The Use of Blood Counts and Blood Cultures to Screen Neonates Born to Partially Treated Group B *Streptococcus*-carrier Mothers for Early-onset Sepsis

Is It Justified?

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Background: No clear recommendations exist regarding the approach to evaluate neonates born to partially treated group B *Streptococcus* (GBS)-carrier mothers for early-onset GBS (EO-GBS) sepsis.

Objective: To determine the yield and drawbacks of screening, all neonates born to GBS-carrier mothers who received only one dose of IV antibiotic, less than 4 hours, before delivery (partially treated).

Methods: A retrospective analysis was performed of all complete blood counts (CBCs) and blood cultures obtained from infants born during the period 2005 to 2009 to GBS-positive screened mothers treated with only one dose of antibiotic prior to delivery. A review was conducted of all neonatal EO-GBS sepsis cases during the study period.

Results: Of 5845 GBS-carrier mothers, 1648 (28%) received only one dose of antibiotic less than 4 hours before delivery. We traced the CBCs and blood cultures, which were taken from 1413/1648 (86%) infants after birth. In 234 (18%) of these 1413 neonates, a second CBC sample was taken due to abnormal result of the CBC (leukocytosis, leukopenia, or thrombocytopenia) or secondary to technical failure in obtaining the blood. None of the blood cultures taken in that screening protocol was GBS positive, but in 10 cases contamination with coagulase-negative *Staphylococcus* was reported. During the study period, EO-GBS sepsis was diagnosed in 11 neonates; all had clinical symptoms upon presentation.

Conclusions: The use of CBC and blood culture to screen neonates born to GBS-carrier mothers who received only one dose of IV antibiotic before delivery led to a negligible clinical yield and a high rate of technical failure. Although these findings are in line with the recent change in the Centers for Disease Control guidelines, they put in question the cost of this practice in terms of neonatal pain and parental anxiety.

Key Words: neonatal GBS screening, GBS-carrier mothers, partially treated mothers, blood counts, blood cultures.

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Implementation of the Centers for Disease Control (CDC) guidelines regarding prevention of early-onset group B *Streptococcus* (EO-GBS) disease in newborns,[1–3] while accepting the approach of maternal screening at 35 to 37 weeks of gestation, has led to a dramatic decrease in the rate of neonatal infections from 1:1000 to 0.3:1000 live births. It was recently shown that EO-GBS neonatal infections occur mostly in infants born to mothers who had a false-negative screening for GBS[4–6] and in preterm infants whose mothers were not tested for GBS before birth.[6]

Despite unequivocal clinical guidelines recommending at least 4 hours of intrapartum antibiotic to increase the prophylactic effect, there are no well-designed studies examining the safe duration of intrapartum antibiotic treatment for the prevention of EO-GBS disease in the newborn.[7] Moreover, data regarding the fate of infants born to GBS-carrier mothers who received antibiotics for less than 4 hours prior to delivery are even more sparse.[8] In the current[3] as well as the former guidelines,[1,2] there is an optional recommendation to obtain a blood count and a blood culture from neonates >37 weeks of GBS-carrier mothers with rupture of membranes for <18 hours who were given only one dose of intravenous antibiotics less than 4 hours before labor (partially treated), although the lack of evidence-based data to support this practice is acknowledged. In the new guidelines, this practice is recommended for infants <37 weeks and/or with rupture of membranes for >18 hours.

The aim of this study was to determine the clinical importance of obtaining a blood count and a blood culture from all neonates (symptomatic and asymptomatic) born to GBS-carrier mothers who received only one dose of antibiotic less than 4 hours before delivery and to examine the side effects and effectiveness of this practice (eg, blood culture contamination and the need for drawing a second sample for blood cell count).

METHODS

This study was conducted at the Hadassah-Hebrew University Medical Center, Jerusalem; a tertiary referral center for the local city population, which is religiously and socioeconomically diverse. The hospital has 2 campuses, Ein Kerem and Mt. Scopus, and each has a neonatology unit. The average annual birth rate in both hospitals combined is about 11,000.

