CEOG Clinical and Experimental Obstetrics & Gynecology

Original Research

Screening for group B hemolytic streptococcal infection in pregnancy in a low-resourced country

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Summary

Objectives: The objectives of this study conducted in a low-resourced country were to determine the feasibility and acceptability among pregnant women of universal screening for group B streptococcus (GBS), the prevalence of GBS, to calculate the risk of vertical transmission, and to study the neonatal outcome of early onset group B streptococcus disease (EOGBSD). *Materials and Methods:* All pregnant women between 35-37 weeks of gestation who attended the Port-of-Spain General Hospital during a six-month interval were enrolled in a study involving universal screening for group B streptococcus from vaginal and ano-rectal swabs. After appropriate laboratory preparation, inspection of the plate for GBS was performed. Patients found to be GBS screen-positive received intrapartum antibiotic prophylaxis (IAP). *Results:* Among the 420 eligible patients, 341 women (81.2%) agreed to participate. A total of 52 maternities (15.2%) were confirmed as GBS screen-positive. The highest rate of positive results were observed in Afro-Caribbean women, although this difference was not statistically significant ($p > 0.05$). Intrapartum antibiotic prophylaxis (IAP) was administered to 37 patients (71.1%). *Conclusion:* This study reveals that despite the relatively low prevalence rate of GBS, a policy of universal screening and IAP in low-resourced countries, it is possible to address the major burden of EOGBSD.

Key words: Group B streptococcus; Neonatal sepsis; Screening; Antibiotic prophylaxis.

Introduction

Although there have been vast improvements in the quality of care administered to pregnant women in both developed and developing countries, perinatal morbidity and mortality remain high in many low-resourced countries. For example, whereas in the United Kingdom, perinatal mortality rate declined from 32.8 in 1960 to 7.6 per 1,000 total births in 1993, in many Caribbean countries, the corresponding rate continues to exceed 25 per 1,000 total births [1]. A major factor contributing to this high rate is neonatal infection. This is partly due to lack of agreed policies and protocols on dealing with vertical transmission of infection from mother to the baby, and even where such agreement exists, there is lack of implementation in a timely manner.

A key factor in the management of neonatal sepsis is an awareness of the likely causative micro-organisms [2]. Two recent UK population-based neonatal surveillance studies found that after exclusion of coagulase negative staphylococci, the most common bacteria implicated in neonatal infection are group B (GBS), non-pyogenic streptococci, *Staphylococcus aureus*, and *Escherichia coli* [3, 4].

Group B hemolytic streptococcus (GBS), also known as *Streptococcus agalactiae,* has been recognized for several decades as a leading cause of neonatal morbidity and mortality [5]. In the United States, despite substantial decline over the past 20 years as a result of widespread use of intrapartum antibiotic prophylaxis (IAP), GBS is still ranked number one in terms of neonatal sepsis [6]. In the UK, the incidence of GBS is 0.4-0.57 per 1,000 live births (PT Heath, personal communication). In the USA, the neonatal mortality when early onset GBS disease (EOGBSD) occurs has declined from a high of 50% in the 1970s to about 5% in 2000 [7] but in the UK, as many as 10-20% of affected babies succumb. In a retrospective study in Trinidad, five out of 31 infected neonates died [8]. Furthermore, among survivors, permanent neurological sequelae are observed in 15-50% of cases.

Two distinct syndromes are described with neonatal invasive disease. Firstly, EOGBSD presents within the first seven days of life (often within the first 12 hours), usually as severe neonatal pneumonia [9]. This pattern of infection is due to vertical transmission to the offspring during childbirth in a mother colonized with the bacteria. The second pattern of infection termed late-onset disease occurs after the first week of life and up to 90 days after birth. The pathogenesis of the late-onset syndrome is thought to be due to nosocomial spread from the mother to the baby after birth [10].

Various strategies have been proposed to reduce the bur-

Revised manuscript accepted for publication July 18, 2019

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLVI, n. 1, 2019
doi: 10.12891/ceog4319.2019

7847050 Canada Inc.
www.irog.net

Published: 10 February 2019

den of GBS on neonates. The implementation of any such risk-reduction strategy must take into consideration the prevalence of the micro-organism in the vaginal flora, the presence of other risk factors, the incidence of EOGBSD, cost-benefit analysis, impact on the microbial ecology of the mother and the infant, and development of resistant strains. A balance has to be achieved between maximizing benefit to the infant but at the same time minimizing intervention to the mother.

