

Incidence of Group B *Streptococcus* Vaginal Colonization Causing Preterm Births and Early Onset Sepsis

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Abstract: This study was conducted to investigate the incidence and prevalence of maternal Group B *Streptococcus* (GBS) colonization between 35 and 37 weeks of gestation which is associated with increased neonatal mortality and preterm birth for a period of six months to appropriate intervention and monitoring of GBS status during pregnancy and to reduce the rate of early onset neonatal mortality. During the study period 250 antenatal mothers delivering at term at Govt Mohan Kumaramangalam Hospital in SALEM, TN, GBS status and other clinical data were obtained from medical records. Exposed women were those testing positive for GBS (GBS positive [n=80]) and the unexposed tested negative for GBS (GBS negative [n=134]). other infections tested 26. Out of 250 antenatal mothers studied 80 were tested positive for GBS colonization and 134 were tested culture negative for GBS, the remaining 36 were mixed infections. The incidence of 32% GBS colonization was recorded. out of 80 GBS positive cases, the early onset sepsis was observed in retrospectively from the medical records. The incidence of invasive infections verified with blood or CSF culture with "traditional neonatal pathogens" in the first 28 days of life was 18 neonates denoted by positive blood culture or CSF. Thus determined association between GBS status and early term delivery and other neonatal infections. Colonization with GBS may have detrimental effects to the term infant through shortening of the gestational age contributing to infant morbidity and mortality warranting appropriate intervention and monitoring of GBS status during pregnancy.

Keywords: pregnancy, infection, preterm birth, vaginal colonization, GBS

1. Introduction

Group B streptococcal disease remains a leading infectious cause of morbidity and mortality among newborns. Intrauterine infection of the foetus results from ascending spread of *Streptococcus agalactiae* (Group B streptococci: GBS) from the vagina of a colonized woman, who is typically asymptomatic. Foetal aspiration of infected amniotic fluid can lead to stillbirth, neonatal pneumonia, meningitis or sepsis (Schuchat 1999).

Approximately 10%-30% of women are asymptomatic carriers of GBS in the genital and gastrointestinal tracts. Infants can also get infected with GBS during passage through the birth canal, although the majority of infants who are exposed to the organism through this route become colonized on skin or mucous membranes, but remain asymptomatic.

One strategy for the prevention of the disease is via screening of pregnant women for both vaginal and rectal carriage of GBS, and administration of suitable antibiotics to eradicate colonization, prior to delivery (Schrag et al. 2002). Group B *Streptococcus* (GBS) is one bacterium that is normally screened between 35 – 37 weeks of pregnancy and has the highest rate of infant mortality due to early onset disease leading to sepsis.

2. Early Onset Disease

There are two types of GBS disease cases among infants: early onset disease and late onset disease. Early onset is classified as cases in which group B *Streptococcus* was isolated from infants younger than one week old (2, 10). Most early onset cases present within the first 48 hours after

delivery (11). Early onset disease presents as respiratory distress in infants, cardiovascular instability and apnea. The most common clinical symptoms observed are bacteremia, pneumonia, and meningitis found by one study to have been present in 83%, 9% and 7% of cases respectively (2). Early-onset disease usually results in rapid clinical deterioration and sepsis.

Late Onset Disease

Late onset-disease is cases that occur between one week and 3 months (2, 10). One study found 52% of infants with late-onset GBS disease were preterm births. Unlike early-onset disease, late-onset disease is not always acquired from the mother (11). One study found approximately 50% of cases of late onset disease were acquired from their colonized mother (14). Similar to early-onset disease, late-onset disease manifests as bacteremia (65%), meningitis (27%), and pneumonia (3%)

In 2002, the Centres for Disease Control and Prevention (CDC, USA) recommended 'universal prenatal screening for vaginal and rectal GBS colonization of all pregnant women at 35–37 weeks gestation'. In the same guidelines, CDC identified various research priorities, including 'the development of media with a reliable colour indicator to signal presence of GBS to improve accuracy of prenatal culture results and facilitate prenatal culture processing at clinical laboratories with limited technical capacity' (Schrag et al. 2002).