We performed a historical cohort analysis of all GBS-positive screened mothers and their infants for the period January 1, 2005 to December 31, 2009. At that time, the Hadassah Medical Center nurseries and the neonatal intensive care units were already practicing the 1996 and 2002 CDC guidelines; thus, all GBS-carrier pregnant women upon admission to labor were immediately given empirical antibiotic treatment consisting of IV penicillin or ampicillin (and clindamycin or vancomycin for penicillin-allergic patients). Mothers who received only one dose of antibiotics (less than 4 hours before delivery) were termed as partially treated.

All neonates born to these partially treated mothers were closely followed clinically. In addition, a complete blood count (CBC) and a blood culture (aerobic and anaerobic bottles, conven-

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tional BACTEC) were obtained within 6 hours after delivery from each such neonate.

All CBCs and blood culture results of neonates born to partially treated GBS-carrier mothers were extracted from the hospital computerized database and evaluated. Blood culture evaluation included discrimination of blood culture contaminations mainly by coagulase-negative *Staphylococcus*. Contamination versus true infection was confirmed after a close clinical observation revealing an asymptomatic infant, while a repeated blood culture, before the commencement of antibiotic, was sterile. Abnormal CBC parameters were defined as either a total white blood cell (WBC) count of less than 5000 cells/mm^3 or more than 30,000 cells/mm^3 and a platelet count of less than 150,000 cells/mm^3. Technical failures in obtaining the CBC samples were also recorded. The medical records of all neonates with positive blood or cerebrospinal fluid cultures for GBS were reviewed for the presence of maternal GBS carrier status, clinical signs and symptoms, abnormalities in CBC, and neonatal outcome.

Statistical analysis was performed to calculate the effectiveness of the CBC in diagnosing neonatal GBS infections, the relative number of invalid blood counts (due to technical failures in obtaining the blood resulting in laboratory errors and abnormal laboratory parameters), and the blood culture contamination rate. A descriptive statistical analysis was performed using PASW 17 software of SPSS.

RESULTS

Of 53,788 women who delivered during the study period (January 1, 2005– December 31, 2009), 5845 (11%) were found to be GBS carriers and 10,187 (19%) were negative for GBS colonization in the antenatal screening. The status of 37,756 (70%) was unknown. The records of 3819 GBS carriers were reviewed. Of them, 1648 (43%) were partially treated, 1851 (48%) were given at least 2 doses of antibiotic (full treatment), and 320 (8%) were not treated prior to delivery (Fig. 1).

According to the protocol, CBCs and blood cultures were obtained from 1413 (86%) infants born to partially treated mothers. The screening blood work was performed within 6 hours after delivery. Repeated CBCs were obtained from 324 infants (18%); 90 (6%) due to technical failures (inability to analyze the blood sample due to insufficient amount or iatrogenic coagulation of the sample), and 234 (12%) due to abnormal result of the CBC (leukocytosis, leukopenia, or thrombocytopenia).

The major indices of the CBCs obtained from neonates born to partially treated mothers and the percentage of abnormal value of each CBC parameter are presented in Table 1. Low platelet count (thrombocytopenia) was documented in 86 (6%) and abnormal WBC count (leukopenia) in only one (0.07%) of the initial CBCs taken. A second and even a third CBC were obtained due to technical failures or abnormal results in 34/176 (19%) and 5/28 (17%) of the cases, respectively. None of these infants developed EO-GBS sepsis.

None of the cultures taken in the screening within 6 hours of birth proved positive for GBS; in 10 of the 1413 infants (0.7%), coagulase-negative *Staphylococcus* was isolated, considered as contamination, after conductive an intensive clinical observation and having sterile repeated blood cultures. In 1 infant, later diagnosed with EO-GBS sepsis, the initial blood culture, which was part of the sepsis screening protocol, was sterile.

