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Late-onset Group B *Streptococcus* in NM Infants, 2006–2011

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Group B *Streptococcus* (GBS) infection is a leading cause of neonatal sepsis in developed and developing countries around the world. GBS neonatal infection can be classified as either early-onset, which occurs within the first six days of life, or late-onset which occurs between 7–89 days of life. Over the last 40 years, early-onset GBS mortality has dropped from 50% to 10–15% in Europe and the United States.[1] The decrease in both disease incidence and subsequent mortality has largely resulted from development of an intrapartum antibiotic regimen given to high-risk mothers during pregnancy to prevent vertical transmission of the bacteria during childbirth.[1-2]

Although the incidence of early-onset GBS has decreased following the use of prophylaxis, the incidence of late-onset has remained the same.[3] Transmission of the organism from mother to infant during childbirth, leading to early-onset GBS, is well understood. However, the source of infection during late-onset GBS infection is not well characterized, and needs to be further investigated. Infants born prematurely or with a low birth weight are at higher risk of developing late-onset GBS infection than other infants.[4–6] Additionally, transmission from mother to infant can occur during breastfeeding through a feedback cycle when the mother has mastitis caused by GBS.[7] Infants spending extra time in the hospital have also been shown to develop healthcare-associated GBS due to potential infection control breaches by hospital staff.[8] While these are some possible sources of infant infection, these sources do not explain all cases of late-onset GBS in infants.

Specialized surveillance systems in the United States monitor trends in GBS infection including the Centers for Disease Control and Prevention (CDC) Active Bacterial Core surveillance (ABCs) program. Data collected by the national ABCs program in 2012 estimated the incidence of late-onset GBS disease in the US at 0.32 cases per 1000 live births.[9] The ABCs program GBS data is used to assess the current perinatal disease prevention guidelines, monitor the effectiveness of intrapartum prophylaxis, and examine trends in GBS invasive disease in other age groups. An in-depth analysis of late-onset GBS disease has not been conducted using ABCs program data for the state of New Mexico.

Methods

Data from the NM ABCs program was utilized for this analysis. NM ABCs is one of 10 sites which conduct active laboratory-based surveillance for Group B *Streptococcus*. This type of disease surveillance allows for better disease burden estimates in NM, through data and bacterial isolate collection. The medical records of mothers with infants who develop late-onset GBS are reviewed by the NM ABCs program to collect data on specific risk factors. For this analysis, cases were defined as NM ABCs GBS-infected infants born between January 1, 2006 and December 31, 2011 with GBS isolated from a sterile body site, and disease onset between 7-89 days of life.

A descriptive epidemiologic analysis was performed among late-onset GBS cases in order to characterize potential risk factors. Demographic information examined included the infant's age, sex, race/ethnicity, county of birth, and insurance status. GBS disease was classified by the body site of the positive GBS culture, the length of time the infant spent in the hospital following GBS diagnosis, and mortality outcome. Known risk factors for late-onset GBS were evaluated, including: maternal prenatal care, low birth weight, gestational age, and whether the mother breastfed the infant prior to disease onset.

Results

From January 1, 2006 through December 31, 2011,

there were 75 cases of late-onset GBS disease reported in New Mexico infants aged 7 – 89 days. The US rate of late-onset GBS from 2006–2011 was 0.28 cases per 1000 live births, and in NM the rate was 0.43 cases per 1000 live births (Figure). Median age of cases was 40 days (range 10─84 days). Of 72 cases with known insurance status, 88% were covered by some type of insurance; of these, 54% utilized Medicaid. The survival rate was 95%; two cases resulted in death, one each in 2007 and 2009. Of infants with late-onset GBS, 60% were delivered vaginally, 46% were premature (<37 weeks of gestation), and 37% were low birth weight (<2500 g). Infants with late-onset GBS, born <37 weeks of gestation had an 8 times (95% CI: 2.7 – 23.5) greater risk of being low birth weight than babies born >37 weeks. Group B *Streptococcus* was isolated from five normally sterile body sites resulting in 57% bacteremia, 32% meningitis, 3% otitis, 3% pneumonia, and 5% cellulitis; some infants had more than one type of manifestation of illness. The median length of hospital stay was 25 days among the 71 cases without missing values. Among all cases, 59% had received breast milk from the mother and 56% were being breastfed before the onset of disease.