Although several studies have confirmed that intrapartum antibiotic prophylaxis (IAP) results in as much as a 30-fold reduction in GBS disease [11-14], there is still uncertainty with respect to an appropriate IAP policy. Selection of women for IAP can follow either a risk-based policy in which antibiotic is administered to those mothers with particular risk factors or alternately, a screening policy whereby all pregnant women between 35-37 weeks of gestation have low vaginal and anorectal swabs taken and mothers who are GBS screen-positive are offered IAP. Both policies have been endorsed by the American Academy of Pediatrics [15] and the American College of Obstetricians and Gynecologists [16], although from 2003 the recommendation was for antenatal screening. With this strategy, the default is that women who are unscreened in the antenatal period, or their culture results are unavailable, receive IAP when they present in labor. A third possibility is a combined approach which involves administering antibiotic to only those women who have risk factors and also have been found GBS screen-positive.

In the UK, the National Screening Committee in 2012 [17] did not recommend either routine or universal screening. However, it advised that women with GBS bacteriuria and/or a positive vaginal swab in the current pregnancy should receive IAP. Further recommendations for IAP include pyrexia in labor (> 38°C) and a history of a previous baby affected with GBS disease.

In the Caribbean as in many other low-resourced countries, there is no consensus on which policy we should adopt to address the problem of GBS disease. Even within the same institution, obstetricians and neonatologists disagree on which strategy to utilize. However, there is universal agreement that IAP should be given to mothers with an incidental finding of GBS carriage during pregnancy, pyrexia in labor (> 38 °C), chorioamnionitis, prolonged rupture of membranes (>18 hours) and a past history of EOGBSD in a previous pregnancy.

The objectives of this prospective study at a teaching tertiary institution were to determine the feasibility and acceptance among pregnant women of universal screening for GBS, the prevalence of GBS in the pregnant population in North Trinidad, to calculate the risk of vertical transmission despite the administration of antibiotic prophylaxis, and to study the neonatal outcome of EOGBS sepsis.

The present authors hope that the findings of this study may prove instructive in the formulation of a policy to address the problem of GBS in pregnancy, especially in low-resourced countries.

Materials and Methods

The study population comprised all pregnant women whose gestational age was 35-37 weeks and who attended the Antenatal clinics at the Port-of-Spain General Hospital during the six-month interval commencing August 1st, 2012. This institution is a tertiary teaching hospital affiliated to the University of the West Indies. It serves a wide cross-section of the population especially those from the adjacent lower socio-economic and deprived communities. Exclusion criteria included a confirmed diagnosis of GBS in the present pregnancy, and the use of broad-spectrum antibiotics during the previous two weeks. Of the 420 eligible patients, 341 women (81%) agreed to participate.

Two culturette rayon swabs were used by the attending doctor to obtain samples from both the lower vagina and the ano-rectum. The specimens were inoculated immediately into separate labelled tubes which contained Todd-Hewitt broth supplemented with antibiotics (gentamicin and metronidazole). The broth was incubated at 35-37°C for 18-24 hours in 5% CO_2. Culture was then performed on a blood agar plate. Subsequently, the plate was inspected for organisms suggestive of GBS. A CAMP test was then carried out to obtain a presumptive diagnosis. When GBS was not identified, the plate was re-incubated and inspected after a further 48 hours. Streptex was utilized for the determination of the particular group of GBS.

Patients who were found to be GBS screened-positive received benzyl penicillin 3 grams intravenously on admission to the Labor ward and 1.5 grams every four hours until delivery. All babies from GBS positive mothers had a septic screen comprising cultures from skin, throat, umbilicus, and blood.

Ethical approval was obtained from the relevant Ethics Committee of the Northwest Regional Health Authority under whose purview comes the Port-of-Spain General Hospital. Statistical analysis was conducted with SPSS version 16. Absolute and relative frequencies were calculated initially followed by Pearson's Chi Square and Fisher's exact tests. A p value of < 0.05 was deemed statistically significant.