During the study period, 11 of 53,788 neonates (0.2 per 1000 live births) were diagnosed with EO-GBS infection; only 2 were born to GBS-carrier mothers (0.3 per 1000 live birth) (Table 2). One was born to a partially treated mother and his initial CBC as part of the screening was unremarkable; the other was born in an urgent cesarean section and the mother was not given antibiotic treatment prior to delivery. Although symptomatic at birth, his initial CBC was within the normal range.

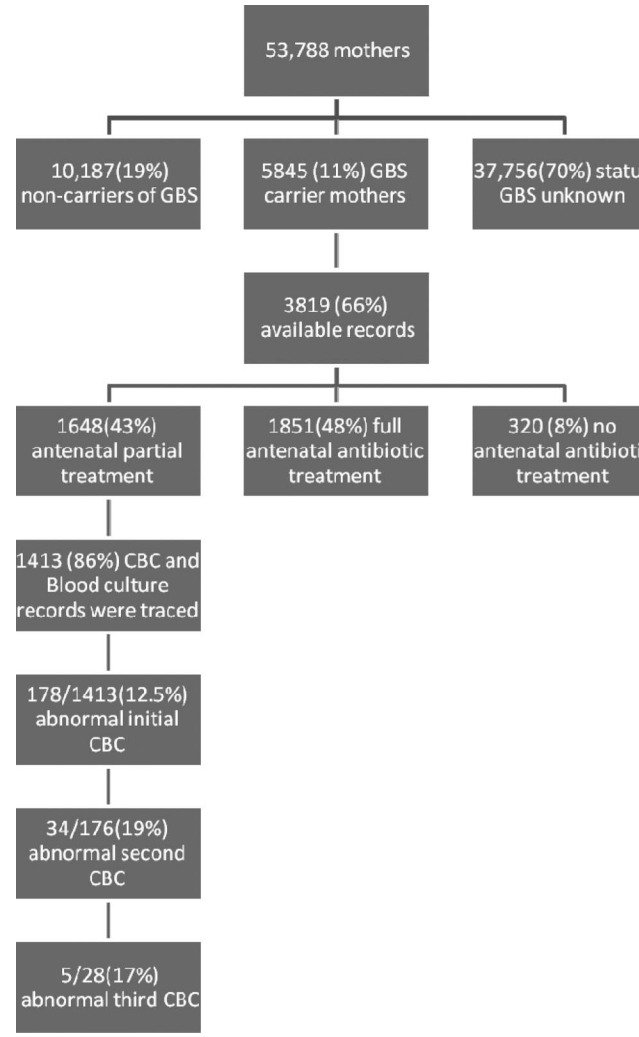

FIGURE 1. Maternal GBS status, antenatal antibiotic treatment, and CBC screening evaluation of neonates born to partially treated mothers.

The clinical characteristics of the GBS-infected neonates are presented in Table 2. Four (36%) were premature twins, 5 (45%) became symptomatic immediately after birth, and 5 (45%) became symptomatic within 12 hours after birth. Of 11, 5 (45%) had mainly respiratory symptoms at presentation. Three infants had central nervous system involvement, including one infant who developed grunting and seizures on the second day of life and had an abnormal CBC. Four of the 11 neonates (36%) died, 3 of whom were preterm.

DISCUSSION

Following the introduction of the CDC guidelines in 1996 regarding interventions to prevent EO-GBS neonatal infections, the CDC revised the guidelines with an algorithm suggesting 2 approaches for the evaluation of a well-appearing infant born to a partially treated GBS-carrier mother: one approach favored expectant observation, whereas the other suggested evaluation by a

TABLE 1. White Blood Cell (WBC) and Platelet (PLT) Values Obtained From Neonates Born to GBS-positive Partially Treated Mothers

	N*	SD†	Median (Range) × 10^3	Technical Failure	Abnormal Indices (%)
First WBC count	1413	2.14	19.8 (4.2–26.4)	90 (6%)	1 (0.07%)
First PLT count	1413	84.82	282 (7–650)	92 (6%)	85 (6%)
Second WBC count	176	2.74	20 (9.8–25.8)	11 (6%)	0 (0%)
Second PLT count	176	87.37	252 (36–475)	11 (6%)	23 (13%)
Third WBC count	28	2.63	18.8 (11.8–23.8)	1 (3%)	0 (0%)
Third PLT count	28	89.79	237 (21–336)	1 (3%)	4 (14%)

*Number of samples taken.
†Standard deviation.

