Watt JP, Schuchat A, Erickson K, et al. Group B streptococcal disease prevention practices of obstetrician-gynecologists. *Obstet Gynecol.* 2001; 98:7–13.
- Ramus RM, McIntire DD, Wendel GD Jr. Antibiotic chemoprophylaxis for group B strep is not necessary with elective cesarean section at term [abstract]. Obstet Gynecol. 1999;180:S85.
- 23. Håkansson S, Axemo P, Bremme K, et al. Swedish Working Group for the Prevention of Perinatal Group B Streptococcal Infections. Group B streptococcal carriage in Sweden: a national study on risk factors for mother and infant colonisation. *Acta Obstet Gynecol Scand.* 2008;87:50–58.
- Lin FY, Troendle JF. Hypothesis: neonatal respiratory distress may be related to asymptomatic colonization with group B streptococci. *Pediatr Infect Dis J.* 2006;25:884–888.
- Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2008. Natl Vital Stat Rep. 2010;58.
- Hansen SM, Uldbjerg N, Kilian M, et al. Dynamics of *Streptococcus* agalactiae colonization in women during and after pregnancy and in their infants. *J Clin Microbiol*. 2004;42:83–89.
- Honest H, Sharma S, Khan KS. Rapid tests for group B *Streptococcus* colonization in laboring women: a systematic review. *Pediatrics*. 2006;117: 1055–1066.
- Chan KL, Levi K, Towner KJ, et al. Evaluation of the sensitivity of a rapid polymerase chain reaction for detection of group B *Streptococcus. J Obstet Gynaecol.* 2006;26:402–406.
- Aziz N, Baron EJ, D'Souza H, et al. Comparison of rapid intrapartum screening methods for group B streptococcal vaginal colonization. *J Matern Fetal Neonatal Med.* 2005;18:225–229.
- Money D, Dobson S, Cole L, et al. An evaluation of a rapid real time polymerase chain reaction assay for detection of group B *Streptococcus* as part of a neonatal group B *Streptococcus* prevention strategy. *J Obstet Gynaecol Can.* 2008;30:770–775.
- Atkins KL, Atkinson RM, Shanks A, et al. Evaluation of polymerase chain reaction for group B *Streptococcus* detection using an improved culture method. *Obstet Gynecol.* 2006;108:488–491.

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