Results

Of 420 eligible patients, 341 women (81%) agreed to participate in the study. The ethnicity of these participants was 241 Afro-Caribbean (70.7%), 82 mixed (24.0%), and 18 Indo-Caribbean (5.3%). The demographic characteristics among the study group were similar to the background figures for the institution and both are shown in Table 1.

The patients' ages ranged from 15 to 44 years, with a median of 26.3 years. Table 1 demonstrates that teenage pregnant women and parturients belonging to the advanced maternal age group (>35 years) accounted for 12.3% and 13.2%, respectively ($p > 0.05$). This is similar to the background data of the general population served by this institution. There were 115 nulliparae (33.7%), 217 of parity 1-5 (63.7%), and the remainder (2.6%) were grand-multiparous. Two hundred and nineteen mothers (64.2%) were delivered vaginally whereas the remainder (35.8%) had Cesarean section. The rate of abdominal delivery among the

Table 1. — *Demographic characteristics.*

Demographic characteristics	GBS screen-positive (%)	GBS screen-negative (%)	Total cases (%)
Age, years	n=52	n=289	n=341
<19	8 (15.4)	34 (11.8)	42 (12.3)
20-24	18 (34.6)	93 (32.2)	111 (32.6)
28-29	9 (17.3)	76 (23.3)	85 (24.9)
30-34	11 (21.2)	47 (16.2)	58 (17.0)
>35	6 (11.5)	39 (13.5)	45 (13.2)
			$p = 0.605$
Ethnicity			
Afro-Caribbean	39 (75.0)	202 (69.9)	241 (70.7)
Mixed	11 (21.2)	71 (24.6)	82 (24.0)
Indo-Caribbean	2 (3.8)	16 (5.5)	18 (5.3)
		16 (5.5)	$p = 0.797$
Parity			
0	18 (34.6)	97 (33.5)	115 (33.7)
1-4	34 (65.5)	183 (63.3)	217 (63.7)
>5	0 (0.0)	9 (3.2)	9 (2.6)

participants was higher than that of the background rate for the institution which currently stands at 21%.

A total of 52 women (15.2%) were confirmed as GBS screen-positive. There were 51 singleton pregnancies and one twin gestation. None of the women had an abnormal vaginal discharge. No cases of preterm labor, pre-labor rupture of membranes or evidence of chorioamnionitis were noted. Positive GBS results were noted in 39 out of 241 (16.2%) Afro-Caribbean women compared with 13 (13%) in the other ethnic groups ($p = 0.451$). There was no statistically significant trend associated with maternal age (17% in women aged < 25 *vs.* 13.8% in women aged 25 or more).

Among the mothers who were GBS screen-positive, 37 received IAP. The remaining 15 women had an emergency cesarean section shortly after admission did not receive IAP or received sub-optimal IAP.

Cesarean section was performed in 17 GBS positive maternities (32.7%), and the remainder (67.3%) had vaginal deliveries. This rate of abdominal delivery is twice that of the background rate for the institution. The indications for the abdominal deliveries included fetal distress (n=9), suspected cephalo-pelvic disproportion (n=3), breech presentation (n=2), previous Cesarean section (n=2), and HIV in one case. Among the 53 babies delivered to GBS positive mothers, eight (15.4%) were of low birth weight (< 2,500 grams), and seven (13.5%) were macrosomic (> 4,000 grams). These were similar to those of the general population.

One healthy neonate was found to be GBS positive from culture of the throat swab despite negative cultures from elsewhere. His mother had received only one dose of penicillin in labor. She had progressed very rapidly in the intrapartum period and delivered vaginally after having been in labor for only two hours, and had thus received sub-optimal IAP (recommended to be at least four hours). The baby received a seven-day course of parenteral antibiotics comprising ampicillin and gentamicin twice daily. During his stay in the Neonatal unit, the baby did not exhibit any clinical features of sepsis such as poor feeding, lethargy, fever nor respiratory distress. Prior to discharge, repeat swabs were negative.