TABLE 2. Clinical Characteristics of EO-GBS–infected Neonates

Case Number	Gestational Age (wk)/Birth Weight (g)	Maternal GBS Status at Delivery	PROM +/−/ Maternal Fever	Mode of Delivery	Time to Clinical Presentation (h)	Clinical Signs at Presentation/Final Diagnosis	Characteristics of Initial CBC	Outcome
1	38/3540	Unknown	−/38.3	Vaginal	12	Tachypnea, grunting/ sepsis and meningitis	Leukopenia	Good
2	39/3702	Positive	−/−	Vaginal	11	Fever/sepsis and meningitis	Normal	Good
3	42/3686	Unknown	−/−	Vaginal	6	Tachypnea, grunting, hypothermia/sepsis	Normal (part of routine screening)	Good
4	29/1370	Unknown	−/−	CS	Immediate	Resuscitation/sepsis	Leukopenia	Died
5	29/1410	Unknown	−/−	CS	Immediate	Resuscitation/sepsis	Leukopenia	Good
6	26/910	Unknown	−/−	Vaginal	Immediate	Resuscitation/sepsis	Normal	Died
7	26/1110	Unknown	−/−	Vaginal	Immediate	Resuscitation/sepsis	Normal	Died
8	33/2190	Positive	−/−	CS	Immediate	Hypoxemia, PPHN/ sepsis	Normal	Good
9	41/3285	Unknown	−/−	Vaginal	8	Grunting/sepsis	Leukopenia	Good
10	38/3035	Unknown	−/−	Vaginal	48	Grunting, seizures/ sepsis and meningitis	Leukopenia and thrombocytopenia	Died
11	42/4195	Unknown	−/38.1	Vaginal	9	Cyanosis, fever/ sepsis	Normal	Good

CS indicates cesarean section; PPHN, persistent pulmonary hypertension of the newborn.

CBC and blood culture.[1,2] Although the recent updated guidelines favor the observational approach, the screening approach is still recommended by the CDC algorithm as an alternative. However, compared with the previous recommendations, a more specific time frame for this evaluation, at 6 to 12 hours after the delivery, is provided in the 2010 guidelines.[3]

We evaluated the neonatal screening approach (ie, obtaining a CBC and blood culture from infants at risk) and found that it had zero positive predictive value when taken early (within 6 hours) after birth; in fact, it had a confounding effect as a result of blood culture contamination with coagulase-negative *Staphylococcus*. This finding strongly supports the current guidelines recommending on blood test evaluation not earlier than 6 hours after birth, when practicing the screening approach.

To the best of our knowledge, there are no well-designed studies that examined the optimal duration of intrapartum prophylaxis for the prevention of EO-GBS disease in the newborn.[7] Furthermore, it was previously shown that even the short duration of less than 4 hours of antibiotic prophylaxis achieved significantly high levels of antibiotics above the minimal inhibitory concentration in the fetus, thus making the claim that infants exposed to less than 4 hours of prophylaxis are particularly at risk for GBS sepsis pharmacokinetically inaccurate.[9] It was also shown that inadequate prophylaxis of either less than 2 hours or less than 4 hours before delivery significantly interrupted vertical colonization of the newborn (60% colonization of untreated neonates vs. 3.6% and 2.4% in neonates born to mothers who received partial treatment at 2 and 4 hours before birth, respectively).[4]