Risk factors for GBS

Many risk factors of GBS disease have been identified in the research over the past decades. Maternal vaginal colonization is the primary risk factor associated with early onset GBS disease. The prevalence of GBS colonization in

pregnant women is 10-30%. Women who are more heavily colonized have an increased risk of having a child with early-onset disease than women who have light colonization (16, 17). Other factors that increase the risk for early-onset disease include gestational age of < 37 completed weeks (preterm birth), premature rupture of the fetal membranes lasting more than 18 hours, intra-amniotic infection, previous delivery of a newborn with early-onset disease, low levels of circulating antibodies against group B *Streptococcus*, young maternal age, and high intrapartum temperatures (18-21).

Clinical risk factors for GBS transmission to neonates [Sch 02]

Chorioamnionitis
GBS bacteriuria in current pregnancy
Maternal rectovaginal colonization
Maternal temperature of Q 38° C
Preterm labor or preterm rupture of membranes < 37 weeks of gestation
Previous delivery of infant with early-onset GBS sepsis
Prolonged (> 18 hours) interval between rupture of membranes and delivery

Prevention and treatment during pregnancy

The CDC developed guidelines in 2002 (updated in 2010) on screening for and prevention of adverse infant and maternal outcomes due to GBS (18). There are two primary strategies for determining if a pregnant woman is at risk of giving birth to a GBS positive infant. The first is a risk-based assessment technique. A woman who has the presence of any of the following is offered intrapartum antibiotic prophylaxis: delivery at less than 37 weeks, intrapartum temperature of greater than 100.4°F or rupture of membrane for more than 18 hours (18).

The second is a universal screening strategy which consists of all pregnant women having a recto-vaginal swab taken at 35-37 weeks. If a woman has a positive culture she is given intrapartum antibiotic prophylaxis. The positive predictive value of the culture taken within 5 weeks of delivery is 77-87% and the negative predictive value is 94-96% (25, 26). Colonization can be transient during the course of a pregnancy and therefore early colonization and positive swabs are not predictive of the risk of early-onset GBS disease in infants.

3. Materials and Methods

The study was approved by the ethical committee of our institute and informed consent was obtained from all patients involved in the study. It was carried out in Government Mohan Kumara Mangalam medical college hospital from February 2016 to July 2016 for six months.

A total of 250 samples, as vaginal swabs, were inoculated onto culture plates. A selective blood agar with STREPTO B ID for the isolation of Group B streptococci. All media, both directly and after selective broth enrichment, and the cultures were observed after both 24- and 48-h incubation. A chromogenic medium, STREPTO B ID, has been made commercially available, as recommended in the CDC protocol ([Roure et al. 2006](#)). Selective agents can be

employed for the inhibition of commensal bacteria (e.g. most Enterobacteriaceae) and both media offer a high specificity for visualization of GBS colonies. All swabs were high vaginal swabs from distinct patients. Each swab was emulsified in 0.75 ml of sterile 0.85% saline. A 50- μ l sample of the resulting suspension was then inoculated onto Medium B, Granada medium and blood agar. The inoculum on each plate was then spread to obtain individual colonies.

Cultures on Medium B were incubated for 18–20 h in air at 37°C. Blood agar and Granada medium were incubated for 18–20 h under anaerobic conditions at 37°C. All plates were interpreted again after a total of 48-h incubation. The cultures were examined for ‘presumptive positive’ colonies, which were defined as haemolytic colonies on blood agar; pink or red colonies on Medium B; or colonies showing any shade of orange/red colouration on Granada medium. Such colonies were subcultured onto blood agar for subsequent testing with Slidex Strepto kit. Any strain demonstrating typical colonial appearance and specific reaction with Group B latex reagent was regarded as GBS. Medium B incorporates a combination of chromogenic enzyme substrates that results in strains of GBS-forming red colonies. Other species are either inhibited by selective agents or appear as blue or green colonies.