Discussion

In the present study, the prevalence of GBS was 15.2%, which is lower than that reported by Orrett *et al.* [18] who conducted a similar study in southern half of the country and found a prevalence of 31.4%. This difference may have been to a less robust method of laboratory diagnosis of GBS in the latter study which led to over-diagnosis. In contrast the present findings concur with those of Martin *et al.* [19] who reported that 14 out of 163 vaginal swabs (8.6%) performed in pregnancy at Holberton Hospital in Antigua were positive for group B streptococcus. In Kingston, Jamaica, the prevalence of EOGBSD was 0.66 per 1,000 [20]. Similarly, Mahadeo *et al.* [21] documented that GBS was an infrequent cause of neonatal sepsis in Guyana. These findings suggest that GBS may be relatively uncommon in the Caribbean although the major ethnic group is Afro-Caribbean. These findings beg the question is GBS more closely related to geographical background of the population than its ethnicity.

Over 80% of eligible patients accepted screening which is in sharp contrast to the belief that screening is not practical in low-resourced countries or among poorly-educated population. Furthermore, the present authors also found that screening for GBS is feasible in our antenatal clinic. They suggest that cost analysis be conducted to investigate cost of screening and that of treating a newborn with EOGBSD.

The present finding that one out of every six to seven women was screen-positive is similar to that reported by others [22]. Whereas teenage pregnancies are considered a risk factor for GBS, in this study the authors found no statistically significant effect of maternal age on GBS carrier status. Approximately 50% of babies of mothers who are carriers for GBS become colonized, and one per cent progress to develop invasive disease if preventative measures are not instituted.

The rate of abdominal delivery among the participants in this study is higher than that of the background rate of the institution. This is due to the fact that those women who were recruited were attending high-risk antenatal clinics and hence it is expected that their caesarean section rate would be higher than that of the general population.

That among 52 GBS screen-positive women only one possible case of EOGBS sepsis was diagnosed, is consistent with the known protective effect of IAP [22, 23]. Furthermore, 14 patients who were GBS positive did not receive optimal IAP and had cesarean births. Septic screening for their babies was all negative. This supports the view that cesarean section also protects against GBS.

One of the major hurdles to overcome is to whom IAP must be administered. The Centers for Disease Control and Prevention [24] in collaboration with the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatricians (AAP) in 1996 advocated the following guidelines for IAP either: culture-based screening for pregnant women between 35-37 weeks of gestation or risk-based screening for women with intrapartum risk factors (including gestational age less than 37 weeks, temperature > 100.4°F, or rupture of membranes for more than 18 hours). Furthermore, IAP was also recommended with GBS bacteriuria which is suggestive of heavy colonization, and with a history of previous infant with invasive GBS disease. With the adoption of these guidelines, IAP was administered to 27% of mothers, and EOGBS disease declined by approximately 70% [25].

Six years later, those guidelines were revised with a recommendation for universal culture-based screening. Adoption of universal screening was reported by Van Dyke *et al.* [25] in which as much as 85% of patients were screened which thus reveals that this policy is feasible.

At this time, while we await the results of further studies on the rapid test or on a vaccine, the present authors recommend a policy of universal screening of pregnant women in the Caribbean despite the low prevalence of GBS in pregnancy in view of the serious morbidity and mortality in infants. With training, self-testing by patients may be feasible and hence there would no extra demand on the medical staff or an increase in the time taken for an antenatal consultation. Self-screening would also decrease the cost of testing.

Women who are screen-positive should receive IAP. It is also suggested that all women tested positive in the antenatal period should carry on them documentary evidence of such when they present in labor. Furthermore, for mothers with GBS bacteriuria in the current pregnancy or a past history of an affected neonate, a 'passport' with this information should also be presented to the admitting officer in the labor suite, thus allowing for timely administration of antibiotic prophylaxis.

One limitation of this study is that it was a hospital-based study, but the country is fairly homogenous especially in terms of ethnic background and socio-economic status and it is reasonable to extrapolate the findings nationally. Also, despite a high acceptance rate of screening, 20% of women declined and hence the authors do not know their carrier status of GBS.

The present authors recommend a study to determine whether women in developing countries would be willing to conduct self-testing. If this is acceptable, then the problem of refusing screening at antenatal clinics may be addressed. There is a need to study 'knowledge, perceptions, and attitudes' on GBS and screening in this population who may not be aware of the serious problem of this infection in newborns. This study reveals that even in a low-resourced country where antenatal clinics are busy, universal screening for GBS and IAP are possible in the quest to reduce the major burden of EOGBS disease.

Acknowledgments

The authors would like to thank Professor Phil Steer for assisting with editing and Ms. Alyssa Maharaj for preparing the manuscript.

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