As previously documented, a single CBC may not be an adequate screening tool for the diagnosis of EO-GBS sepsis,[10,11] particularly when obtained in the first 4 hours postdelivery.[12] To the best of our knowledge, only 2 studies have assessed the yield of CBC and blood cultures in screening newborns of partially treated mothers at risk for sepsis. In 1 study performed by Ottolini et al, the specificity and sensitivity of abnormal WBC count were 73% and 41%, respectively.[8] However, this study was conducted while locally using the risk-based approach and not the maternal screening-based approach, which is currently proposed by the 2010 guidelines. In addition, the potential emotional and economic burden resulting from possible technical failures and blood culture contamination when obtaining the blood samples were not addressed. The other study, although evaluating a small cohort, demonstrated no yield with regard to this practice.[13]

We reviewed 1648 cases of partially treated mothers and their infants, analyzing 1413 (86%) CBCs and blood cultures obtained from those infants. In the single case of an infant with EO-GBS sepsis born to a partially treated mother, the initial CBC and blood culture taken while the neonate was asymptomatic were unremarkable. In 5 of 11 EO-GBS infected neonates, the initial CBC was abnormal, but on evaluation they had clinical symptoms indicative of sepsis, in line with previously reported data. However, it should be emphasized that our analysis was not performed on this specific group.[8,14]

Although the CBCs were taken by senior pediatric residents and neonatologists, technical failures were recorded in 18% of the samples, necessitating additional testing. Taken together, the ab-

sence of any yield of CBC taken at less than 6 hours of birth in asymptomatic infants, the risk of technical failure, and the risk of contaminants in blood cultures, all leading to numerous painful procedures and parental anxiety demonstrate that this practice is unnecessary.

A majority of our EO-GBS sepsis cases were born to mothers with unknown GBS carriage status, an observation that has been constantly reinforced since the wide application of the CDC guidelines.[5,6,15] Five of the 11 (45%) EO-GBS septic neonates were preterm, a slightly higher rate than that reported in the United States (25.6%)[6] and Europe (23%).[15] In our cohort as previously reported, clinical symptoms were proven more sensitive than hematological findings.[14] In all but one of the EO-GBS cases, symptoms occurred within 24 hours of birth and were mainly respiratory, as previously reported[5]; however, one neonate developed clinical symptoms on the second day of life, reinforcing the recommendation of clinical observation for at least 48 hours after birth in the asymptomatic neonate born to a GBS-carrier mother.

Our study has some limitations. Initially, as we cross-matched 2 separate database systems, 2026 files of GBS-carrier patients could not be reached. We cannot assume that any selection bias had occurred in this process, since it was fully computerized. To overcome the possibility that these files contained a screen that yielded a positive GBS-culture result, we reviewed all our EO-GBS cases for their prior maternal status and treatment, thus, eliminating the possibility of missing a positive screen. We might, however, still have confounded results regarding technical failures and contaminations when obtaining the blood. Second, 68% of the pregnant women were not tested for GBS before labor, a considerably higher percentage than reported elsewhere.[6] This could be the result of the current Israeli guidelines and the Israel Obstetrics and Gynecology Association practice recommendations that are based on the high-risk approach for GBS. However, the practice within the Jerusalem district, including our center, was different, as gynecologists increasingly adopted the screening approach.[16,17] In addition, the incidence of EO-GBS sepsis in our study was 0.2 per 1000 live births, a lower incidence than reported in the United States (0.32 cases per 1000 live births)[6] and Europe (0.50 per 1000 live births),[4] a fact that further diminishes the yield from screening infants born to partially treated GBS-carrier mothers.

In summary, since the optimal approach to a term neonate born to a GBS-carrier mother partially treated with antibiotic before delivery is still under investigation, our findings support the practice of expectant observation, which was considered the preferred alternative by the revised guidelines published in 2010.[3] Our study highlights the negligible yield of the early screening (<6 hours of birth) protocol in asymptomatic newborns of partially treated mothers. More importantly, it shows the drawbacks in terms of unnecessary stress to the newborn and his or her family. Nevertheless, our findings support the current guidelines for laboratory evaluation by CBC and blood culture of partially treated preterm infants born to GBS-carrier mothers and the need of clinical observation of at least 48 hours for all infants at risk for EO-GBS infection.

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