Inclusion Criteria

Subjects included in this report had spontaneous onset of labor followed by vaginal delivery.

Exclusion Criteria

All subjects with labor induction or cesarean sections at term (irrespective of GBS status) were excluded. Subjects with multiple gestations, preeclampsia, placenta previa, fetal anomalies, and/or medical (such as gestational diabetes mellitus)/ surgical complications of pregnancy and delivering at term were excluded. Gestational age was determined by date of last menstrual period.

Participants without gestational age were excluded. Only patients who delivered at term (37/0 weeks to 42/0 weeks) were included in our study.

4. Results

A hospital based retrospective study in this tertiary care hospital following 250 antenatal mothers and live births and infants with early-onset GBS, concluded that the screening approach is over 50% more effective at preventing early-onset GBS disease than the risk based approach. Out of 250 antenatal mothers studied 80 were tested positive for GBS colonization and 134 were tested culture negative for GBS, the remaining 36 were mixed infections. The incidence of 32% GBS colonization was recorded. Out of 80 GBS positive cases, the early onset sepsis was observed in retrospectively from the medical records. The incidence of invasive infections verified with blood or CSF culture with “traditional neonatal pathogens” in the first 28 days of life was 18 neonates denoted by positive blood culture or CSF culture over time. In 90 % of the cases only the blood culture was positive. Meningitis occurred in 10 %, most often together with a positive blood culture (72 %). Maternal vaginal colonization is the primary risk factor

associated with early onset GBS disease. The prevalence of GBS colonization in pregnant women is 10-30%.

The overall case fatality rate in infections day 0-27 was 9%. Only 18 cases (22.5%) with invasive infections day 0-27 had a gestational age 37 weeks, birth weight Q 2 500 g and no known predisposing conditions. Premature birth and VLBW resulted in an increased risk of invasive infections with an incidence in the 28 first days of life of 162.8/1 000 live births among neonates. The case fatality rate in patients with culture verified infections was 23 % in neonates with a gestational age < 29 weeks and 3 % among neonates Q 37 weeks.

Number and Incidence of GBS (%) of incidence of GBS:

Name of the organisms	No of isolates	% of isolates
Group B streptococci	80	32
Mixed infections	36	14.4
Culture negative	134	53.6

Number and (%) of all infections in relation to gestational age:

Onset of infection days	< 30 weeks	30-36 weeks	> 36 weeks
0	3 (15)	6 (25)	10 (60)
6-Jan	2(12)	6 (26)	11 (62)
27-Jul	9 (50)	3 (16)	7 (38)

Number and (%) of all infections in relation to birth weight

Onset of infection days	< 1 500g	1 500 -2 499g	> 2 499g < 3,599g
0	3(16)	4(21)	11 (65)
6-Jan	3(15)	4(19)	12(66)
27-Jul	9 (50)	3 (15)	6 (33)

5. Discussion

GBS as a possible determinant of gestational age

The results of our study, based on screening of 250 antenatal mothers from Govt Mohan kumara mangalam medical college hospital Salem, TN, illustrate that women who are GBS positive between 35-37 weeks gestation are more likely to have an early term birth and a child with a lower birth weight. In our population, GBS positive women are 3 times more likely to deliver between 37 and 39 weeks compared to delivering 39 to 41 weeks. Our results suggest that women who are GBS positive have a greater risk of an early term birth and it is also associated with significant reduction in birth weight. Both of which can contribute to morbidities similar to that seen in infection associated with preterm birth.