Maternal risk factors for infant late-onset GBS were examined among NM cases (Table). The median age of mothers of cases was 23 years (range 14─39 years). Many mothers (49%) were Hispanic. Of mothers of infants with late-onset GBS, 89% reported receiving some prenatal care. Of those who received prenatal care, 48% were screened for GBS during their prenatal care visit; 15% of those had positive GBS cultures prior to delivery hospital admission, and 5% were culture positive after hospital admission. Among mothers with a positive screen for GBS, 10% were given antibiotic prophylaxis, as recommended in the Prevention of Perinatal Group B Streptococcal Disease Revised Guidelines.[2]

Discussion

According to the literature, low birth weight and prematurity are both risk factors for late-onset GBS. Among the 75 cases of late-onset GBS in NM from 2006–2011, the percentage of cases that were low birth weight was similar to those cases that were not low birth weight. Among cases, the percentage of infants who were premature was slightly less than those cases who were not premature. Breastfeeding has also been shown to be a risk factor for disease if the mother has mastitis caused by GBS. Late-onset GBS cases in NM breastfed less (56%) compared to the NM Pregnancy Risk Assessment Monitoring System (PRAMS) data for breastfeeding (84%). Women who give birth to babies in NM might participate in PRAMS - a questionnaire distributed to women who have recently given birth, which collects information about different aspects of prenatal care, demographic information about the mothers, as well as health information of the mothers and infants. Currently, the PRAMS questionnaire does not include questions about GBS screening or diagnosis. To better understand the relationship between GBS screening, positive cultures, and the onset of GBS disease among the general population, questions about GBS could be included on the PRAMS questionnaire.

Screening for GBS during pregnancy is an important aspect of prenatal care for pregnant women. Most NM mothers of infants with late-onset GBS received at least some prenatal care during pregnancy. However, less than half of mothers reported being screened for GBS during their prenatal care visits. At this time, data is not available regarding rates of screening for GBS among expectant mothers in NM. Of those women who screened positive for GBS, very few reported receiving prophylaxis for disease during delivery which prompts the question, why did mothers known to screen GBS-positive not receive prophylaxis? Further study is ongoing at a national level to better answer this question and determine potential reasons for missed prophylaxis opportunities.

One limitation of this analysis is that only 75 cases were reported in NM during the six year period. This small number of cases makes it difficult to determine the statistical significance of the reported results. Another limitation is the relatively large number of missing results for some of the variables. Variables such as birth weight, whether a baby received breast milk from its mother, and whether a mother was screened for GBS are important data. Without this information, it is difficult to determine which potential factors might contribute to GBS-disease among infants.

Risk factors for late-onset GBS disease are not fully understood. There are some risk factors in the literature, both maternal and infant, that appear to increase an infant's risk of developing late-onset disease. These risk factors, such as maternal smoking and drinking, breastfeeding, and potential healthcare-associated infection, need to be further investigated and compared among infants with and without late-onset GBS. A

case-control study comparing birth certificate data risk factors among late-onset GBS cases and healthy controls is ongoing to help determine potential additional risk factors for late-onset GBS in NM.

Table. Infant and Maternal Characteristics of Late-onset Group B *Streptococcus* cases, New Mexico, 2006–2011

Variable	Yes (%)	No (%)	Missing (%)
Infant's Demographics			
Infant sex (Male)	43 (57.3)	32 (42.7)	
Gestational age < 37 wks	33 (45.8)	39 (54.2)	3 (1.4)
Birth weight < 2500g	28 (37.3)	27 (36.0)	20 (26.7)
Breast milk from mother	44 (58.7)	14 (18.7)	17 (22.6)
Breastfed before GBS onset	42 (56.0)	32 (42.7)	1 (1.3)
Died	2 (2.7)	71 (94.6)	2 (2.7)
Mother's Demographics			
Mother's Race/Ethnicity			
Hispanic	37 (49.3)		10 (13.3)
White	13 (17.3)		
American Indian	13 (17.3)		
Asian	1 (1.4)		
Black	1 (1.4)		
Received prenatal care	67 (89.3)	2 (2.7)	6 (8.0)
Had insurance	66 (88.0)	6 (8.0)	3 (4.0)
Vaginal delivery	45 (60.0)	30 (40.0)	0
Screened for GBS	36 (48.0)	27 (36.0)	12 (16.0)
GBS positive before admission	11 (14.7)	55 (73.3)	9 (12.0)
GBS positive after admission	4 (5.3)	67 (89.4)	4 (5.3)
Received prophylaxis for GBS	8 (10.7)	47 (62.6)	20 (26.7)

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Figure. Rate of Late-onset Group B *Streptococcus*, New Mexico and United States, 2006–2011