In addition to its association with higher rates of infant morbidity and mortality early term birth can affect the development of the child, the cost of healthcare and may prolong hospital stays. GBS is a very potent inflammatory agent and the infected host suffers from all consequences of hyper-inflammation and inflammatory cytokines. Neonates have low levels of both antibodies and complement proteins and this negatively affects recognition, chemotaxis and phagocytosis of the bacteria. The CPS is a major virulence factor since it surrounds the organism and the cell wall

antigen will be covered. CPS protects the bacteria from opsonization and phagocytosis

The Centers for Disease Control and Prevention (CDC) Active Bacterial Core Surveillance reported in 2008 approximately 1,200 cases of early-onset disease per year with almost 70% of cases born at term (≥ 37 weeks), (12). This is equivalent to 0.28 cases of early-onset GBS disease per 1,000 live births. In the early 1990's, prior to implementation of preventative measures, there was an annual incidence of 1.7 early-onset cases per 1,000 live births (13). In 2002 the CDC released revised guidelines for the prevention of early-onset disease causing the incidence of GBS early-onset in infants to decrease 27% from 0.47 cases per 1,000 live births in 2000 to 0.34 cases per 1,000 live births in 2004 with further decline by 2008. The case fatality rate for early onset disease has decreased from 50% in the 1970s to about 5% in 2009.

In the CDC guidelines in 2002 they adopted this conclusion and recommend culture-based screenings in the 35-37 gestational week to determine the women who should be offered intrapartum antibiotics. Women who have GBS bacteriuria (presence of bacteria in the urine) at any point during pregnancy and women with a history of a previous infant with early-onset GBS should be given intrapartum antibiotic prophylaxis.

Studies found that even when using the maternal screening method and the appropriate antibiotic regime, early-onset group B streptococcal disease in infants still occurred (30, 31). This could partially be explained by women who have false negative screening results and therefore are not offered antibiotics, insufficient screening, suboptimal antibiotics given, and screening prior to the recommended time (31-34). In addition to preventing the transmission of bacteria from the mother to the child (primary prevention), the CDC has recommended guidelines for preventing disease in the infant if he/she does acquire the bacteria (secondary prevention). Signs of sepsis include: respiratory distress, apnea, fever or unstable temperature, acidosis, and pallor (35). If any of these early signs occur the CDC recommends performing blood and cerebrospinal fluid cultures (18). Some recommend giving the infant broad spectrum antibiotics prior to obtaining culture results.

Prevention and treatment during pregnancy

The CDC developed guidelines in 2002 (updated in 2010) on screening for and prevention of adverse infant and maternal outcomes due to GBS (18). There are two primary strategies for determining if a pregnant woman is at risk of giving birth to a GBS positive infant. The first is a risk-based assessment technique. A woman who has the presence of any of the following is offered **intrapartum antibiotic prophylaxis**: delivery at less than 37 weeks, intrapartum temperature of greater than 100.4°F or rupture of membrane for more than 18 hours (18).

The second is a universal screening strategy which consists of all pregnant women having a vaginal swab taken at 35-37 weeks. If a woman has a positive culture she is given intrapartum antibiotic prophylaxis. A vaccine would decrease the concern over antimicrobial resistance as well as

help to prevent late-onset GBS disease in infants, and GBS disease in non-pregnant adults (13, 42). Vaccines against GBS are being developed and researched. Vaccine trials in pregnant woman are slow due to the added ethical and health issues associated with research on pregnant women.

Chemoprophylaxis to prevent GBS disease

In the 1980s, it was found that effective treatment with chemoprophylaxis of GBS colonized women resulted in reduced rates of neonatal colonization and early-onset sepsis. Preventive strategies should be used: (1) universal prenatal GBS screening of all women at 35-37 weeks of gestation followed by intrapartum chemoprophylaxis of all (2) The antibiotic recommended by the CDC is penicillin. Women who are allergic to penicillin should receive cefazolin (if no history of anaphylaxis) or clindamycin (if high risk of anaphylaxis) (18, 37). (3) Antimicrobial susceptibility testing should be done on the culture in cases with women who are allergic to penicillin. Intrapartum antibiotic prophylaxis should be given for at least 4 hours prior to delivery if possible. In addition, GBS resistance to macrolides such as clindamycin appears to be rising.

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